

# HEALTH SCIENCE CENTER 28<sup>TH</sup> ANNUAL RESEARCH DAY AT MARSHALL UNIVERSITY MARCH 11, 2016

Oral and Poster Presentations

Marshall University Medical Center • Huntington, West Virginia

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**This event is supported annually by educational grants from the following Endowments:**

Thelma V. Owen Memorial  
Richard J. Stevens Memorial

**Faculty Disclosure Policy 2016**

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**No Faculty Disclosure or conflicts of interest are indicated for this CME activity.**

**Disclosure of Conflicts of Interest**

Marshall University Joan C. Edwards School of Medicine (MUJCESOM) requires instructors, planners, managers and other individuals who are in a position to control the content of this activity to disclose any real or apparent conflict of interest they may have as related to the content of this activity. All identified real or apparent conflicts of interest are thoroughly reviewed and resolved by MUJCESOM's planning process for fair balance, scientific objectivity of studies mentioned in the materials or used as the basis of content, and appropriateness of patient care recommendations. Disclosure information will be presented verbally or in print to participants before presentation of the agenda lectures.

Completed faculty disclosure forms are on file in the CME Office.



Marshall University Joan C. Edwards School of Medicine is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education for physicians.

The conference will consist of a series of oral and poster presentations highlighting basic and clinical research performed by School of Medicine students, residents and fellows. Please use pages 11 through 25, to locate presenters, their abstracts, presentation times and location of presentation. The complete agenda is available at <http://www.musom.marshall.edu> (research link)

### **INTENDED AUDIENCE**

The Health Science Center 28th Annual Research Day at Marshall University is designed for physicians, residents, basic scientists, medical students, graduate students, and other interested health professionals.

### **GOALS**

- 1) To involve faculty, medical and graduate students in the process required to formally present their research in either oral or poster presentations.
- 2) To inform and involve the community in ongoing research at Marshall University Joan C. Edwards School of Medicine.
- 3) To encourage the attitude among faculty, residents, and students for Continuing Medical Education in the area of clinical research.

### **GLOBAL LEARNING OBJECTIVES**

By the end of these lectures the participant will be able to:

- 1) Compare different approaches to medical investigation.
- 2) Compare and contrast the importance of basic research and cellular mechanisms as it relates to human disease.
- 3) Discuss and review research related to current and future improvements in the clinical management of patients.
- 4) Interpret and analyze data for medical investigation to potentially determine the effectiveness towards improving patient care.
- 5) Stress the importance of translational research benefits to the basic scientist in support of the practicing physician.

## CREDIT STATEMENT

Marshall University Joan C. Edwards School of Medicine designates this live educational activity for a maximum of 5.0 AMA PRA Category 1 Credits™. Physicians should only claim credit commensurate with the extent of their participation in the activity. (Session Registration and Evaluation are required).

## EVALUATION FORM Completion

Please follow specific instructions for completing the bar coded evaluation form. Keep your “X’s” in the bubbles and your written comments in the designated boxes. Your input is needed for planning future events.

## ASSISTED SERVICES

If special arrangements are required for an individual with a disability to attend these events, please contact Continuing Medical Education at (304) 691-1770 no later than 1 week before the event date or See a CME Representative at the Registration Area on the day of the event.

### PLANNING COMMITTEE - NO CONFLICTS INDICATED

**Uma Sundaram, MD**, Conference Chair, Vice-Dean, Research and Graduate Education

**Todd Gress, MD**, Co-Chair, Assistant Dean, Clinical and Translational Research

**David N. Bailey, MBA**, Assistant Dean, CME

**Richard Egleton, PhD**, Co-Director, Biomedical Sciences Graduate Programs

**Brian Patton, Director**, Digital Media Services

**William F. Pewen, PhD**, Associate, College of Health Professions

**Inder Sehgal, PharmD**, Professor, School of Pharmacy

### STAFF COORDINATORS - NO CONFLICTS INDICATED

Anita Mathis .....BMS Coordination & Registration

Patricia “Trish” Martin ....Registration

Brian Patton .....Web Publications, Online Abstract  
Submission Form Design and Content  
Retrieval, Judging tabulations summary

## RESEARCH DAY



## PAST INVITED LECTURERS

### **2015 Richard J. Johnson, MD**

Tomas Berl Professor and Chief  
Division of Renal Diseases and Hypertension  
University of Colorado Anschutz Campus  
Aurora, CO

1) *The Role of Sugar (fructose) in the Great Epidemics of Diabetes and Obesity*

### **2014 - Jose S. Pulido, MD, MS, MBA, MPH**

Professor of Ophthalmology and Molecular Medicine  
Associate in Neuro-oncology  
Mayo Clinic Cancer Center  
Rochester, MN

1) *The Topology of Blinding Eye Disease*

2) *Breaking bad and Breaking good*

### **2013 - John J. Cannell, MD**

Executive Director  
Vitamin D Council  
San Luis Obispo, CA

1) *The Use of Vitamin D in Clinical Practice*

### **2012 - William Thies, Ph.D.**

Vice President, Medical Scientific Affairs  
Alzheimer's Association  
Chicago, IL

1) *Alzheimers Today and the Future*

### **2011 – Susan S. Smyth, MD, Ph.D.**

Professor of Medicine  
Director, MD/Ph.D. Program  
University of Kentucky

1) *Cardiovascular Complications of Obesity*

### **2010 – Gregory Germino, MD**

Deputy Director of the National Institute of Diabetes and Digestive  
& Kidney Disease (NIDDK) at the National Institutes of Health (NIH)  
Bethesda, Maryland

1) *Dia-besity: converging problems, emerging science*

### **2008 – Gregory Alan Hale, MD**

Associate Professor of Pediatrics  
University of Tennessee

1) *Transplantation and Cellular Therapies: Current Research  
and Future Opportunities*

2) *An introduction to Hematopoietic Cell Transplantation*

### **2007 –Daniel D. Bikle, M.D., Ph.D.**

Professor of Medicine and Dermatology  
In residence University of California

1) *The skin game: Calcium and vitamin D regulated cellular  
differentiation*

2) *Vitamin D: how much do we need and why*

## PAST INVITED LECTURERS

### **2006 - Mark E. Shirtliff, Ph.D.**

Assistant Professor, Department of Biomedical Sciences  
Dental School, University of Maryland-Baltimore  
Baltimore, Maryland

- 1) *Staphylococcus aureus* biofilms: *in vitro* and *in vivo* studies

### **2006 - J. William Costerton, Ph.D.**

Director & Professor, Center for Biofilms, School of Dentistry  
University of Southern California  
Los Angeles, California

- 1) *Biofilms in Device-related and other Chronic Bacterial Diseases*

### **2005 – William F. Balistreri, MD**

Director, Gastroenterology  
Cincinnati Children's Hospital Medical Center

- 1) *Inborn Errors of Bile Acid Biosynthesis*
- 2) *Viral Hepatitis 2005*

### **2004 – Joseph S. McLaughlin, MD**

Professor Emeritus of Surgery  
University of Maryland

- 1) *Traumatic Ruptured Aorta*
- 2) *Strange Tumor I Have Known*

### **2003 – W. Jackson Pledger, Ph.D.**

Professor, Interdisciplinary Oncology  
University of South Florida College of Medicine  
Tampa, Florida

- 1) *Regulation of proliferation by cyclin dependent kinase*
- 2) *Functional genomics and cancer therapy*

### **2002 – Alan H. Jobe, M.D., Ph.D.**

Professor of Pediatrics  
Cincinnati Children's Hospital Medical Center  
Cincinnati, Ohio

- 1) *Mechanisms of lung injury in the preterm*
- 2) *Translational research on lung maturation based on clinical observations*

### **2001 - Arnold Starr, M.D.**

Director, Alzheimers' Research Center  
Institute Brain Research of California, Irvine

- 1) *Hearing but not understanding: auditory nerve dysfunction in the presence of preserved cochlear receptors*
- 2) *Patients' stories and their seminal importance for research*

### **2000–Fredrick L. Brancati, M.D., M.H.S.**

Associate Professor, Medicine and Epidemiology  
John Hopkins Medical Institute

- 1) *Novel risk factors for type 2 diabetes mellitus and their implications for treatment*
- 2) *Prevention and clinical epidemiology in the new millennium*

## PAST INVITED LECTURERS

### **1999 – Robert B. Belshe, MD**

Director and Professor, Div. of Infectious Diseases and Immunology  
St. Louis University

- 1) *Live attenuated influenza vaccine: using genetics to defeat the flu*
- 2) *Vaccines for the 21<sup>st</sup> century*

### **1998 – Jerome S. Brody, MD**

Vice-Chairman of Medicine for Research, Professor of Medicine  
Director, Pulmonary Center  
Boston University School of Medicine

- 1) *Lung development: lesson from flies connections to cancer*
- 2) *Molecular approaches to the diagnosis of lung cancer*

### **1997 – Rochelle Hirschhorn, MD**

Professor of Medicine, Department of Medicine  
NYU School of Medicine

- 1) *Advances in defects in host defense*
- 2) *Reflection on the changing face of medicine*

### **1996 – Stuart F. Schlossman, MD**

Baruj Benacerraf Professor of Medicine  
Harvard Medical School  
Chief, Division of Tumor Immunology  
Dana-Barber Cancer Institute, Boston

- 1) *Human T-cell activation*
- 2) *What's in a name – cd nomenclature*

### **1995 – Frank M. Torti, MPH, MD, FACP**

Director, Comprehensive Cancer Center  
Professor Charles L. Spurr Professor of Medicine  
Section Head for Hematology/Oncology, Wake Forest University  
Chairman, Department of Cancer Biology  
Bowman Gray School of Medicine

- 1) *New pathways for the regulation of iron*
- 2) *Popeye spinach and iron: the politics*

### **1994 – Abner Louis Notkins, MDB**

Director, Intramural Research Program  
Chief, Laboratory of Oral Medicine National Institute of Dental Research,  
National Institutes of Health, Bethesda, MD

- 1) *Polyreactive antibody molecules and matter*
- 2) *The Bethesda experiment*

### **1993 – Erling Norrby, MD, Ph.D.**

Dean of Research and Professor of Virology  
Karolinska Institute, Department of Virology Sweden

- 1) *Immunization against HIV-2/SIV in monkeys*
- 2) *The selection of Nobel Prize winners*



## PAST INVITED LECTURERS

### **1992 – Simon Karpatkin, MD**

Professor of Medicine

New York University School of Medicine

- 1) *Role of thrombin, integrins and oncogenes*
- 2) *How scientific discoveries are made*

### **1991 – Robert M. Chanock, MD**

Chief, Laboratory of Infectious Diseases

National Institute of Allergy & Infectious Diseases

National Institutes of Health, Bethesda, MD

- 1) *Epidemiology, pathogenesis, therapy*
- 2) *New approaches to development of treatment plans*

### **1990 – Dewitt S. Goodman, MD**

Director, Institute of Human Nutrition

Director, Arteriosclerosis Research Center

Tiden-Weger-Bieler Professor of Preventative Medicine

Professor of Medicine, Columbia University,

College of Physicians and Surgeons

Director, Division of Metabolism and Nutrition

Department of Medicine

Columbia-Presbyterian Medical Center, New York

*Retinoid and retinoid-binding proteins*

### **1989 – Michael A. Zasloff, MD, Ph.D.**

Charles E.H. Upham, Professor of Pediatrics

University of Pennsylvania School of Medicine

Chief, Division of Human Genetics & Molecular Biology

The Children's Hospital of Philadelphia

- 1) *The flow of genetic information*
- 2) *Magainin peptides*

## 2015 RESEARCH DAY CONFERENCE PRESENTATION WINNERS

### **Winner of Basic Science Oral Presentation • Kristeena Ray Wright**

"Polycomb group and associated proteins as potential therapeutic targets for endometriosis"

Other Authors and Mentor: Brenda Mitchell and Nalini Santanam

*Department of Pharmacology, Physiology, and Toxicology and Department of Obstetrics and Gynecology, JCESOM*

### **Winner of Clinical Science Oral Presentation, Student Category • Brandon J. Smith**

"Impact of influenza vaccination on clinical outcomes of patients admitted in a university affiliated large medical center in Pittsburgh, Pennsylvania"

Other Authors and Mentor: Todd Gress, Mohamed Yassin, Rahman Hariri, Juliet Ferrelli, and Hector Bonilla

*Department of Internal Medicine, JCESOM and Division of Infectious Diseases, UPMC Mercy*

### **Winner of Clinical Science Oral Presentation, Resident Category • A. Allison Roy**

"Evaluating Buprenorphine Metabolism in Cord Blood from Neonates Born to Opiate Addicted Mothers as a Predictor of Neonatal Abstinence Syndrome in Rural Appalachia"

Other Authors and Mentor: Allison Hamilton, Ryan Stone, Anne Silvis, and

Lauren Richards-Waugh

*Department of Obstetrics and Gynecology, JCESOM*

### **Winner of Basic Science Poster Presentation • Adam P. Fischer**

"Normoxic accumulation and activity of HIF-1 is associated with ascorbic acid transporter expression and localization in human melanoma"

Other authors and Mentor: Sarah L. Miles

*Department of Biochemistry and Microbiology, JCESOM*

### **Winner of Clinical Case Poster Presentation, Student Category • Paul Viscuse**

"Fatigue, bruising, and weight loss in a teenage female with previously diagnosed thrombocytopenia"

Authors and Mentor: Jacob Kilgore and Mark Mogul

*Department of Pediatrics, JCESOM*

### **Winner of Clinical Case Poster Presentation, Post-Graduate Category • Zain Qazi**

"Atypical Growth of an Osteochondroma in a 31 year old female"

Authors and Mentor: Russell Odone, Jacob Hamm, Franklin Shuler, and Felix Cheung

*Department of Orthopaedic Surgery, JCESOM*

### **Winner of Clinical Science Poster Presentation, Student Category • Maria Espiridon**

"The Medicare Annual Wellness Visit: Barriers and Patient Perceptions"

Other Authors and Mentor: Raghavendra Mulinti and Lynne J Goebel

*Departments of Internal Medicine, JCESOM and West Virginia University (Charleston)*

### **Winner of Clinical Science Poster Presentation, Post-Graduate Category • Jared Brownfield**

"Placental ADRB1 mRNA as a Potential Predictor of Outcome and Possible Therapeutic Target in High Risk Pregnancies"

Other Authors and Mentor: Anne Silvis, Ryan Stone, Nalini Santanam, and David Jude

*Department of Obstetrics and Gynecology, JCESOM*

# RICHARD J. STEVENS, MD MEMORIAL LECTURE

RESEARCH DAY | INVITED LECTURER



## **NAJI ABUMRAD, MD**

**Chairman Emeritus,  
Department of Surgery  
John L. Sawyers  
Professor of Surgery  
Vanderbilt University  
School of Medicine  
Nashville, TN**

***“The Life of an Academic  
Surgeon” Persevere,  
Don’t be afraid, Explore***

*No Conflicts Indicated*

**MARCH 11, 2016  
11:30 AM  
HARLESS  
AUDITORIUM**

### **Suggested reading:**

*The Elusive Work/Family Life Balance in  
Academic Surgery: Notes to Female Surgeons*  
<http://www.urologymatch.com/node/2508>  
*Comparison of private versus academic  
practice for general surgeons: a guide for  
medical students and residents*  
<http://www.ncbi.nlm.nih.gov/pubmed/14644289>

## ABOUT THE RICHARD J. STEVENS, MD MEMORIAL LECTURE

The Richard J. Stevens, MD Memorial Lecture is supported annually by the family of Dr. Stevens. Dr. Stevens was an outstanding medical practitioner characterized by former Dean Charles H. McKown, Jr., of the Marshall University Joan C. Edwards School of Medicine as a pioneer “who was never in a hurry but always on the move.”

Born in Portsmouth, Ohio, Dr. Stevens received his undergraduate degree from Marshall University, attended West Virginia School of Medicine for two years, then went on to earn his medical degree from Rush Medical School in Chicago.

Dr. Stevens returned to Huntington in 1941 as one of the first board certified practitioners in internal medicine in the area. He was a member of the Alpha Omega Alpha, the medical honorary, as well as gastroenterology and research societies.

Dr. Stevens was one of three physicians who first researched prothrombin testing for guidance in administering anticoagulants to patients with coronary occlusion.

Remembered as genuinely committed to his profession, his community and those around him, he had the unique ability to bring about a meeting of the minds among colleagues, patients and families.

The memorial lecture is presented each year at the Marshall University Joan C. Edwards School of Medicine’s Research Day. It was established by Dr. Steven’s wife, Dr. Sarah Louise Cockrell Stevens, and their seven children: Chari Louise Stevens Singleton, Mary Alice Stevens, Richard J. Stevens II, Johanna Stevens Holswade, Robert C. Stevens, and Randall C. Stevens.

## List of Presenters' Abstracts

No relevant Conflicts of Interest as supported by Disclosure

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			Zill	85	P32

## RESEARCH DAY AGENDA

**MARCH 11, 2016**

Specific learning objectives will be presented with each oral presentation.

Questions and answers encouraged throughout all sessions.

No apparent speaker conflicts indicated as supported by disclosure.

7:00AM	Registration	AM & PM registration required
8:15AM	Welcome	Joseph I. Shapiro, MD, Dean
8:20AM	Opening Remarks	Uma Sundaram, MD, Vice Dean and Research Day Chair

Oral Session I		Page 27	
Time	Format	Presentation Order	Name/ <b>Abstract Title</b> /Department
8:30AM	Oral	1	Taha Ahmad <b><i>The Significance of CYP2B6 Genetic Polymorphisms in Unexpected Fatalities of Methadone Users in Caucasians of WV and KY Appalachia Region</i></b> <i>Dept. of Pharmacology, Physiology, and Toxicology, Marshall University, Huntington, WV and 2 Marshall University Forensic Science Graduate Program, Marshall University</i>
8:42AM	Oral	2	Daniel Kahn <b><i>Rural West Virginia teen perception of texting and driving</i></b> <i>Orthopaedics</i>
8:54AM	Oral	3	Funda Kartal <b><i>Enhanced Mitochondrial Biogenesis in ER/PR Positive Breast Cancers</i></b> <i>Departments of Biochemistry and Microbiology and Pathology† and School of Pharmacy, Department of Pharmaceutical Research and Science</i>
9:06AM	Oral	4	Amrita Mallick <b><i>Na/K_ ATPase Mimetic pNaKtide Peptide attenuates aging in adult human dermal fibroblasts</i></b> <i>Departments of Medicine, Surgery and Pharmacology</i>
9:18AM	Oral	5	Sarah L. Miles <b><i>Defining the role of Hepatocyte Growth Factor (MET) Receptor and PI3K/AKT signaling activation in Bilateral Diffuse Uveal Melanocytic Proliferation syndrome</i></b> <i>Biochemistry and Microbiology</i>

## RESEARCH DAY AGENDA

9:30AM	Oral	6	<p>Justin K. Tomblin</p> <p><b>2,3,7,8 tetrachlorodibenzo p dioxin (TCDD)/ Aryl Hydrocarbon Receptor (AHR) Regulation of Large Neutral Amino Acid Transporter 1 (LAT1) in Breast Cancer Cells</b></p> <p><i>Departments of Pharmacology, Physiology and Toxicology, Clinical &amp; Translational Science, and Biochemistry and Microbiology</i></p>
<b>9:45AM BREAK</b>			<b>Poster Session 1, Page 53 - Atrium</b>
<b>Oral Session 2</b>		<b>Page 35</b>	
10:30AM	Oral	7	<p>Alexandra Nichols</p> <p><b>Role of Serum Biomarkers in Early Detection of Diabetic Cardiomyopathy in West Virginian Population</b></p> <p><i>Department of Medicine, Department of Internal Medicine, Department of Surgery</i></p>
10:42AM	Oral	8	<p>Andrew Vess</p> <p><b>Does intravenous acetaminophen used as adjunctive treatment for postoperative pain management in patients undergoing joint replacement affect clinical outcomes?</b></p> <p><i>Department of Translational Sciences and Cabell Huntington Hospital Pharmacy</i></p>
10:54AM	Oral	9	<p>Lexie C. Keding</p> <p><b>A Novel In Vitro Assay to Assess Antibiotic Penetration in Respiratory Mucus</b></p> <p><i>Department of Biochemistry and Microbiology Marshall University, Department of Pharmaceutical Science and Research Marshall University, Department of Pediatrics University of Kentucky, Department of Biochemistry and Microbiology; Pediatrics</i></p>
11:06AM	Oral	10	<p>Mohit Harsh</p> <p><b>Locally Advanced and Invasive Prostate Cancer is More Common in Appalachia: Results of a Single Surgeon over 15 years</b></p> <p><i>Departments of Surgery/Urology &amp; Anatomical Pathology</i></p>
11:18AM	Oral	11	<p>Kristeena Wright</p> <p><b>The epigenetic role of Ezh2_FoxP3 crosstalk in endometriosis and its associated pain</b></p> <p><i>Department of Pharmacology, Physiology, and Toxicology, Department of Obstetrics and Gynecology</i></p>

## RESEARCH DAY AGENDA

11:30AM	Keynote	<p><b>Naji Abumrad, MD</b>  <b><i>The Life of an Academic Surgeon</i></b>  <i>Chairment Emeritus, Department of Surgery,          John L. Sawyers Professor of Surgery, Vanderbilt          University School of Medicine, Nashville, TN</i>  <i>"Persevere, Don't be afraid, Explore</i></p>
		No Conflicts

### 12:40PM BOX LUNCH

Oral Session 3		Page 41	
1:15PM	Oral	12	<p>Naveed Iqbal  <b><i>Anti-Cyclic Citrullinated Peptide Antibodies are Not Elevated in A Heart Failure Population without Rheumatoid Arthritis</i></b>  <i>MUSchool of Medicine, Cleveland Clinic Foundation</i></p>
1:27PM	Oral	13	<p>Molly Butts  <b><i>Enteroids: An in_vitro three dimensional model of the intestinal epithelium</i></b>  <i>Clinical Translational Sciences</i></p>
1:39PM	Oral	14	<p>Jason Childress  <b><i>Robotic Laparoscopic Partial Nephrectomy with Cold versus Warm Ischemia</i></b>  <i>Departments of Surgery/Urology and Internal Medicine/Nephrology</i></p>
1:51PM	Oral	15	<p>Rachael Starcher  <b><i>Use of telehealth to teach reproductive health and life skills to rural high school females</i></b>  <i>Obstetrics and Gynecology</i></p>
2:03PM	Oral	16	<p>Rahman Barry  <b><i>Laparoscopic Vertical Sleeve Gastrectomy: A 5_year VA Review</i></b>  <i>Surgery</i></p>

### 2:30PM BREAK Poster Session 2, Page 97- Atrium

Oral Session 4		Page 47	
3:15PM	Oral	17	<p>Andrew Feyh  <b><i>Role of Serum Biomarkers in Early Detection of Non_Alcoholic Steatohepatitis and Fibrosis in West Virginian Children</i></b>  <i>Medicine, Pediatrics, Surgery, Pharmacology</i></p>



## RESEARCH DAY AGENDA

3:27PM	Oral	18	James Lewis <b>Long Term Effect of Successful Stimulant Medication Treatment on the Body Mass Index (BMI) of Pediatric Patients with Attention Deficit Hyperactivity Disorder (ADHD)</b> <i>Pediatrics</i>
3:39PM	Oral	19	Brent Smith <b>In Melanoma the RET G691S Polymorphism is a Germline Variant</b> <i>Division of Medical Oncology, University of Colorado School of Medicine</i>
3:51PM	Oral	20	Jacaline K. Parkman <b>Congenitc Mice Confirmed QTL Linked to Obesity and Hyperlipidemia on Chromosome 1 in the TALLYHO Mouse</b> <i>Department of Pharmacology, Physiology, and Toxicology</i>

**4:30PM Awards Presentation**

**Harless Auditorium**

### 9:45AM-10:30AM POSTER PRESENTATIONS SESSION 1 - ATRIUM - PAGE 53

No.	Name/ <b>Abstract</b> /Department
1	Grant Buchanan <b>Dementia in hip fracture patients: a risk factor for in_hospital complications?</b> <i>Department of Orthopaedic Surgery</i>
2	James M Lewis <b>Attention Hyperactivity Deficit Disorder and Co_existing Anxiety: Long_Term Response to Stimulant Therapy</b> <i>Pediatrics</i>
3	William D. Rollyson <b>Capsaicin inhibits invasion of human non_small cell lung cancer cells in a TRPV1 receptor independent manner</b> <i>Department of Pharmacology, Physiology, and Toxicology</i>
4	Keegan Mullins <b>Oral HPV: An Exploration and Assessment of Young males' Knowledge, Risk Perceptions, Behaviors, and Vaccination Compliance</b> <i>Public Health, University of South Carolina</i>
5	Vishal Hari Lakhani <b>A Positive Correlation between High Levels of Inflammatory Markers and 20_HETE in Obese Appalachian Females</b> <i>Surgery and Pharmacology</i>

## RESEARCH DAY AGENDA

- 6 A. Allison Roy  
**Determining Optimal Ovarian Cancer Treatment by Age**  
*Obstetrics and Gynecology*
- 7 Krithika Srikanthan  
**Heme Oxygenase Induction Suppresses Hepatic Hecpudin and Rescues Ferroportin and Ferritin Expression in Obese Mice**  
*Medicine, Surgery and Pharmacology*
- 8 Adam P. Fischer and Sarah L. Miles  
**Comparison of the use of ascorbic acid vs. dehydroascorbic acid to reduce HIF\_1 alpha stabilization in human melanoma**  
*Biochemistry and Microbiology*
- 9 Ebrahim Sabbagh  
**Incidence of hypomagnesemia on proton pump inhibitors at the Huntington Veterans Affairs Medical Center – IHOP**  
*Internal Medicine*
- 10 Franklin D. Shuler  
**Killing of MRSA using IlluminOss: Blue Light and Sterilization of Orthopaedically Relevant Pathogenic Bacteria**  
*Orthopaedic Surgery*
- 11 Fang Bai  
**Measurement of Endogenous Cardiotonic Steroids, MBG and TCB, by LC\_MS**  
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- 12 Ahmed Amro  
**Not A Straight Forward Atrioventricular (AV) Node Ablation**  
*Internal Medicine*
- 13 Laura Kutz  
**Role of the Na/K ATPase a1 Isoform in Skeletal Muscle**  
*Marshall Institute for Interdisciplinary Research*
- 14 Sarah Govender  
**Hypoxic Effects on Hematopoietic Stem Cells**  
*Biochemistry and Molecular Biology*
- 15 Fathia Alfakeri  
**A Case Report of Benzocaine\_induced methemoglobinemia: a life threatening complication after a transesophageal echocardiogram**  
*Internal Medicine*
- 16 Yara E. Tovar  
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**Utilization of a clinical data warehouse for use as a primary data source for clinical studies**  
*Department of Clinical and Translational Sciences. Appalachian Clinical and Translational Science Institute*
- 18 Joseph C. Hart and Kalpana Miriyala  
**Psychiatric manifestations co-occurring in a father-son pair with Waardenburg Syndrome**  
*Psychiatry*
- 19 Niraj Nepal  
**Functional and molecular transition of Na<sub>2</sub>K<sub>2</sub>ATPase during the growth and maturation of intestinal epithelial cells**  
*Clinical and Translational Sciences*
- 20 Melissa Rowe  
**Barriers to HPV Vaccination Among Females with Physical and Mental Limitation**  
*OB/GYN, Marshall Health*
- 21 Kevin White  
**Late Severe Postpartum Preeclampsia 18 Days After Delivery: A Case Report**  
*Obstetrics and Gynecology*
- 22 Raj Singh  
**Evaluating the Implications of Changes in PSA Screening Guidelines on Prostate Cancer-Related Mortality, Utility, and Cost: A Decision Analysis Approach**  
*Department of Oncological Sciences, Division of Urologic Oncology*
- 23 Travis Parkulo  
**Differential expression of glutamine absorption in the small intestine**  
*Clinical Translational Sciences, Marshall University*
- 24 Tamara Murphy  
**Alteration of Mitochondrial Biogenesis in the Kidneys of TALLYHO Mice**  
*Departments of Biochemistry and Microbiology and Pharmacology, Physiology, and Toxicology, Joan C. Edwards School of Medicine, Huntington, WV, and Department of Pharmaceutical Research and Science*
- 25 Racine HL  
**Thermal Imaging Reveals Temperature Retention in Hindlimbs of Mice up to 4 Hours after Targeted Intermittent Limb Heating**  
*Anatomy and Pathology*
- 26 Charles Clements  
**Determination of the Impact of Counseling on Smoking Cessation Rates in Urban and Rural Appalachians Taking Nicotine Replacement Therapy**  
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- 27 Khalid Al Katranji  
**Improving Resident Knowledge and Awareness of Utilization of MDI Spacer Device in Asthma Management**  
*Pediatrics*

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***Anti\_Viral Medication Tenofovir Induces Oxidative Stress and Apoptosis in HK\_2 Cells***  
*Department of Pharmacology, Physiology and Toxicology, Joan C. Edwards School of Medicine, Marshall University, Huntington, WV; West Virginia Wesleyan College*
- 29 Matthew D. Thompson  
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*Ophthalmology*
- 30 Sean Piwarski  
***Exploring the Mechanism by Which 2,3,7,8\_tetrachlorodibenzodioxin (TCDD) Regulates Jagged\_1 via the Aryl Hydrocarbon Receptor***  
*Pharmacology, Toxicology, and Physiology*
- 31 Matthew Boyer  
***Late\_Onset Bipolar Disorder: A Case Report and Literature Review***  
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- 32 S.N. Zill  
***Common mechanisms and specializations in force detection and control in cockroaches, stick insects and Drosophila***  
*Anat. and Pathology, J.C. Edwards Sch. Med., Huntington, WV; Dept. of Animal Physiology, Zoological Inst., Univ. of Cologne, Cologne, Germany; Dept. of Biol. Cybernetics, Univ. of Bielefeld, Bielefeld, Germany; Dept. of Chem., Marshall University, Huntington, WV, Forensic Science Center*
- 33 Scott Murphy  
***Neuropsychiatric Features of Urea Cycle Disorder***  
*Psychiatry*
- 34 James Lewis  
***Teaching Interpersonal and Communication Skills: Results of a Parent\_Directed Resident Education Program on Children and Youth with Special Health Care Needs (CYSHCN)***  
*Pediatrics*
- 35 Haresh Visweshwar  
***Superior Mesenteric Artery Syndrome in an athletic 22 year old female***  
*Medicine*
- 36 N. Seemaladinne  
***Mycoplasma Pneumonia Associated Mucositis: A Diagnostic Challenge***  
*Pediatrics*
- 37 Hilary Cornell  
***Interstitial Microduplication of 16p13.3 – A case report***  
*Psychiatry*

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- 38 Casey Summers  
***The Removal of Zolpidem from Standardized Order Sets and its Effect on the Rate of Inpatient Falls in a Community Teaching Hospital***  
Marshall Health Neuroscience Department, Marshall University School of Pharmacy, Marshall University, Joan C. Edwards School of Medicine, Cabell Huntington Hospital
- 39 Yanling Yan  
***Pro224 Ala mutation of the Rat Na/K\_ATPase a1 Subunit Prevents Na/K\_ATPase Signaling Without Affecting Ouabain\_Sensitive Ion\_Exchange Function***  
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- 40 Deborah L. Amos  
***Excess Catalase modulates hypothalamic appetite regulation***  
College of Arts and Sciences, Bluefield State College, Bluefield, WV; Department of Pharmacology, Physiology and Toxicology, Joan C. Edwards School of Medicine, Marshall University
- 41 Preeya T. Shah  
***MBS,an Analogue of Ouabain, Ameliorated PNx\_Mediated Cardiac Fibrosis and Function***  
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- 42 Harsh M.  
***Response of Family Medicine Residents to An Educational Intervention About Patient\_Physician Communication***  
Family Medicine
- 43 Victoria Watson  
***Prospective, open\_label study of Andexanet Alfa in patients receiving a Factor Xa inhibitor who have acute major bleeding: A case report and clinical trial review***  
Neuroscience

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Neuroscience Department, School of Pharmacy and Cabell Huntington Hospital
- 45 Johnson Walker  
***An Update on Pediatric All\_Terrain Vehicle Trauma: A Two\_Decade Statewide Experience***  
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- 46 Zeynep C. Koc  
***Reduced iron intake protects mitochondrial energy metabolism in ethanol consumption***  
Departments of Anatomy and Pathology# and Biochemistry and Microbiology
- 47 Raj Singh  
***Initial Treatment Outcomes for Types 1 and 2 Trigeminal Neuralgia following Stereotactic Radiosurgery: A Retrospective Analysis***  
Radiation Oncology

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- 48      Binh Le  
***Clinical utility of methicillin-resistant Staphylococcus aureus nasal polymerase chain reaction (PCR) in intensive care unit patients with pneumonia***  
*School of Pharmacy*
- 49      Yanling Yan  
***Measurement of Protein Carbonylation of the Na/K-ATPase  $\alpha$ 1 Subunit by Gel-Filtration HPLC***  
*Pharmacology, MIIR*
- 50      Ahmed fahala  
***diagnostic value of cardiac computed tomography angiography in patients with left bundle branch block and abnormal single photon emission computed tomography***  
*Internal\_Medicine*
- 51      Zachary Sanford  
***Orthopaedic Surgeon Density in West Virginia***  
*Orthopaedic Surgery*
- 52      Aladdin Tarakji  
***Retrospective analysis of outcomes from use of a novel carbon fiber implant for oncologic and fracture outcomes***  
*Orthopedic Surgery*
- 53      Muhammad A. Chaudhry  
***pNaKtide, an antagonist of Na/K-ATPase Signaling, Ameliorated PNx-Mediated Cardiac Function***  
*Pharmacology, MIIR*
- 54      Maria Espiridion  
***Distance to care is associated with lower healthcare maintenance and survival in patients with gynecologic malignancies***  
*Obstetrics and Gynecology*
- 55      Egleton Richard  
***Buprenorphine modulates angiogenesis***  
*Pharmacology and Physiology*
- 56      Emad Alkhankan  
***Giant Cell Interstitial Pneumonia is a rare manifestation of chronic Nitrofurantoin lung toxicity***  
*Internal Medicine*
- 57      Grant Buchanan  
***Geriatric trauma: are the elderly undertriaged?***  
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- 58      Yousef Abdel\_Aziz  
***PanColitis with ileitis caused by Methicillin-Resistant Staphylococcus Aureus (MRSA)***  
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- 59 S. Mohan  
***Morphine mediated neuroprotection from hemin using an in vitro model of intracerebral hemorrhage***
- 60 Sinan Ozgur  
***Intra-operative total knee arthroplasty distraction significantly reduces visible particulate debris***  
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- 61 Cody Stover  
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*Orthopaedic Surgery*
- 62 Elise Anderson  
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- 63 Jack Wang  
***Homicidal Ideation in Psychiatric Emergency Room***  
*Psychiatry and Behavioral Medicine*
- 64 Crystal D. Heise  
***Introductory Performance Improvement Evaluation to Optimize Door to Needle Time for IV Thrombolysis Therapy in Acute Ischemic Stroke***  
*Marshall Health Neuroscience Department, Marshall University School of Pharmacy*
- 65 Mohit Harsh  
***Robotic Partial Nephrectomy in 119 Consecutive Cases***  
*Surgery/Urology and Internal Medicine/Nephrology*
- 66 Krista Allen  
***Cost of Care for the Surviving Periviable Neonate***  
*Pediatrics*
- 67 Lawrence M. Wyner  
***Tumor to Tumor Metastasis (TTM) Occurring in the Penis***  
*Department of Surgery, Joan C. Edwards School of Medicine, Huntington, WV,  
Department of Laboratory Medicine and Pathology, Mayo Clinic*
- 68 Scott Studeny  
***A Quality Improvement Project: Improving Patient Safety by Standardizing the Handoff Process***  
*Marshall Pediatrics, Hoops Family Children's Hospital*
- 69 Kristin Sinning  
***Pregnancy After Endometrial Ablation Complicated by Placenta Accrete***  
*Obstetrics and Gynecology*
- 70 Justin M. Pacor  
***Prevalence of Ideal Cardiovascular Health Metrics in Children & Adolescents: A Systematic Review***  
*Center for Healthcare Advancement & Outcomes, Baptist Health South Florida, Miami, FL*

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- 71 Brooke Andrews  
**Effects of Maternal Polydrug Exposure on Fetal Neonatal Abstinence Syndrome Severity**  
*Pediatrics*
- 72 Dakota Ward and Monica Valentovic  
**Characterization of Renal Cytotoxicity and Oxidative Stress Induced by the Radiocontrast Agent Diatrizoate**  
*Pharmacology, Physiology and Toxicology*
- 73 Kevin S. McCann  
**Observational Study of the Structured and Monitored Management of Chronic Non\_Malignant Pain with Opiates in a Rural Primary Care Office in a High Opiate Abuse Region**  
*Family and Community Health*
- 74 Abdalla Lawag and Vincent Sollars  
**Phenotypic Plsticity associated with Hsp90 inhibition**  
*Biochemistry and Microbiology*
- 75 Makenzie E. Hatfield Kresch  
**A Pilot Time\_Motion Study of Academic Family Physician's Patient Care Activity**  
*Family and Community Health*
- 76 Mina Shenouda  
**Achieving Complete Response on Post\_Therapy PET Scan Might Inversely Correlate with Survival in Small Cell Lung Cancer**  
*Internal Medicine*
- 77 Ashley D. Collins  
**Tobacco Use and Associated Factors Among Patients Presenting to a Psychiatric ER**  
*Psychiatry*
- 78 Alisha Milton Lewis  
**Reciprocal regulation of IL\_17 and IL\_22 secretion by CD4 T cells through the Aryl Hydrocarbon Receptor**  
*School of Pharmacy*
- 79 Rodhan Khthir  
**How Safe is Healthcare? Patient and Family Exposure and Perceptions Medicine Epigenetic Histone Modifications**  
*Biological Sciences*
- 80 Diane Dawley  
**Effects of Opioid Abuse Potentially Mediated by Epigenetic Histone Modifications**  
*Department of Biological Sciences*
- 81 James Lewis  
**IMPROVING HEALTH CARE OUTCOMES FOR HOMELESS APALACHIAN CHILDREN: Care Coordination by Parents of Children with Special Health Care Needs. A West Virginia CARES (Coordination Access to Resource and Emergency Services) Project from the Healthy Tomorrows Partnership for Children Program**  
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- 83 Grant S. Buchanan  
***Body mass index as a predictor of tibial component size in unicompartmental knee arthroplasty***  
*Orthopaedic Surgery*
- 84 Caroline A. Hunter  
***Role of antioxidants in kinase-dependent regulation of mitochondrial energy metabolism***  
*Biochemistry and Microbiology*
- 85 M. Harsh  
***A Survey of African American Men in Chicago Barbershops: Implications for the Effectiveness of the Barbershop Model in the Health Promotion of African American Men***  
*Marshall University Joan C. Edwards School of Medicine, Department of Clinical Psychology, Adler University, Department of Urology, Northwestern University Feinberg School of Medicine, Project Brotherhood Inc. Woodlawn Health Center*





**ORAL SESSION I • 8:30 AM – 9:45 AM**

# **28TH ANNUAL RESEARCH DAY ORAL SESSION**

## **The Significance of CYP2B6 Genetic Polymorphisms in Unexpected Fatalities of Methadone Users in Caucasians of WV and KY Appalachia Region**

Taha Ahmad 1, Lauren Richards-Waugh 2, Samie Sabet 1, and Gary O. Rankin 1

1 Dept. of Pharmacology, Physiology, and Toxicology, Marshall University, Huntington, WV and 2 Marshall University Forensic Science Graduate Program, Marshall University, Huntington, WV

### **Background**

Cytochrome P450 enzyme 2B6 (CYP2B6) is one of the key enzymes involved in the stereo-selective metabolism of (S)-methadone to 2-ethyl-1,5-dimethyl-3,3-diphenylpyrrolidine (EDDP), an inactive methadone metabolite. Elevated (S)-methadone can cause cardiotoxicity by prolonging the QT interval of the heart's electrical cycle. The large confounding interindividual variability in the pharmacokinetics of methadone contributes to the ambiguity in the relationship between dose, plasma concentration levels, and side effects.

### **Hypothesis**

The hypothesis of this study is that one or more single nucleotide polymorphisms (SNPs) located within the CYP2B6 gene contributes to or is linked to the methadone poor metabolizer phenotype resulting in an overdose.

### **Methods**

The genotypic frequencies of eight exonic and intronic CYP2B6 gene SNPs (rs2279344, rs3211371, rs3745274, rs4803419, rs8192709, rs8192719, rs12721655 and rs35979566) were determined using real time polymerase chain reaction utilizing TaqMan Allelic Discrimination Analysis. The examination was conducted on Appalachian Caucasian methadone only intoxication (125) and control (255) cases obtained from the West Virginia (WV) and Kentucky (KY) Offices of the Chief Medical Examiner. Based on a Chi-squared goodness of fit test with two degrees of freedom, Hardy-Weinberg equilibrium was determined for each of the eight SNPs genotyped.

### **Results**

SNP rs8192709 of the control group was determined to be in disequilibrium ( $p < 0.05$ ). Further analysis indicated a significant difference ( $p < 0.05$ ) in the frequencies of SNPs rs3745274, rs4803419, rs8192709, and rs8192719 of the control group when compared to the general Caucasian population. These observations indicate that the Caucasians of the WV and KY Appalachia region embody a unique gene pool. The genetic frequency of methadone only fatality cases were thus compared to the control group, showing an apparent increase ( $p < 0.05$ ) in the minor allele frequency for SNPs rs3745274 (\*9, 516G>T), and rs8192719 (C>T).

### **Conclusion**

These results indicate that there are two SNPs on the CYP2B6 gene that may be linked to methadone fatalities.

## **Rural West Virginia teen perception of texting and driving.**

Daniel Kahn MSIII, Frank Fofie MSIII, Grant Buchanan MD, Zain Qazi MD, Timothy Wilson-Byrne MD, Tracy Legrow PsyD, Franklin Shuler MD, PhD  
Orthopaedics, Marshall University

### **Background**

Texting and driving has developed into a severe problem among the adolescent population. Motor vehicle accidents kill over 2000 teenagers annually, and it has been estimated that 58% of accidents are due to distracted driving. The purpose of this study was to evaluate teen perception of texting and driving among rural West Virginia high school students, and see if education could reduce this dangerous behavior.

### **Hypothesis**

The authors hypothesize that texting and driving is prevalent among rural high school students and that education will improve their perception of its dangers and reduce this risky behavior.

### **Methods**

143 rural WV high school students completed a 20 question survey regarding their perception and participation in texting and driving. These students underwent an educational session and later were asked to fill out another survey to see if their perception had changed.

### **Results**

This research found that 95% of teens acknowledged the danger of texting and driving, yet 36% still regularly did so; education did not significantly alter their perception of the dangers of texting and driving ( $p=0.2$ ) or reduce the frequency of this behavior ( $p=0.6$ ).

### **Conclusion**

Although the hypothesis of educating students on the dangers of texting and driving in order to effect change in driving habits was sound, it appears to be ineffective. It is reasonable to assume that teens knowing accept the risk of texting and driving and feel that personally they can text and drive without any impairment. It is clear that education alone is not sufficient for reducing a dangerous driving behavior and more effective strategies are needed to effect change.

## **Enhanced Mitochondrial Biogenesis in ER/PR Positive Breast Cancers**

Funda Kartal\*, Doreen Griswald†, Hasan Koc#, and Emine C. Koc\*

Marshall University Joan C. Edwards School of Medicine, Departments of Biochemistry and Microbiology \*, and Pathology† and School of Pharmacy, Department of Pharmaceutical Research and Science#

### **Background**

Mitochondria have critical functions in eukaryotic cells such as compartmentalization of metabolic pathways, generation of cellular energy, regulation of redox state, production of reactive oxygen species (ROS), buffering cellular Ca<sup>2+</sup>, and initiation of apoptosis. According to the Warburg hypothesis, mitochondrial dysfunction is interpreted as one of the leading factors in cancer. However, recent studies revealed that the mitochondrial energy metabolism was altered in tumors to support their high energy demand. Understanding the mechanism behind the altered mitochondrial energy metabolism and biogenesis may lead to discovery of novel therapeutic targets. In this study, we investigated the alterations in expression and post-translational modifications of mitochondrial translation components in breast tumor biopsies.

### **Hypothesis**

Altered regulation of mitochondrial biogenesis, specifically the translation machinery components, supports development and progression of ER/PR positive breast carcinomas.

### **Methods**

Breast tumor biopsies were obtained from Marshall University Joan C. Edwards School of Medicine immediately after surgical resection. After tumor staging and detection of ER, PR, and HER2 expression, frozen tissue samples were sliced and sonicated for preparation of protein lysates. Protein determination of lysates were carried out with BCA assays to ensure equal loading of samples onto SDS gels for immunoblotting analysis.

### **Results**

An increase in oxidative phosphorylation (OXPHOS) complexes was observed in the majority of tumor samples with high ER/PR expression. Altered expression of mitochondrial translation components, mainly ribosomal proteins, allowed us to correlate the mitochondrial protein synthesis to the expression of complex I and IV subunits in tumor biopsies.

### **Conclusion**

Our results indicate that the enhanced mitochondrial biogenesis and/or translation could be one of the key regulatory points of tumor metabolism in breast carcinoma. Unrevealing the mechanism behind this regulation will allow us to devise new strategies to treat cancer.

## **Na/K-ATPase Mimetic pNaKtide Peptide attenuates aging in adult human dermal fibroblasts**

Amrita Mallick, Krithika Srikanthan, Alexandra Nichols and Komal Sodhi

Department of Medicine, Surgery and Pharmacology

### **Background**

Aging is characterized by inevitable but progressive decline of physiological integrity. Cellular senescence is evident by a number of physiological changes that occur in the cells including loss of cell division, increases in size, nuclear changes and senescence-associated gene overexpression.

### **Hypothesis**

This study addresses the effect of novel drug, pNaKtide, a peptide derived from  $\alpha 1$  Na/K-ATPase, has on senescence-associated features in HDF induced by exposure to oxidative stress caused by hydrogen peroxide ( $H_2O_2$ ).

### **Methods**

Two groups of adult HDF cells were exposed to a sub lethal dose of  $H_2O_2$  for 2 hours to induce cellular senescence. One group was then treated with different concentrations of pNaKtide for 48hours. Progression to senescence was evaluated in treated and untreated cells by: studying morphology changes, RT-PCR, T-BARs assay to assess lipid peroxidation, superoxide assay to measure the level of ROS, and senescence associated  $\beta$  galactosidase assay.

### **Results**

$H_2O_2$  exposed senescent cells showed significantly elevated levels of mRNAs (p21, apolipoprotein J, Collagenase 1, fibronectin) that are indicators of DNA damage confirming senescence through alterations in gene expression. Morphological symptoms such as loss of cell replication, increased size of nucleus was evident through Dapi staining in aged cells. Additionally, activation of senescence associated  $\beta$ -galactosidase and increase in ROS level were also significant in these cells as expected. On the contrary, cells exposed to  $H_2O_2$  and treated with pNaKtide showed similar morphology and gene expression profile comparable to pre senescent control cells that were not exposed to  $H_2O_2$ .

### **Conclusion**

Taken together, our study demonstrates for the first time that Na/K-ATPase Mimetic pNaKtide Peptide significantly alleviate the genetic and phenotypic attributes of aging. pNaKtide is a novel drug for treating cellular damage responses that may contribute to manifestations of aging.

# **Defining the role of Hepatocyte Growth Factor (MET) Receptor and PI3K/AKT signaling activation in Bilateral Diffuse Uveal Melanocytic Proliferation syndrome**

Sarah L. Miles

Biochemistry and Microbiology, Joan C. Edwards School of Medicine, Marshall University

## **Background**

Bilateral diffuse uveal melanocytic proliferation (BDUMP) is a paraneoplastic ocular syndrome characterized by profound bilateral vision loss as a result of benign pigmented and non-pigmented uveal melanocytic tumors, exudative retinal detachment and rapid cataract formation. Ocular symptoms frequently appear prior to the discovery of a primary malignancy, delaying proper diagnosis. The lack of a molecular diagnostic marker or molecular target for therapy severely limits the clinical management of this syndrome. Previous analysis of BDUMP factor-dependent melanocyte signaling activation revealed activation of the hepatocyte growth factor (MET) receptor with subsequent robust downstream activation of PI3K/AKT signaling.

## **Hypothesis**

The objectives of these studies were to further investigate MET receptor and PI3K/AKT activation as the critical molecular mechanisms responsible for initiation and potentiation of BDUMP syndrome, and analyze the melanocyte selectivity of BDUMP activated signaling mechanism.

## **Methods**

To investigate melanocyte specific sensitivity, time sensitive BDUMP-dependent signaling activation was analyzed in normal melanocytes vs. keratinocytes. Antibody signaling arrays, coupled with comprehensive western blot analysis of MET and PI3K/AKT phosphorylation status were used to characterize the differential activation of the MET/PI3K/AKT axis by BDUMP factor stimulation. To further establish the role of MET receptor and PI3K activation, chemical antagonists of MET and PI3K were used were used to inhibit BDUMP dependent proliferation and signaling activation.

## **Results**

BDUMP dependent signaling activation and western blot analysis of activating phosphorylation of both the MET receptor and downstream AKT reveal differential phosphorylation status in response to BDUMP serum in melanocytes and keratinocytes. Pretreatment with both MET receptor and PI3K inhibitors prevent BDUMP stimulated proliferation and signaling activation in normal melanocytes.

## **Conclusion**

Despite the rarity of BDUMP, these studies have substantially furthered our current understanding of melanocyte-sensitive mechanisms that may drive the initiation and progression of BDUMP syndrome. Furthermore, MET receptor inhibition may provide a potential therapeutic target, and warrants further investigation.



## **2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)/Aryl Hydrocarbon Receptor (AHR) Regulation of Large Neutral Amino Acid Transporter 1 (LAT1) in Breast Cancer Cells.**

Justin K. Tomblin<sup>1</sup>, Subha Arthur<sup>2</sup>, Donald A. Primerano<sup>3</sup>, Ateeq R. Chaudhry<sup>1</sup>, Jun Fan<sup>3</sup>, James Denvir<sup>3</sup> and Travis B. Salisbury<sup>1</sup>.

<sup>1</sup>Departments of Pharmacology, Physiology and Toxicology, <sup>2</sup>Clinical & Translational Science, and <sup>3</sup>Biochemistry and Microbiology, Joan C. Edwards School of Medicine, Marshall University, 1 John Marshall Drive, Huntington, WV 25755, USA.

### **Background**

The aryl hydrocarbon receptor (AHR) is a ligand-activated transcription factor that is regulated by environmental toxicants that function as AHR agonists such as 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD). AHR also plays a role in cancer cell cycle progression. L-Type Amino Acid Transporter 1 (LAT1) is overexpressed in cancer, which has been attributed to its ability to promote leucine uptake by tumor cells.

### **Hypothesis**

In this study, we hypothesized that TCDD regulated the expression of LAT1 in breast cancer cells (BCCs) through an AHR dependent mechanism.

### **Methods**

RNA sequencing followed by Ingenuity Pathway Analysis (IPA), western blotting, quantitative real time PCR, radioactive leucine uptake experiments and chromatin immunoprecipitation studies were all implemented to study our hypothesis. Our model cell line was MCF-7 BCCs.

### **Results**

TCDD RNA-seq coupled with published TCDD-ChIP-seq identified LAT1 as a potential TCDD/AHR target gene. Pathway analysis of TCDD-RNA-seq data revealed a significant association between TCDD and molecular transport. Short interfering RNA (siRNA)-directed knockdown of AHR confirmed that TCDD-induction of LAT1 mRNA and protein required AHR. The AHR antagonist CH-223191 blocked TCDD-stimulated increases in LAT1 mRNA, indicating that TCDD binding to AHR is required to induce LAT1 expression. Leucine uptake experiments established TCDD-induction of leucine uptake by MCF-7 BCCs. Chromatin immunoprecipitation-quantitative PCR (ChIP-qPCR) assays revealed recruitment of AHR/AHR nuclear translocator (ARNT) heterodimers as well as the histone acetyltransferase p300 to an AHR binding site in the LAT1 gene, which caused increases in histone H3 acetylation.

### **Conclusion**

This study is the first to fully characterize TCDD/AHR regulation of the LAT1 gene in breast cancer cells. We have demonstrated LAT1 to be a direct TCDD/AHR target. Experiments in other breast cancer cell lines, including the triple-negative breast cancer line, MDA-MB-231, are ongoing.





**ORAL SESSION II • 10:30 AM – 11:30 AM**

# 28TH ANNUAL RESEARCH DAY ORAL SESSION

## **Role of Serum Biomarkers in Early Detection of Diabetic Cardiomyopathy in West Virginian Population.**

Alexandra Nichols, Adam Shaver, Kristen Payne, Komal Sodhi

Department of Medicine, Department of Internal Medicine, Department of Surgery

### **Background**

Diabetic cardiomyopathy (DCM) is an established complication of diabetes mellitus. In West Virginia, the especially high incidence of diabetes and heart failure validate the necessity of developing new strategies for earlier detection of DCM. Since most DCM patients remain asymptomatic until the later stages of the disease when the fibrotic complications become irreversible, we aimed to explore biomarkers that can identify early-stage DCM.

### **Hypothesis**

Patients with both diabetes and diastolic dysfunction will exhibit elevated levels of serum biomarkers that indicate the potential for the development of diabetic cardiomyopathy.

### **Methods**

The patients were grouped into four categories based on clinical diabetic and cardiac parameters: Control, Diabetes (DM), Diastolic dysfunction (DD), and Diabetes with diastolic dysfunction (DM+DD), the last group being the preclinical DCM group.

### **Results**

Echocardiography images indicated severe diastolic dysfunction in patients with DD+DM and DD compared to DM or control patients. In the DM and DM+DD groups, TNF $\alpha$ , isoprostane, and leptin were elevated compared to control ( $p < 0.05$ ), as were clinical markers HDL, glucose and hemoglobin A1C. Fibrotic markers IGFBP7 and TGF- $\beta$  followed the same trend. The Control group showed higher beneficial levels of adiponectin and bilirubin, which were reduced in the DM and DM+DD groups ( $p < 0.05$ ).

### **Conclusion**

Our results identified elevated levels of specific biomarkers, including IGFBP7 and TGF- $\beta$ , in West Virginia patients with diastolic dysfunction. Therefore, this novel study support the clinical application of biomarkers in diagnosing early stage DCM, which will enable attenuation of disease progression prior to the onset of irreversible complications.

**Does intravenous acetaminophen used as adjunctive treatment for postoperative pain management in patients undergoing joint replacement affect clinical outcomes?**

Andrew Vess, Alexandria Cremeans, Ganga Navada, Todd Gress, and Derek Grimm  
Department of Translational Sciences and Cabell Huntington Hospital Pharmacy,  
Marshall University Joan C. Edwards School of Medicine

**Background**

Although standardized protocols have advanced the care of the postoperative joint replacement patient, pain management remains a challenge. Intravenous acetaminophen is an attractive analgesic option and is hypothesized to potentially spare opioid use minimizing their adverse effects.

**Hypothesis**

Intravenous acetaminophen used as adjunctive treatment to control postoperative pain in joint replacement does not affect clinical outcomes.

**Methods**

We randomly selected 601 patients undergoing joint replacement surgery into three postoperative pain management groups: Group 1) Narcotic only (N=200); Group 2) Narcotic/intravenous acetaminophen (N=200); and Group 3) Narcotic/intravenous acetaminophen/intra-articular bupivacaine (N=201). We collected data on prior narcotic use, post-operative narcotic use for first 24 hours (morphine equivalents (me)), pain score (1 to 10 Likert scale), time to ambulation, and length of stay.

**Results**

Our study groups were similar for age (median 65.0, iqr 13.4), gender (36.4% male; N=219), body mass index (median 32.2 kg/m<sup>2</sup>, iqr 9.0 kg/m<sup>2</sup>), and prior narcotic use (23.6%, N=142)(all p>0.20). Time to ambulation was significantly longer in Group 2 (median 20.2 hours) compared to Groups 1 and 3 (median 18.8 and 18.9 hours, respectively)(overall p<0.001), while length of stay was significantly shorter in group 3 (median 2.1 days) compared to groups 1 and 2 (median 3.0 days for both)(overall p<0.001). Although narcotic use was higher in group 2 (median 139 me), it was not significantly different from groups 1 and 3 (122.5 and 123.5 me, respectively) (p=0.08). Interestingly, pain scores were better in group 2 (median 4.5 vs. 5 for both groups 1 and 3; p=0.007).

**Conclusion**

Adjunctive treatment with intravenous acetaminophen was associated with slightly better pain scores, but appeared to have no impact on the use of narcotics, time to ambulation, or hospital length of stay. Based on our data and previous reports, the use of intravenous acetaminophen for post-operative pain management in joint replacement is no longer warranted.

## **A Novel In Vitro Assay to Assess Antibiotic Penetration in Respiratory Mucus**

Lexie C. Keding, Timothy E. Long, Michael I. Anstead, Hongwei D. Yu

Department of Biochemistry and Microbiology Marshall University, Department of Pharmaceutical Science and Research Marshall University, Department of Pediatrics University of Kentucky, Department of Biochemistry and Microbiology; Pediatrics Marshall University

### **Background**

A hallmark of chronic pulmonary diseases is the hypersecretion of mucus that can facilitate persistent lung infections by bacterial pathogens. Currently, there is no in vitro assay to gauge the bioavailability of an antibiotic to penetrate mucus and inhibit bacterial growth. This unmet need prompted us to design a microdiffusion method that utilizes patient sputum to screen for antibiotic efficacy. This work describes the assay design and results obtained using the respiratory pathogen *Pseudomonas aeruginosa* and sputum from cystic fibrosis (CF) patients.

### **Hypothesis**

It is hypothesized that antibiotics carrying an overall neutral charge (e.g., ciprofloxacin) will achieve higher bioavailability levels compared to cationic antibiotics (e.g., tobramycin) due to the influence of ionic and electrostatic interactions with anionic constituents (e.g. DNA, actin) in CF mucus.

### **Methods**

The penetrating ability of standard antibiotics was evaluated using centrifuge filter columns containing 1% CF sputum in Noble agar. The columns were inserted into a 1.5 mL centrifuge tube containing a  $5 \times 10^5$  broth inoculum of *P. aeruginosa* and 50  $\mu$ L of 10-25  $\mu$ M antibiotic was applied to the agar surface. Comparison of antibiotic diffusion was assessed following overnight incubation by determining inhibition of antibiotic activity using optical density measurements of the broth inoculum with Noble agar alone representing 100% drug diffusion into the broth culture.

### **Results**

The results from the assay revealed that penetration of tobramycin in sputum is lower than ciprofloxacin. These preliminary findings suggest that the bioavailability of zwitterionic antibiotics to inhibit bacterial growth is higher than that for charged antibiotics in respiratory mucus.

### **Conclusion**

This study revealed that the constituents in CF sputum modulates antibiotic bioavailability. Follow up studies using sputum from different CF patient populations will be performed to further corroborate these findings.

## **Locally Advanced and Invasive Prostate Cancer is More Common in**

### **Appalachia: Results of a Single Surgeon over 15 years**

Mohit Harsh, MS-II, Krista Denning MD, Teresa Limjoco MD, Doreen Griswald MD

Linda Brown, MD, James C. Jensen, MD

Departments of Surgery/Urology & Anatomical Pathology, Marshall University Joan

C. Edwards School of Medicine, Huntington, WV

#### **Background**

The USPSTF has recommended abandoning efforts to find and treat prostate cancer (PCa). One key assumption in the analysis leading to this recommendation is that the natural history of PCa is uniform across the nation.

#### **Hypothesis**

PCa pathology is not homogenous across the nation.

#### **Methods**

Clinical and pathological data relating to radical prostatectomy by the senior surgeon of this report has been collected prospectively with IRB approval over a 14 year period. These data reflect two groups of patients at risk, differing markedly in fitness, demographics of smoking, obesity, heart disease, diabetes, and access to healthcare. Pathological data from this series was analyzed in Excel using Students t-test and Chi-Squared analysis, as appropriate. High grade PCa (HGPCA) was defined as any Grade 5 cancer. High Stage PCa (HSPCA) was defined as T3/T4 disease. Positive surgical margins (PSM) was defined as tumor present at the margin of the surgical specimen.

#### **Results**

A total of 837 patients were operated from 1993 through 2010. Data was available from 361 UT patients and 476 WV patients. The average age among UT patients was 62.6 years v 61.5 years among WV patients ( $p > 0.05$ ). Average PSA was 6.2 ng/ml among UT patients v 6.5 ng/ml in WV ( $p > 0.05$ ).

HGPCA was present in 7/361 UT patients compared to 31/476 WV patients ( $p = 0.002$ ). HSPCA was present 13/361 UT patients compared to 98/476 WV patients ( $p < 0.01$ ). PSM were present in 65/371 UT patients compared to 123/476 WV patients ( $p < 0.01$ ).

#### **Conclusion**

Patients in the WV arm of this study were significantly more likely to have HGPCA, HSPCA, and PSM compared to patients in the Intermountain West, while age and PSA were not different. This brings into question the fundamental assumptions of the USPSTF in an area already challenged by availability of healthcare and highly prevalent and injurious local health customs such as smoking.

## **The epigenetic role of Ezh2-FoxP3 crosstalk in endometriosis and its associated pain**

Kristeena Wright<sup>1</sup>; Brenda Mitchell, MD<sup>2</sup>; Nalini Santanam, PhD, MPH<sup>1</sup>

<sup>1</sup>Department of Pharmacology, Physiology, and Toxicology, <sup>2</sup>Department of Obstetrics and Gynecology, Joan C. Edwards School of Medicine, Marshall University

### **Background**

Nearly 10% of young women have endometriosis and many are afflicted with chronic pelvic pain. Understanding the mechanisms of pain at play would allow for more effective treatments.

### **Hypothesis**

Epigenetic mechanisms involved with polycomb group proteins and associated genes play a major role in the development and progression of endometriosis and its associated pain.

### **Methods**

This study involved tissues from non-endometriosis subjects without pain (n=4), as well as non-lesion (n=7) and endometriotic (n=4) tissues from patients with endometriosis and pain. Real-time PCR was used to analyze gene expression of polycomb repressor complex 2 (PRC2) components and Western blot was used to determine the relative protein levels. Interaction of tumor suppressor Forkhead box P3 (FOXP3) as a potential target for the PRC2 catalytic subunit, Enhancer of zeste 2 (EZH2), was also measured using chromatin immunoprecipitation and immunoblotting. Lastly, Qiagen EpiTect Methyl II Array was also used to identify methylation patterns of genes associated with inflammation and autoimmunity in endometriotic fluids compared to controls.

### **Results**

Expression of EZH2 was elevated in ectopic tissues compared to controls, while lowered in eutopic tissue in endometriosis patients (fold change = 3.54, 0.11, respectively). Western blots also revealed increased levels of the tri-methylation of lysine 27 on histone 3 (H3K27me3). FOXP3 gene expression was much lower in both ectopic and eutopic tissues compared to controls. DNA methylation arrays showed heightened methylation of this gene's promoter region in tissues from endometriosis patients with pain compared to controls.

### **Conclusion**

Our results thus far suggest that the upregulation of polycomb proteins in endometriotic tissues modulates DNA methylation of the forkhead protein resulting in its decreased expression. This likely leads to increased growth of the endometriotic tissue in the peritoneal environment, as well as increased pain. Our results have uncovered a network of proteins that may aid in the progression of endometriotic lesions.





**ORAL SESSION III • 1:15 PM – 2:30 PM**

# **28TH ANNUAL RESEARCH DAY ORAL SESSION**

## **Anti-Cyclic Citrullinated Peptide Antibodies are Not Elevated in A Heart Failure Population without Rheumatoid Arthritis**

Naveed Iqbal MD, Yiping Wu PhD, Stanley L. Hazen, MD PhD, W. H. Wilson Tang MD

Marshall University School of Medicine, Cleveland Clinic Foundation, Cleveland State University

### **Background**

Anti-cyclic citrullinated peptide autoantibodies (anti-CCP) have been associated with erosive arthritis in patients with rheumatoid arthritis (RA), a population with overall increased cardiovascular risk. Our group has recently identified protein carbamylation and citrulline levels (that may cross-react with anti-CCP) linking to increased major adverse cardiac events (MACE = death, myocardial infarction, stroke) in cardiac patients with depressed systolic function. The prognostic value of anti-CCP in non-RA heart failure cohort remains unknown.

### **Hypothesis**

We conducted this clinical investigation to explore the potential link between aCCP antibodies and cardiovascular risk in a large cohort of non-RA patients within the confines of a heart failure population undergoing coronary evaluation

### **Methods**

We measured anti-CCP in 720 subjects with an ejection fraction less than 50% undergoing elective coronary angiography, without an acute coronary event. Adjudicated MACE outcomes were ascertained over the ensuing 3 years for all subjects following enrollment

### **Results**

In our study population (mean age  $63 \pm 11$  years, 65% male), the median and mean anti-CCP levels were 0.2 U/mL and  $0.0 \text{ U/mL} \pm 0.1 \text{ U/mL}$ , respectively. Overall, anti-CCP did not predict future MACE, either alone (Hazard ratio [HR] 1.3 [95%CI 0.81-2.1],  $p=NS$ ) or after adjusting for traditional risk factors and renal function (HR: 1.21 [95%CI 0.74-2.01],  $p=NS$ ) nor was it present at significant levels in the nonselective population undergoing cardiac catheterization. Only 1% patients had elevated anti-CCP levels ( $=0.6 \text{ U/mL}$ ).

### **Conclusion**

In stable heart failure population without RA, anti-CCP antibodies are not detectable at significant levels and do not predict future MACE.

## **Enteroids: An in-vitro three dimensional model of the intestinal epithelium**

Molly Butts, Soudamani Singh, Subha Arthur and Uma Sundaram

Clinical Translational Sciences, Marshall University

### **Background**

The mammalian intestinal mucosa is made of secretory crypt and absorptive villus epithelial cells. An enteroid is an organoid, or a miniature organ, of the intestinal epithelium that is grown in-vitro. Similar to the in-vivo adult mammalian intestinal epithelium, enteroids also have the undifferentiated stem cells that are in a constant state of proliferation, differentiation and maturation from a secretory crypt cell into mature villus epithelial cells. This unique self-renewal mechanism makes enteroids one of the unique models of a sustainable in-vitro three dimensional organ system.

### **Hypothesis**

In order to ideally determine the mechanisms of secretion and absorption in-vitro without the confounding effects of blood flow, enteric nervous system, motility etc. it is necessary to have an in-vitro model of the intestinal epithelium.

### **Methods**

Here we report that we have been able to successfully isolate intestinal crypts from mouse intestinal epithelium and grow them in-vitro as enteroids. Isolated crypt cells were seeded on matrigel and grown in a medium containing essential growth factors such as EGF, Noggin and R-spondin.

### **Results**

The isolated crypts formed enterospheres on day 1. On day 2, the enterospheres produced new buds of crypt domains which became fully grown crypt units by day 4.

### **Conclusion**

Culturing enteroids is the closest model system to the actual mammalian physiological condition possible in a laboratory setting. Therefore, these enteroids may now be used to study and understand the differential expression and function of nutrient transporters during the maturation of intestinal epithelial cells in a three dimensional in-vitro system analogous to the in-vivo intestine.

## **Robotic Laparoscopic Partial Nephrectomy with Cold versus Warm Ischemia**

Jason Childress, Todd Gress, Zeid Khitan, Hala Alshyeb, Neha Garg, James C. Jensen

Departments of Surgery/Urology and Internal Medicine/Nephrology, Marshall University Joan C. Edwards School of Medicine, Huntington, WV

### **Background**

Cold ischemia is the gold standard in open partial nephrectomy and is advocated for laparoscopic cold ischemia. However, scant data exists to demonstrate that this is necessary, desirable or effective using the robotic laparoscopic interface.

### **Hypothesis**

We examine this issue in a case controlled series of patients having robotic-assisted laparoscopic partial nephrectomy (RALPN) using the warm ischemia (WI) method and compare it to a cohort consisting of size matched lesions have the same technique using cold ischemia (CI).

### **Methods**

Patients with renal mass since September 2006 have been offered RALPN providing a) no significant tumor thrombus; b) > 50% of the affected kidney was potentially salvageable by CT/MRI; c) no limiting nodal metastases; and d) no specific contraindications to surgery. A case control method matching patients by greatest renal tumor dimension was used comparing RALPN+WI versus those having RALPN+CI. MDRD calculated GFR was measured at baseline, daily x 4 following the procedure, and at > 1 month post operatively. Statistical analysis was performed in Excel using Students t-Test, and the Chi-squared analysis, as appropriate. IRB approval was given for this project.

### **Results**

Of 119 patients undergoing RALPN since September 2006, 35 have had RALPN+CI, while 49 have had RALPN+WI. Twenty-five patients from each group were matched by the tumor size +/- 0.5cm. No differences were noted in patient age, tumor size, or baseline GFR among RALPN+CI v RALPN+WI ( $p > 0.05$ ). Moreover, no differences developed in GFR on any of post-op days 1, 2, 3, or 4, or at > one month post operatively. Resection time in the RALPN+CI group was 39.9 minutes versus 22.3 min in the RALPN+WI group ( $p=0.029$ ).

### **Conclusion**

RALPN+CI allows for longer resection time without compromising renal function among those having RALPN.

## **Use of telehealth to teach reproductive health and life skills to rural high school females**

Rachael Starcher, Becca King, Jennie Yoost  
Obstetrics and Gynecology (Marshall University)

### **Background**

While national teen pregnancy (26.5 per 1000) and school dropout (7%) rates have declined in recent years, in McDowell County, there exists a teen birth rate of 78.1 per 1000 and a school dropout rate of 17.8%.

### **Hypothesis**

The goal of the study was to evaluate the novel use of telehealth in influencing health knowledge and behavior in a rural underserved community by teaching life skill topics to female high school students.

### **Methods**

Telehealth sessions, each emphasizing a different topic, were incorporated into an existing after school program at two McDowell County high schools. Surveys assessed teen pregnancy risk factors and behaviors both before and 6-months after completion of the program. Session pre-tests assessed pre-existing knowledge and perceptions. Post-tests assessed knowledge gained and self-efficacy. The use of telehealth was also evaluated.

### **Results**

Fifty-five subjects participated with an average age of 16.1 (SD 1.2). Only 20.4% of subjects' mothers and 12.2% of subjects' fathers achieved education beyond high school. Of subjects' mothers, 20% had experienced teen pregnancies (age =18). Sexual activity was reported among 52.7% of subjects, 4 (7.2%) reported a desire to become pregnant within the next year, and 4 (7.2%) reported already pregnant.

Thirty-seven subjects completed the 6-month follow up survey. Report of compliance with both condom and contraception use increased from 20% to 40% ( $p=.04$ ) and 22% to 38% ( $p=0.12$ ), respectively. Report of HPV vaccine initiation or completion increased from 38% to 71.4% ( $p=.03$ ) among participants of the STD session ( $n=28$ ). There were no school dropouts among subjects and one additional pregnancy reported. Over 96% of subjects reported "very confident" that the material was accurate, 86.4% reported that telehealth was "very effective" for teaching the material, and 92.8% reported they were "very likely" to participate again.

### **Conclusion**

Telehealth is a promising way to provide educational health outreach to remote underserved areas.

## Laparoscopic Vertical Sleeve Gastrectomy: A 5-year VA Review

Rahman Barry, Todd Gress, Farzad Amiri, Timothy Canterbury  
Surgery, Marshall University

### Background

Laparoscopic sleeve gastrectomy(LSG) has recently gained popularity as a definitive bariatric surgery procedure. Data is lacking on long-term outcomes after LSG, particularly in a Veterans Affairs population.

### Hypothesis

To review all LSG surgeries performed over the past 5 years, focusing on weight-loss outcomes and impact on obesity-related comorbidities.

### Methods

We retrospectively reviewed 223 patients undergoing LSG between January 2009 and June 2014 for morbid obesity. All met NIH criteria. Data on length-of-stay(LOS), complications, interval weight loss up to 5 years postoperatively, comorbidities, and number of therapies preoperatively and at long-term follow-up(LTFU) were collected. The data were analyzed using simple descriptive statistics, the Student's t-test, and ANOVA.

### Results

There were 164 males and 59 females(74% vs. 26%) with an average age of 53 years who underwent LSG. The mean weight and body mass index(BMI) were 139.4 kg and 45.4kg/m<sup>2</sup>, respectively. The average American Society of Anesthesiologists(ASA) score was 2.6. The mean weight loss at 1 year was 85.4 lbs(38.8kg) and at 5 years was 65.4lbs(29.7kg). Weight loss continued until 12-18 months, when there was a nadir in weight loss (P<0.001). There were 4 deaths and 4 staple-line leaks. 3 deaths were related to late cardiac events. One early death occurred in a very high-risk patient. All staple-line leaks were managed non-operatively. Of the 223 patients, 193 had hypertension,137 diabetes,158 hyperlipidemia,119 obstructive sleep apnea(OSA) and 125 gastroesophageal reflux disease. Preoperatively, patients were on a mean of 1.9 anti-hypertensive medications,0.9 hyperlipidemic agents,0.9 anti-reflux agents and 0.9 oral hypoglycemics. 50% of diabetics were on insulin and 68% with OSA used CPAP/BiPAP. We found significant absolute reductions in mean anti-hypertensive medications(-0.8),anti-hyperlipidemic agents(-0.4),anti-reflux agents(-0.4),oral hypoglycemics(-0.6), insulin use(-25%),and use of CPAP/BiPAP(-55%)(All P<0.001).

### Conclusion

Laparoscopic sleeve gastrectomy is a safe and effective bariatric surgery procedure, resulting in significant early weight-loss up to 18 months and long-term improvement in all obesity-related comorbid conditions.



**ORAL SESSION IIII • 3:15 PM – 4:03 PM**

# **28TH ANNUAL RESEARCH DAY ORAL SESSION**

## **Role of Serum Biomarkers in Early Detection of Non-Alcoholic Steatohepatitis and Fibrosis in West Virginian Children**

Andrew Feyh, Lucas Bracero, Tariq Latif, Alexandra Nichols, Krithika Srikanthan, Deborah L Preston, Yoram Elitsur and Komal Sodhi  
department of Medicine, Pediatrics, Surgery and Pharmacology

### **Background**

Obesity, an epidemic among West Virginia children, is well-established contributors to nonalcoholic steatohepatitis (NASH). The reported prevalence of NASH among children is 2.6%, but this increases to as much as 53% among obese children. Progression of NASH can lead to hepatic fibrosis and cirrhosis, making early detection imperative. The standard for diagnosing NASH is histologically via liver biopsy, but it is not well suited for screening or monitoring children because of its invasive nature, cost, and complications.

### **Hypothesis**

A panel of serum biomarkers were previously used in adults and showed close correlation with histology. We aim to explore those serum biomarkers to detect NASH and early stage hepatic fibrosis in at-risk children.

### **Methods**

Children who attended the gastroenterology clinic were prospectively recruited to the study. Fasting serum samples were drawn and biomarker levels were assessed via ELISA and RT-PCR.

### **Results**

The children were divided into 3 groups: Normal weight without insulin resistance (IR) (Control, group 1, #28), Obese without IR (group 2, #15), and Obese with IR (group 3, #27).

Obese (both with and without IR) patients had significantly elevated levels of oxidative markers (malondialdehyde [MDA], IL-6), fibrotic markers (CK-18), lipid metabolism markers (FGF-21), lipid inflow and outflow markers (triglycerides [TG], ApoB), and ALT compared to the control ( $p < 0.05$ ). These biomarkers were even more significantly elevated when comparing the obese with IR to obese without IR patients ( $p < 0.05$ ). Bilirubin and GLUT-1 levels were significantly decreased in both obese groups compared to the control ( $p < 0.05$ ).

### **Conclusion**

NASH associated biomarkers significantly correlated with obese children especially with those who developed IR. This study may support the use of this panel of biomarkers in obese children without the need for liver biopsy, and thereby, can play an important role in screening and monitoring obese children, which are at risk of developing NASH and hepatic fibrosis.



**Long Term Effect of Successful Stimulant Medication Treatment on the Body  
Mass Index (BMI) of Pediatric Patients with Attention Deficit Hyperactivity  
Disorder (ADHD)**

James Lewis, Brittany Woodall, Niccia Ditrapano, Anu Pokharel, Michael Matheney  
Pediatrics, Joan C. Edwards School of Medicine

**Background**

Children and adolescents with ADHD have been reported to be at risk for increased BMI despite the growth suppression and weight loss often associated with stimulant medication treatment. The long term result of effective stimulant treatment for ADHD on BMI has not been studied.

**Hypothesis**

To identify BMI trends in pediatric patients with ADHD on effective stimulant therapy.

**Methods**

Patients were identified who had been diagnosed with ADHD during 2012 and successfully treated with stimulant medication by one behavioral pediatrician following current American Academy of Pediatrics guidelines through June 2015. BMIs recorded on the initial visit and subsequent 3 to 6 month intervals were tabulated over a 30 to 42 month follow-up period.

**Results**

The total of 188 patients were divided into four groups: Obese (BMI>95%) 46 (25%), Overweight (BMI 85-95%) 33 (17%), Normal (BMI 5-85%) 104 (55%), and Underweight (BMI<5%) 5 (3%). The change in mean BMI from initial visit to end of treatment period was: Obese 98.1 to 88.6, Overweight 89.1 to 66.2, Normal 49.9 to 37.1 and Underweight 1.3 to 2.0.

**Conclusion**

Although almost one half of ADHD patients had BMIs higher than normal at outset, all groups except for those who were underweight showed a decrease in BMI over the first year which persisted over the treatment period. In this study, stimulant medication therapy that was effective for ADHD reduced BMI as well.

## **In Melanoma the RET G691S Polymorphism is a Germline Variant**

Brent Smith, Carol Amato, Stephen Robinson, and William Robinson

Division of Medical Oncology, University of Colorado School of Medicine

### **Background**

The RET protooncogene encodes for a receptor tyrosine kinase that is activated by glial cell derived neurotrophic factor (GDNF). Previous studies have found that a single nucleotide polymorphism (SNP), RETp (G691S), in the juxtamembrane portion enhances the signaling pathway and promotes tumor growth by GDNF in pancreatic and thyroid cancer in addition to melanoma. It is uncertain however whether this SNP is a germline variant or a somatic mutation. Paired peripheral blood samples and tumor biopsy samples were sequenced and their concordancy was used to determine if RETp is a germline variant or a true somatic mutation.

### **Hypothesis**

If the genotypes in blood and tissue are found to be concordant it would clearly indicate that RETp is a germline variant. On the contrary, if the samples are found to be discordant with a higher frequency of RETp in tissue then it would suggest that this occurs as the result of a somatic mutation.

### **Methods**

In this study, we examined both melanoma tissue samples and matching peripheral blood DNA for RETp. Clinical characteristics of the patients were also cross-referenced to determine if there were any trends in age, location of the primary lesion, family history, patient ethnicity or the pathological type of melanoma. Using PCR sequencing, we examined 180 different pairs of peripheral blood DNA and matched tissue samples to determine concordance.

### **Results**

Of the 180 paired samples we tested 94.4% of the samples were found to be genotypically concordant indicating that in most instances this is a germline variation. However, discordance was found in 5.6% of the paired samples and suggests that in melanoma RETp can also arise as the result of a somatic mutation and could subsequently be targeted for molecular based treatment.

### **Conclusion**

In this study it was shown that the RETp variant was a germline SNP in desmoplastic and non-desmoplastic melanomas.

## **Congenetic Mice Confirmed QTL Linked to Obesity and Hyperlipidemia on Chromosome 1 in the TALLYHO Mouse**

Jacaline K. Parkman, Xia Mao, Kristy Dillon, and Jung Han Kim

Department of Pharmacology, Physiology, and Toxicology, Joan C. Edwards School of Medicine

### **Background**

The TALLYHO (TH) mouse presents a syndrome of obesity, insulin resistance, type 2 diabetes, and hyperlipidemia. In a genome-wide scan of a [THxC57BL/6 (B6)]F<sub>2</sub> population, we previously identified quantitative trait loci (QTL) linked to obesity and hyperlipidemia on mouse chromosome (Chr) 1. To confirm the QTL and develop a strategy for positional cloning of the responsible gene(s), we generated a congenic mouse strain that carries the Chr 1 QTL, 128 Mb in size, derived from TH on a B6 background (B6.TH-Chr1-128Mb) and a second congenic strain carrying only the proximal segment, 92 Mb, of the original congenic interval (B6.TH-Chr1-92Mb).

### **Hypothesis**

The purpose of this study was to characterize these congenic mice on chow and high fat diets (HFD) and evaluate gene expression levels of interferon activated gene 202B (Ifi202b) as a positional candidate gene.

### **Methods**

B6.TH-Chr1-128Mb, B6.TH-Chr1-92Mb, and B6 mice were weaned onto chow or HFD and maintained. Body composition, plasma cholesterol, and triglyceride levels were determined. Indirect calorimetry was conducted. Ifi202b mRNA levels were measured in adipose tissue by qRT-PCR.

### **Results**

On chow, B6.TH-Chr1-128Mb mice exhibited significantly larger body fat mass compared with B6.TH-Chr1-92Mb and B6 mice. Similar trends were seen for plasma total cholesterol and true triglyceride levels, suggesting the Chr1 QTL candidate region is likely within the distal segment of the TH congenic interval where the Ifi202b gene, associated with obesity and down-regulated in B6 mice due to a microdeletion, maps. All animals gained more body fat when fed HFD. B6.TH-Chr1-128Mb mice showed lower energy expenditure (kcal/kg/hr) than B6.TH-Chr1-92Mb and B6 mice on chow and HFD, without food intake differences. The Ifi202b mRNA levels were 5-fold higher in adipose tissue of B6.TH-Chr1-128Mb mice than B6 mice on chow, and even higher on HFD.

### **Conclusion**

In summary, TH mice carry QTL conferring obesity and hyperlipidemia on the distal part of Chr 1.





**POSTER PRESENTATIONS • SESSION I • 9:45 AM – 10:30 AM**

# 28TH ANNUAL RESEARCH DAY POSTER SESSION

## **Dementia in hip fracture patients: a risk factor for in-hospital complications?**

Grant Buchanan MD, William Wyatt PhD, Mallorie Hatch PhD, Viorel Raducan MD,  
Franklin Shuler MD, PhD  
Department of Orthopaedic Surgery, Joan C. Edwards School of Medicine;  
Healthgrades

### **Background**

Numerous studies have found that dementia is associated with higher mortality following hip fracture; however, the reason for this increased mortality is less clear. Some have attributed it to comorbidities, while others have cited factors such as delayed time to surgery, activities of daily living impairment, and poor rehabilitation. Little is known about the effect of dementia on postoperative complications. The purpose of this study is to determine whether dementia influences the rate of postoperative complications following hip fracture.

### **Hypothesis**

The authors hypothesize that patients with dementia will have significantly higher in-hospital complication rates; patients with dementia undergoing operative fixation will have higher in-hospital complication rates; patients with dementia admitted from nursing facility will have higher in-hospital complication rates compared to their community dwelling counterparts.

### **Methods**

This research involves a multivariate analysis of Centers for Medicare & Medicaid Services data on patients over the age of 65 with hip fractures treated with operative or nonoperative management. The rate of in-hospital complications was compared between patients with dementia and without dementia. Results were adjusted to account for confounding variables such as age, sex, place of residence prior to injury (community vs. long-term care facility), and medical comorbidities.

### **Results**

Dementia was not found to be a statistically significant risk factor for higher in-hospital complications. There was no significant difference in the rate of in-hospital complications between operative and non-operative management. There was no significant difference between the rate of in-hospital complications in patients with dementia who presented from a nursing home and those who presented from the community.

### **Conclusion**

Dementia is not an independent risk factor for in-hospital complications in patients with hip fracture.

## Attention Hyperactivity Deficit Disorder and Co-existing Anxiety: Long-Term Response to Stimulant Therapy

James M Lewis, Meredith Woodall, Michael Matheney, Niccia Ditrapano, Anu Pokharel, Jesse Lewis  
Pediatrics, Joan C. Edwards School of Medicine, Huntington, WV, United States.

### Background

Although anxiety is a coexisting condition in 30-40% of pediatric patients diagnosed with ADHD, the safety and effectiveness of stimulant medication as the primary treatment for both ADHD and anxiety is not well established.

### Hypothesis

To evaluate the response to stimulant treatment on symptoms of both ADHD and anxiety in the combined group as compared to the ADHD alone group.

### Methods

Parents of new patients referred to the ADHD Center from January 2013 through July 2014 completed the Screen for Child Anxiety Related Disorders (SCARED) documenting the presence of an anxiety disorder by a score of >25. All patients subsequently received multimodal ADHD treatment, including stimulant medication, by one physician following current American Academy of Pediatrics guidelines. Consistent improvement in ADHD and anxiety by parent report was documented by chart review of subsequent office visits through July 2015 for a 12-30 month follow-up period. Attention span and anxious/worried symptoms were graded by parents on each visit as improved, worse, or unchanged.

### Results

Of the 111 patients enrolled and diagnosed with ADHD, 36(34%) received a SCARED score of >25. A total of 104 patients completed the study with 35 in the combined ADHD/anxiety group and 69 in the ADHD alone group. There were no significant differences in median age (10), sex (75% male), ADHD primarily inattentive type (15%) or family history of anxiety (34%).

	Positive Response of anxiety and ADHD ratings to stimulant therapy		
	ADHD and Anxiety (n=35)	ADHD Alone (n=69)	p-value*
Anxious/worried:			
Severe at diagnosis	27 (77%)	16 (23%)	
Improved	24	13	0.66
Unchanged/worse	3/0	3/0	
Attention span:			
Severe at diagnosis	32 (91%)	16 (23%)	
Improved	29	13	0.39
Unchanged/worse	3/0	3/0	

\*Fisher's exact test

### Conclusion

Stimulant treatment of pediatric patients with ADHD and anxiety results in parent-reported improvement in anxious/worried symptoms and attention span equal to patients with ADHD alone.

## **Capsaicin inhibits invasion of human non-small cell lung cancer cells in a TRPV1 receptor independent manner**

William D. Rollyson, Nicholas A. Nolan, Austin T. Akers, Kathleen C. Brown, and Piyali Dasgupta

Department of Pharmacology, Physiology, and Toxicology, Joan C. Edwards School of Medicine, Marshall University

### **Background**

Non-small cell lung cancer (NSCLC) comprises 85% of lung cancer cases and is characterized by aggressive clinical course and rapid metastasis. One of the challenges of NSCLCs is that the tumor has frequently metastasized to distant organs at the time of diagnosis. The invasion of tumor cells is a key step in the metastatic cascade. Dietary compounds like capsaicin have been known to cause apoptosis in human NSCLCs. However, the effect of capsaicin on the pro-invasive ability of NSCLC cells has not yet been studied.

### **Hypothesis**

Capsaicin and its related compounds inhibit the invasion of NSCLC.

### **Methods**

Using a Boyden chamber assay, as described in Dasgupta, P, et al. (2009) *Int J Cancer* 124(1):26-45, NSCLC cells were placed in the upper chamber. They were treated with capsaicin, capsiate, and capsiconiate.

Using a spherical invasion assay, as described in Evensen, NA, et al. (2013) *PloS One* 8(12):e82811, NSCLC cells are mixed in with a 1:1 solution of Matrigel and RPMI containing 20% FBS media and treated with capsaicin, capsiate, and capsiconiate.

### **Results**

Boyden chamber assays show that capsaicin inhibits the invasion of NSCLC in a concentration-dependent and time-dependent manner. The pro-invasive activity of capsaicin was verified by a second invasion assay, the spherical invasion assay, and similar results were obtained. We also examined the anti-invasive activity of two non-pungent capsaicin compounds, namely capsiate and capsiconiate. Capsiate displayed equivalent anti-invasive activity as capsaicin, whereas capsiconiate did not alter the invasion of NSCLC cells. The anti-invasive activity of capsaicin and capsiate were found to be independent of its apoptotic activity and occurs at lower concentrations. The anti-invasive activity of capsaicin and capsiate are independent of TRPV1.

### **Conclusion**

Our results show that capsaicin and its related compounds may be useful to combat invasive human NSCLC.



## **Oral HPV: An Exploration and Assessment of Young males' Knowledge, Risk Perceptions, Behaviors, and Vaccination Compliance**

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### **Background**

Human papillomavirus (HPV) is a common sexually transmitted infection that is linked to cervical cancer. A much less studied complication of HPV infection is oral cancer. "Oral HPV" is transmitted primarily during cunnilingus/fellatio and infects the oropharynx. Oral HPV is 7-times more common in young men compared to young women. In the last decade, the CDC reported a 4-5-fold increase in HPV+ oropharyngeal cancers. There is no FDA-approved method for detecting or diagnosing an oral HPV infection, but there is an FDA-approved prophylactic vaccine.

### **Hypothesis**

Our study aim is to explore and assess young males' knowledge, risk perceptions, behaviors, and vaccination compliance towards oral HPV.

### **Methods**

This was a cross-sectional survey study of 102 male college students enrolled in classes at a southern university in 2015. The IRB of the University of South Carolina approved the protocol for this study.

### **Results**

Majority of the participants' demonstrated low oral HPV knowledge coupled with participation in high-risk sexual behaviors. Notably, 70% of participants were unvaccinated and 74% reported having had oral sex at least once. Of those participating in oral sex, 44% reported never wearing a condom. Although there was poor vaccination compliance, 70% did believe that the HPV vaccine would be helpful in preventing oral HPV. Despite participants' precarious sexual behaviors, poor vaccination compliance and low scores on the oral HPV knowledge survey, 73% of college males surveyed still found it unlikely that they would contract oral HPV.

### **Conclusion**

Our study suggests that education about oral HPV is insufficient for preventing the spread of oral HPV. Male students are at high risk for contracting oral HPV given their participation in risky sexual behavior along with low vaccination rates. Further studies are needed to determine appropriate strategies to promote healthy behavioral changes and improve HPV vaccination compliance.

## **A Positive Correlation between High Levels of Inflammatory Markers and 20-HETE in Obese Appalachian Females**

Vishal Hari Lakhani, Alexandra Nichols, Krithika Srikanthan, Amrita Mallick and Komal Sodhi

Department of Surgery and Pharmacology

### **Background**

Higher body mass index (BMI) increases the risk for developing hypertension. Women are disproportionately more affected by obesity. Obesity increases levels of metabolic syndrome biomarkers (leptin and TNF- $\alpha$ ) in Appalachian women, and leads to vascular dysfunction and atherosclerosis, which is assessed by levels of inflammatory markers 20-HETE, a powerful vasoconstrictor, and serum adiponectin.

### **Hypothesis**

We previously demonstrated a marked increase in levels of inflammatory markers in humans and mice with hypertension, obesity and diabetes, and hypothesize that a high-BMI subject would present with increased levels of 20-HETE, leptin, and TNF- $\alpha$ , and decreased adiponectin.

### **Methods**

Serum adiponectin, 20-HETE, leptin, and TNF- $\alpha$  were assayed in female Appalachian subjects. Linear regression analysis was used to analyze the relationship between BMI, leptin, adiponectin and 20-HETE. Nonlinear regression was used to determine the odds ratio and confidence intervals. The effect on murine pre-adipocytes was also measured.

### **Results**

Lipidomic analysis revealed a significant increase in CYP-derived 20-HETE among high-BMI females (50-72) compared to lower-BMI subjects (32-45) ( $p < 0.05$ ). Treatment of murine pre-adipocytes with 20-HETE decreased serum adiponectin levels and increased adipogenesis by 76% ( $p < 0.05$ ), implicating both 20-HETE and oxidative stress as factors in the pathogenesis of BMI-related disease. Serum leptin and TNF- $\alpha$  were significantly increased in high-BMI subjects ( $p < 0.05$ ) compared to lower-BMI subjects, while adiponectin levels were decreased ( $p < 0.05$ ) in high-BMI subjects compared to lower-BMI subjects.

### **Conclusion**

Increased BMI in Appalachian females correlates with an increase in 20-HETE expression, serum TNF- $\alpha$ , and leptin expression and a decrease in serum adiponectin. This represents a novel mechanism by which high-BMI females with controlled blood pressure remain sensitive to the development of atherogenesis, vascular dysfunction, and metabolic syndrome.

## **Determining Optimal Ovarian Cancer Treatment by Age**

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Huntington, WV

### **Background**

Ovarian cancer is difficult to diagnose because it presents with nonspecific symptoms until reaching late stages. In fact, ¾ of women are stage 3 or greater at diagnosis. Optimal debulking surgery and chemotherapy are the mainstays of treatment. The risk of ovarian cancer increases with age. Older patients are more likely to have comorbidities that result in non-optimal treatment based on cancer stage guidelines. Comparing age and treatment received to months of survival may provide insight into treatment that may be most important in older patients. Chemotherapy and debulking surgery increase survival in ovarian cancer patients. Individual factors need to be identified to guide treatment in older women to optimize individual outcome.

### **Hypothesis**

As age increases and comorbidities increase, surgery becomes more dangerous but chemotherapy is still a viable option for these patients. Providing older patients with chemotherapy increases months of survival.

### **Methods**

Patients at ECCC and CHH who were diagnosed with ovarian cancer between 2004 and 2014 were compared. Age, stage at diagnosis, treatment, months of survival since diagnosis, and comorbidities were compared using multivariate analysis.

### **Results**

Patients with older age were less likely to receive optimal surgery and treatment than younger patients. All patients, regardless of age, that received any chemotherapy had a longer lifespan than those that did not receive any chemotherapy.

### **Conclusion**

Advanced stage patients with ovarian cancer are less likely to receive optimal treatment with debulking surgery and chemotherapy if the patient is older. Most patients diagnosed with ovarian cancer are older than 50, with diagnosis prior to menopause occurring only about 10% of the time. With increasing age, patients become more likely to be diagnosed with ovarian cancer. Mortality from ovarian cancer has only slightly decreased in the past 30 years. Further study to determine guidelines to optimally treat older patients with comorbidities is needed.

## Heme Oxygenase Induction Suppresses Hepatic Hpcidin and Rescues Ferroportin and Ferritin Expression in Obese Mice

Krithika Srikanthan, Alexandra Nichols, Amrita Mallick, Vishal Hari Lakhani and Komal Sodhi

Department of Medicine, Surgery and Pharmacology

### Background

Hepcidin, a phase II reactant secreted by hepatocytes, regulates cellular iron levels by increasing internalization of ferroportin- a transmembrane protein facilitating egress of cellular iron. Chronic low-grade inflammatory states, such as obesity, have been shown to increase oxidative stress and enhance hepcidin secretion from hepatocytes and macrophages.

### Hypothesis

Heme-heme oxygenase (HO) is a stress response system, the induction of which reduces oxidative stress thereby abating patho-physiological conditions such as obesity and metabolic syndrome.

### Methods

8 weeks old male obese (ob) mice and their age- and sex-matched lean mice were used as controls. CoPP was administered intraperitoneally once a week (3 mg/kg) for 6 weeks to obese mice. CoPP plus stannous mesoporphyrin (SnMP) was administered intraperitoneally three times a week (20 mg/kg) for 6 weeks.

### Results

We investigated the effects of HO-1 induction on hepatic hepcidin levels and on iron homeostasis in tissues from lean and obese mice. Obese mice exhibited hyperglycemia along with increased levels of pro-inflammatory cytokines (MCP-1, IL-6,  $p < 0.05$ ), oxidative stress and increased hepatic hepcidin levels ( $p < 0.05$ ). Enhancement of hepcidin was reflected in the reduced expression of ferroportin in obese mice ( $p < 0.05$ ). Further our results showed attenuation of insulin receptor phosphorylation and attenuation of metabolic regulators including pAMPK, pAKT and pLKB1. Cobalt protoporphyrin (CoPP)-induced HO-1 up-regulation in obese mice and reversed these pathophysiological alterations ( $p < 0.05$ ) while attenuating hepatic hepcidin levels and enhancing ferritin expression. These effects of CoPP were prevented in obese mice concurrently exposed to an inhibitor of HO (SnMP) ( $p < 0.05$ ).

### Conclusion

Taken together, our results highlight a modulatory effect of HO on iron homeostasis mediated through the suppression of hepatic hepcidin in conjunction with the rescue of cellular ferritin levels. Therefore these findings may prove an effective strategy in treating the metabolic consequences of obesity including alteration of liver iron homeostasis.

**Comparison of the use of ascorbic acid vs. dehydroascorbic acid to reduce  
HIF-1 alpha stabilization in human melanoma**

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**Background**

Increasing evidence supports the role for hypoxia inducible factor-1 alpha (HIF-1alpha) in melanoma carcinogenesis. We have previously reported that ascorbic acid (AA; vitamin C) significantly decreases HIF-1 alpha accumulation, and reduces the invasive potential of metastatic melanoma, suggesting AA may be a beneficial adjuvant therapy to improve chemotherapeutic response. Intracellular accumulation of AA is accomplished by transport of AA by sodium dependent vitamin C transporters (SVCT) or dehydroascorbate (DHA) via glucose transporters (GLUTs). With the finding that many malignancies have elevated GLUT expression, reports have suggested that DHA supplementation would provide an effective means to deliver and restore intracellular ascorbate. However, these studies do not account for competition of glucose with DHA for GLUT transport, raising question to its value in a clinical setting. These studies will assess the impact of physiological glucose on the ability of AA and DHA to regulate the stability and accumulation of HIF-1 alpha in human metastatic melanoma.

**Hypothesis**

We hypothesize that in the presence of physiological glucose, AA will be more effective than DHA in decreasing the stability and accumulation of HIF-1 alpha, and further augment the response to chemotherapy in metastatic melanoma.

**Methods**

HIF-1 alpha protein accumulation in WM9 and WM239 metastatic melanoma cells was evaluated by western blot following treatment with AA, ascorbate 2-phosphate (A2P), or DHA under physiological or glucose-free conditions. The impact of AA or DHA on chemotherapy response was evaluated by a cyQuant proliferation assay following treatment with temozolomide (TMZ) with or without A2P and DHA.

**Results**

Western blot analysis demonstrates that treatment of melanoma cells with AA and A2P was more effective than DHA in decreasing HIF-1 alpha protein. Furthermore supplementation with A2P further reduced melanoma cell proliferation in response to TMZ.

**Conclusion**

Our studies suggest AA or A2P, but not DHA as a potential adjuvant therapy for metastatic melanoma.

**Incidence of hypomagnesemia on proton pump inhibitors at the Huntington  
Veterans Affairs Medical Center – IHOP**

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**Background**

Proton pump inhibitors (PPIs) are widely used for the treatment of acid-related disease states such as dyspepsia, GERD, esophagitis, and peptic ulcers. These medications are generally considered safe in most patient populations especially in geriatric patients; however, there are several adverse effects that may occur with long-term use. Hypomagnesemia is a newer complication arising in the literature following multiple case reports over the past several years, although the true incidence of hypomagnesemia associated with PPI use remains unclear at this time.

**Hypothesis**

The primary benefit for the current research is to determine the incidence of hypomagnesemia with long-term PPI therapy. This information can be used to determine if supplementation or a change in therapy is needed.

**Methods**

A retrospective chart review was performed on patients enrolled at the Huntington VAMC who are receiving or have received long-term PPI therapy (considered > 3 months). Magnesium levels were reviewed to determine the incidence of hypomagnesemia with PPI use. Other data analyzed included age, PPI prescribed, calcium level, potassium level, and diuretic use (both Loop and thiazide).

**Results**

Of the 331 patient charts reviewed, 192 met the study inclusion criteria and were analyzed for hypomagnesemia while on PPI therapy. There was a total of 51 out of 192 patients (26.6%) with hypomagnesemia reported at least 3 months after starting PPI therapy. The decline in magnesium levels over time while on PPI therapy resulted in a Pearson's Correlation of -0.24 which was statistically significant ( $p < 0.001$ ).

**Conclusion**

Hypomagnesemia may result in patients on long-term PPI therapy regardless of age and diuretics may further contribute to this issue. Low magnesium does not appear to be correlated with hypokalemia or hypocalcemia in this patient population. Baseline and routine monitoring of magnesium should be considered in patients that are being started on PPI therapy or are continued on therapy long-term.

## **Killing of MRSA using IlluminOss: Blue Light and Sterilization of Orthopaedically Relevant Pathogenic Bacteria**

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### **Background**

Blue light, with wavelengths outside of the UV spectrum, has antimicrobial properties for both Gram-negative and Gram-positive bacteria.<sup>1</sup> Currently, there is an FDA approved clinical trial at Marshall University (IRB 704603) that is using blue light for photodynamic bone stabilization – the IlluminOss Light Fix clinical trial. One of the major blue light outputs from the IlluminOss optical fiber is at 405nm (Figure 1, blue peak in yellow oval). This wavelength has been shown to eradicate methicillin-resistant *S. aureus* (MRSA), *S. aureus* and *P. aeruginosa* in a time and dose dependent manner due to the production of cytotoxic reactive oxygen molecules.<sup>1-4</sup>

### **Hypothesis**

IlluminOss Medical asked for me to lead the investigation to determine whether the full spectrum IlluminOss light output during the 400 sec implant curing process is capable of bactericidal activity to Orthopaedically relevant pathogens.

### **Methods**

Bacterial suspension cultures were used to study the effect of IlluminOss blue light on control bacteria: MSSA (ATCC 29213) and MRSA (ATCC 43300). The bacterial strain was diluted in 0.9% NSS until reaching an optical density of 0.5 McFarland units ( $1.5 \times 10^8$  CFU/ml). After final dilutions to a concentration that is relevant to cause orthopaedic related infections, 3ml of bacterial suspension was used for the light dosing experiments. A time-dependent bacterial killing was noted in these control experiments. These suspension culture experiments were repeated in duplicate for patient isolated MRSA and data shown in Figure 2. A 99.9% killing of MRSA was obtained in 400 seconds used for IlluminOss curing at energy levels that are not toxic to mammalian cells (Figure 2).

### **Results**

MRSA is 99.9% inactivated during the 400 sec cure for the IlluminOss implant.

### **Conclusion**

This is the first report of bactericidal activity associated with an Orthopaedic Implant that is not due to the intrinsic material properties of the implant.

## Measurement of Endogenous Cardiotoxic Steroids, MBG and TCB, by LC-MS

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### Background

It has been shown that level of endogenous cardiotoxic steroids (CTS) was elevated under different physiological and pathophysiological conditions in human being and animal studies. However, there are limitations and variations of ELISA methods measuring CTS in plasma samples. We explore the possibility of measuring marinobufagenin (MBG) and telecinobufagenin (TCB), two CTS compounds, in plasma samples.

### Methods

LC-MS system: Agilent 6490 Triple Quad LC/MS with Agilent 1100 HPLC and autosampler. Column (ZORBAX Eclipse Plus C18 rapid resolution HT, 2.1x50mm, 1.8 micron) temperature was set at 40°C. Gradient elution was used to separate CTS with mobile phase A (water with 0.1% formic acid) and B (acetonitrile with 0.1% formic acid). Polarity is positive and scan type is MRM. Extraction methods: liquid-liquid extraction with chloroform and liquid-solid phase extraction with C18 column and water-acetonitrile. Identification of MBG and TCB was performed by three positive transitions.

### Results

The R<sup>2</sup> values for TCB and MBG standard (in mobile phase A) curve are 0.9994 and 0.9996, respectively. For TCB, the detection limit (by standard curve) is 10 pM and quantification detection limit is 25-50 pM. After comparing several extraction methods, we choose liquid-liquid extraction with chloroform which showed a better recovery rate in both MBG- and TCB-spiked plasma samples. In commercially available normal human plasma, both MBG and TCB are detectable. In the normal human plasma spiked with MBG and TCB, the recovery rates are ranging from 83.34% to 126.56%, depending on the CTS standard spiked and CTS concentration spiked. In plasma samples from C57/B6 mice and Dahl salt-resistant and salt-sensitive rats, both endogenous MBG and TCB are detectable.

### Conclusion

With further optimization, LC-MS method might be a more effective and accurate approach for measuring endogenous CTS.



## **Not A Straight Forward Atrioventricular (AV) Node Ablation.**

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Internal Medicine

### **Background**

EP studies and ablations are becoming commonly practiced procedures in heart centers. The AV Node ablation is usually an easy procedure to do, but difficult access can turn this into a challenging case.

### **Case Presentation**

A 77 years old white female with persistent atrial fibrillation, rhythm control failed with multiple antiarrhythmic medications and rate control failed after maximizing AV nodal blockers. She had symptomatic rapid ventricular response, heart rate up to 200bpm noted on device check despite digoxin and Cardizem. A dual chamber pacemaker was implanted in 2009. AV node ablation was planned. To our surprise the inferior vena cava (IVC) was anomalous. The IVC drains into the superior vena cava (SVC) rather than the right atrium. Therefore we could not access the AV node from the right femoral vein; instead we accessed it through the right IJ and SVC. The AV node ablation was successful and the patient was sent home without the AV node blockers.

### **Discussion**

Ablation of AV node in Atrial Fibrillation is a safe therapeutic procedure in electrophysiology with a high success rate. Its aim is to induce permanent block of conduction between the atria and the ventricles. Normally the procedure is performed via the femoral access, which allows practical access to the AV node through the inferior vena cava. In rare cases of congenital anomaly of IVC, ablation of AV node can be performed via the SVC access. We present a case of a patient with drug resistant atrial fibrillation that was ablated through the Right IJ vein due to congenital anomaly of the IVC.

## Role of the Na/K ATPase $\alpha 1$ Isoform in Skeletal Muscle

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### Background

Recent published and unpublished observations from our laboratory in a renal epithelial cell system expressing either Na/K-ATPase  $\alpha 1$  or  $\alpha 2$  isoform suggest that a higher level of expression of the  $\alpha 1$  isoform results in a higher growth rate and a lower glucose utilization rate. The physiological impact of this finding in vivo is unknown. We investigated this issue in the skeletal muscle, a tissue in which the enzymatic function of the predominant (85%)  $\alpha 2$  isoform in contraction is well known, while the role of the remainder (15%)  $\alpha 1$  remains unclear.

### Hypothesis

We expected that in skeletal muscle, decreasing  $\alpha 1$  expression would lead to decreased growth of oxidative muscles.

### Methods

In a genetically engineered mouse model of decreased  $\alpha 1$  expression ( $\alpha 1^{+/-}$ ), we analyzed muscle growth parameters in muscle composed of either fast-twitch (glycolytic) or slow-twitch (oxidative) myofibers. We used Western blots and immunohistochemistry to confirm decreased expression of  $\alpha 1$  in  $\alpha 1^{+/-}$  mice compared to control littermates, while muscle weight and fiber cross sectional area (CSA) were analyzed to compare muscle growth.

### Results

These studies revealed that  $\alpha 1$  expression is drastically limited in the glycolytic myofiber-rich Extensor Digitorum Longus (EDL) muscle compared to the oxidative myofiber-rich soleus muscle and confirmed that  $\alpha 1$  expression is decreased in both muscle types in  $\alpha 1^{+/-}$  mice compared to controls. This reduction of  $\alpha 1$  expression decreased muscle weight/body weight ratio for the soleus by 13% ( $0.214 \pm 0.004$  vs  $0.236 \pm 0.008$  mg/g,  $p < 0.005$ ) without affecting the weight/body weight ratio of the EDL ( $0.307 \pm 0.005$  vs  $0.297 \pm 0.011$  mg/g,  $p = 0.86$ ). These changes were confirmed by a 10% decrease in the CSA of the oxidative fibers of the soleus ( $933 \pm 7$  vs  $1034 \pm 11$   $\mu\text{m}^2$ ,  $p = 0.0001$ ).

### Conclusion

Compared to glycolytic fibers, oxidative fibers play a larger role in modulating insulin sensitivity. Molecular players that may specifically impact oxidative fibers such as Na/K-ATPase  $\alpha 1$  may become targets to address metabolic disease.

## **Hypoxic Effects on Hematopoietic Stem Cells**

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### **Background**

The cells in your body exist at much lower oxygen levels in comparison to ambient oxygen levels of 21%. Physiological oxygen levels vary from 4-8% for normal cells to hypoxic conditions of 1% such as in hematopoietic stem cell (HSC) niches. Existence in hypoxic conditions has profound effects on transcriptional patterns, differentiation and metabolism.

### **Hypothesis**

Keeping these cells at a lower oxygen level will help them differentiate at more physiological levels.

### **Methods**

Using a specialized cell culture model to study the changes associated with this switch from aerobic to anaerobic energy production two cell lines were used. An EML cell line (hematopoietic stem cells) and a BHK cell line (Bavarian Hamster Kidney). The BHK cell lines, which have been transfected with cytokine, secrete stem cell factor into the medium that is used to support the EML cell line. O<sub>2</sub> levels were manipulated using incubators. The EML cells are put in an incubator to monitor and manipulate the O<sub>2</sub>, keeping them at that 1-5% to replicate the oxygen levels present in the human body. We will study the difference at normoxic and acute oxygen levels. The Flow-cytometer was used to immunophenotype native cells in normoxic and hypoxic environments.

### **Results**

Live and dead cell differences were not significant in normoxic versus hypoxic acute. EML cells were of the MPP3 phenotype, indicating they are primed for myeloid development.

### **Conclusion**

The understanding of this process can eventually aid in differentiating the stem cells for healthcare purposes. If this project is successful, it could have ramifications on patient care with diseases such as leukemia, lymphoma, and sickle cell anemia. This data will help understand how hypoxic conditions affect bone marrow transplants.

## **A Case Report of Benzocaine-induced methemoglobinemia: a life threatening complication after a transesophageal echocardiogram**

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### **Background**

Methemoglobinemia (MHb) is defined as abnormal levels of oxidized hemoglobin that cannot bind and transport oxygen. It is clinically characterized by cyanosis, low pulse oximetric readings, and normal arterial PO<sub>2</sub> values. We report a case of methemoglobinemia after a repeated topical benzocaine during a trans esophageal echocardiogram.

### **Case Presentation**

A 43 year old female patient who was referred to our emergency room from the oncology clinic as she was found to have sinus tachycardia (HR =110 bmp), leukocytosis and acute kidney injury on CKD stage III with hyperkalemia. The patient was admitted to the ICU, was diagnosed with MRSA bacteremia related to line sepsis for which a transesophageal echocardiogram (TEE) was ordered to rule out endocarditis. The patient had TEE done, Cetacaine spray as topical anesthetic was used repeatedly. The TEE was uneventful; however, 10 minutes later, she started to complain of dizziness, palpitation, and was found to have central cyanosis on physical exam. Vital sings showed: Pulse rate of 130 bpm, RR: 18, BP: 152/88 mmHg, O<sub>2</sub> saturation: 80%. Chest X -Ray showed no acute cardiopulmonary process, and an EKG was normal. The patient was placed on high flow oxygen therapy through non-rebreather, her O<sub>2</sub> saturation was 80%. ABG on 60% FIO<sub>2</sub>; PH: 7.48, PO<sub>2</sub>: 293, PCO<sub>2</sub>: 31, HCO<sub>3</sub>: 22.4, and O<sub>2</sub> saturation of 100%. methemoglobinemia was suspected. MetHB level was found to be 67.4%, patient received one dose of IV Methylene Blue, 1 mg/kg over 10 minutes after which her symptoms improved. A repeat MetHB level 30 minutes later was 0.5%.

### **Discussion**

Severe methemoglobinemia is a life-threatening condition and if untreated may result in fatal consequences. Early diagnosis and appropriate treatment are crucial in treating this emergency situation.

## **Ketosis-prone diabetes: an emerging category of diabetes that needs more attention.**

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### **Background**

Recently there has been an increase in diabetes cases that do not fit traditional categories. Diabetic ketoacidosis (DKA) has usually been considered a key clinical feature of type 1 diabetes mellitus. There is an increasing number of cases with Type 2 diabetes (T2DM) presenting with DKA. Notably some of these patients can discontinue insulin and maintain good glycemic control with oral agents after sometime.

### **Case Presentation**

33-year-old Caucasian woman admitted to hospital with a diagnosis of DKA. No known past medical or family history of diabetes. Her physical exam was remarkable for a BMI of 36 Kg/m<sup>2</sup>. Laboratory studies revealed a pH 7.06, a glucose level of 924 mg/dL, bicarbonate <5, anion gap 19 and urine ketones. A1c was 12.6%. She required a significant amount of insulin and was discharged Glargine 80 units daily and Lispro 10 units with meals. Glutamic acid decarboxylase antibodies were negative and C-peptide was low normal at 1.5. At her clinic follow up visits, her insulin was gradually decreased over the following months; A1c had improved to 5.1. Metformin was added, she was subsequently able to come off Insulin completely within 15 months. The patient continued only on metformin 500 mg PO twice a day and maintained adequate glycemic control with an A1c of 5.8%. She has remained on this current regimen with good glycemic control.

### **Discussion**

Recently there has been an increase in hospital admission due to DKA. A portion of these patients have ketosis-prone type 2 diabetes. It has been reported mostly in African-Americans and Latinos with a higher prevalence in men. Most patients have clinical and immunogenetic features of T2DM, characterized by severe beta cell dysfunction and a variable clinical course. Majority discontinue insulin and remain off it for months to years and C-peptide response to glucagon appears to be the best predictor of remission.

## **Utilization of a clinical data warehouse for use as a primary data source for clinical studies.**

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### **Background**

Institutional data warehouse of all medical information is valuable to improve patient care, facilitate quality assurance and cost/benefit analysis. It is essential for clinical outcomes research within and between health science centers. Thus, the National Institutes of Health has made formation of an i2b2-based clinical data warehouse a key component of funding for clinical and translational science institutes in this country. Recently at Marshall a data warehouse of all clinical and billing information at Cabell Huntington Hospital and Marshall Health was created. It is currently not clear whether a warehouse may be exclusively used as source data without correlation with medical records.

### **Hypothesis**

Hepatitis-C patients with anemia have more GI tract pathology as etiology for the anemia.

### **Methods**

Query from warehouse patients who had liver function tests (LFTs), hepatitis-C, anemia, and endoscopic procedures. Ascertain from medical records if the Marshall data warehouse may be used as a primary source for retrospective clinical studies.

### **Results**

Between 2010 and 2015, 77,366 patients had LFTs and 37,272 were abnormal and 40,094 were normal. Hepatitis-C was more likely present in patients with abnormal LFTs (2.7 vs 0.4%). Irrespective of LFTs, Hepatitis-C patients had more anemia (75 vs 62% abnormal LFTs and 60 vs 37% normal LFTs). We will determine the presence of GI-tract pathology in each subgroup. Ultimately, we plan to determine the minimum number of randomly selected subgroup patients necessary to validate warehouse-based data with 95% confidence using the individual patient record.

### **Conclusion**

The results of this study will demonstrate that warehouse may be used as primary source for clinical retrospective studies with only a small sampling validation of source data. Secondly this study will validate the warehouse at least for this particular patient group, which will greatly facilitate clinical research at Marshall.

## **Psychiatric manifestations co-occurring in a father-son pair with Waardenburg Syndrome**

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### **Background**

Waardenburg syndrome type I (WS1) is an auditory-pigmentary disorder comprising congenital sensorineural hearing loss, pigmentary disturbances, along with dystopia canthorum (lateral displacement of the inner canthi). It is an autosomal dominant disorder, however, the phenotype of WS1 is highly variable even within a family. Hence, true prevalence of the disorder is undetermined. Sequencing and deletion/duplication analysis of PAX3 gene on chromosome 2 can detect up to 90% of the pathogenic variants of this gene that is determined to cause WS1.

### **Case Presentation**

We describe a four year old male, meeting the clinical criteria of WS1. He exhibited dystopia canthorum, an affected first degree relative, medial eyebrow flare, and broad high nasal root and hypoplastic nasal alae. He did not have hearing loss, pigmentation anomalies or intellectual disability. However, he did have less commonly occurring symptoms of spina bifida and myelomeningocele, with hydrocephalus. Mother reported psychiatric symptoms of attention deficit, hyperactivity, and anxiety. Family history revealed that father, paternal uncle and paternal grandfather also manifested the cardinal symptoms of deafness, white forelock and dystopia canthorum. None were formally diagnosed with WS.

### **Discussion**

Psychiatric symptoms have not commonly been described as part of the syndrome. All case reports describing psychiatric symptoms such as aggression and irritability in patients with WS1 had deafness and/or intellectual disability. We believe this case report adds to the existing literature in several ways. 1. Our patient exhibited psychiatric symptoms in absence of deafness or intellectual disability. 2. Though the father and son have different physical manifestations of the WS1, yet they exhibit a similar psychiatric presentation. Further genetic evaluation may lead to clues regarding the genetic bases for psychiatric disorders.

## **Functional and molecular transition of Na-K-ATPase during the growth and maturation of intestinal epithelial cells**

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Clinical and Translational Sciences, Marshall University

### **Background**

Na-K-ATPase an integral basolateral membrane protein of the intestinal epithelial cells provides the favorable transcellular sodium gradient required for the optimal functioning of the brush border membrane sodium dependent nutrient transporters. We have previously shown that Na-K-ATPase functional activity varies depending on the cell type and function: Villus cells that have the primary function of sodium dependent nutrient absorption have twice the amount of Na-K-ATPase function compared to the crypt cells that have minimal absorptive capacity.

### **Hypothesis**

How the transition in the functional capacity of Na-K-ATPase occurs during the growth and maturation of intestinal cells from crypt to villus is not known.

### **Methods**

An in-vitro model of rat intestinal cell crypt to villus differentiation was used. Na-K-ATPase activity was determined as a measure of <sup>86</sup>Rb uptake and inorganic phosphate release.

### **Results**

Na-K-ATPase activity increased gradually as the cells matured from day 0 through day 4 of post confluence achieving maximal, albeit statistically insignificant, activity on day 3 compared to day 4. Overall Na-K-ATPase activity was increased at least two fold on day 4 compared to day 0. Western blot studies showed that there was a gradual increase in the Na-K-ATPase alpha-1 levels in the whole cell protein preparations from 0-4 day and this increase was 2 fold on 4 day compared to 0 day.

### **Conclusion**

As intestinal cells mature from secretory crypt cells to absorptive villus cells, the functional activity of Na-K-ATPase and the protein expression of its functional a-1 subunit increases, likely to accommodate the functional needs of the intestinal cell type.



## **Barriers to HPV Vaccination Among Females with Physical and Mental Limitation**

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### **Background**

Human papilloma virus vaccine (HPV) is recommended for females age 9-26 because it is the most common sexually transmitted infection in the United States and prolonged infections with high-risk HPV strands cause 96% of cervical, 90% of anal, 60% of oropharyngeal, and 40% of vaginal/vulvar cancers.

In special health care need children, one study suggests, parents have difficulties accepting the vaccine, perceiving their child doesn't need vaccinated due to sexual inactivity. However, another study concluded these children are just as likely to be sexually active.

### **Hypothesis**

A previous study in our institution found that females with physical or mental limitations were less likely to be vaccinated for HPV compared to controls. The purpose of this study is to evaluate reasons for nonvaccination in each group. It is our thought that reasons for nonvaccination will differ between these groups.

### **Methods**

Females age 12-18 presenting to Marshall Pediatric or OBGYN clinics between January 1, 2012 to December 31, 2012 were identified. A database was made using CPT codes for well child and routine health visits through the electronic medical record. Data collected included age, vaccine history, and presence of physical or mental disability. Further study involves a phone survey to guardians of nonvaccinators, evaluating reasons for nonvaccination and HPV vaccination knowledge. Data will be compared between controls and limitation groups. Data will be stored as password protected.

### **Results**

1314 female subjects were identified in the given period. 67 subjects were classified as physically or mentally delayed. Overall HPV vaccination was 54%. Among the controls, 684 of 1247 subjects received at least one HPV vaccine, compared to 27 out of 67 cases (RR 1.36, 95%CI 1.01, 1.83).

### **Conclusion**

HPV vaccination is higher among adolescents without physical or mental delay. Ongoing assessment is determining if reasons are different for nonvaccination among those with delays compared to controls.

## **Late Severe Postpartum Preeclampsia 18 Days After Delivery: A Case Report**

Kevin White MD, Sarah Price MD

Obstetrics and Gynecology

### **Background**

Postpartum preeclampsia presents with symptoms including: thunderclap headache, visual abnormalities such as scotomata, photophobia, blurry vision temporal blindness, epigastric pain, nausea, vomiting, retrosternal chest pain and altered mental status.

### **Case Presentation**

A 40 year old gravida 3 now para 3004 arrived to the emergency department 18 days after a repeat cesarean section at 39 weeks and 6 days. She presented with a new onset severe frontal thunderclap headache, severe range blood pressures and a protein/creatinine ratio of 0.67. The patient was started on magnesium sulfate for 24hours, IV labetalol for severe pressures and oral labetalol. She was discharged in stable condition.

### **Discussion**

Postpartum preeclampsia is a rare condition with potentially life threatening complications such as eclampsia, cerebral hemorrhage, HELLP, renal failure, hepatic failure, hepatic rupture, disseminated intravascular coagulopathy. Worldwide preeclampsia/ecclampsia account for 10-15% of all maternal deaths making it one of the top 4 causes of maternal morbidity and mortality. Thus preeclampsia should be in the differential of a postpartum patient presenting with suggestive symptoms and elevated blood pressures.

**Evaluating the Implications of Changes in PSA-Screening Guidelines on Prostate Cancer-Related Mortality, Utility, and Cost: A Decision Analysis Approach**

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**Background**

In 2012, the US Preventive Services Task Force (USPSTF) recommended against prostate-specific antigen (PSA) screening. In this study we developed methodology to validate this recommendation with the idea of using the model in our unique health care population.

**Methods**

We used the Decision Tree Analysis Method incorporating outcomes derived from a comprehensive literature review of prostate cancer. ARM 1 included those with =1 lifetime PSA screenings. ARM 2 included those having <1 lifetime PSA screenings. We evaluated Median survival, Quality Adjusted Life Years (QALYs) and lifetime cost/QALYs for patients with no prostate cancer, limited prostate cancer, and metastatic disease assuming prostatectomy following a diagnosis and treatment of limited Low Risk Prostate Cancer (LRPCA; Stage I, Gleason 3+3)

**Results**

No significant difference in median survival was seen for those found to have LRPCA treated by radical prostatectomy between screening and non-screening arms (15.70 years for the non-screening arm and 15.78 years for the screening arm;  $p = 1$ ). Similarly, no significant difference was found with regards to QALYs between screening (14.78 QALYs) and non-screening (14.94 QALYs;  $p = 1$ ) arms. The screening arm was found to have a lower cost per QALY (\$2435) compared to the non-screening arm (\$3573) but was not significantly different ( $p = 1$ ).

**Conclusion**

Our model finds no benefit for PSA screening that discovers LRPCA that is then treated by radical prostatectomy (even without considering lead-time bias in the screening arm). Future analysis will look at this question in a population of patients more typical in WV, where analysis of surgical specimens shows that as many as 50% of patients harbor invasive T3/T4 disease, contain Grade 4/5 tumor, experience a high rate of positive margins, harbor more positive lymph nodes, and/or have first degree relatives who died of prostate cancer.

## **Differential expression of glutamine absorption in the small intestine.**

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Clinical Translational Sciences, Marshall University

### **Background**

In the mammalian intestine, secretory crypt cells mature into absorptive villus cells over 4-6 days. Their primary nutrient source, amino acid glutamine, is primarily absorbed through two distinct Na-glutamine co-transporters, SN2 in crypts and B0AT1 in villus. In-vitro, IEC-18 cells resemble in-vivo crypt cells on day 1 of its post-confluence and by day 4 they resemble mature villus cells structurally and functionally.

### **Hypothesis**

How SN2 transitions to B0AT1 during the growth and maturation of intestinal cells is not known.

### **Methods**

Brush border membrane (BBM) protein extracts were prepared from IEC-18 cells using CaCl<sub>2</sub> precipitation and differential centrifugation. Western blot analyses were performed using standard protocols.

### **Results**

The whole cell expression of B0AT1 protein was found to gradually increase from day 1 through days 2 and 3 of post-confluence and became predominant on day 4. However, this pattern of B0AT1 expression was not observed in the BBM protein extracts, where B0AT1 expression was completely absent in days 0, 1 and 2 with faint expression in day 3 and predominant expression in day 4. The expression of SN2 protein was predominant on days 0 and 1 in whole cells with progressive decrease starting day 2. This decrease was also seen in BBM preparations, where SN2 protein expression was completely absent in day 4.

### **Conclusion**

These data indicate that in IEC-18 cells at day 1 post-confluence the predominant Na-glutamine co-transporter is SN2 while B0AT1 becomes the predominant by day 4. Thus, as intestinal cells mature from crypt to villus, two unique co-transporters transport glutamine.

## **Alteration of Mitochondrial Biogenesis in the Kidneys of TALLYHO Mice**

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### **Background**

Between 8-16% of the world's population suffers from Chronic Kidney Disease (CKD), and the epidemics in diabetes, hypertension, and obesity - all important CKD risk factors - are expected further increase the prevalence of this condition. TALLYHO (TH) mice are a strain of inbred, obese mice that exhibit hyperglycemia and insulin resistance. Hyperglycemia due to type 2 diabetes causes kidney injury by altering renal metabolism, physiology, and architecture. TH mice have shown to be an excellent model to investigate diabetes- and obesity-related changes to kidney tissue. In this study, we sought to continue this line of inquiry and investigated the alterations in mitochondrial biogenesis and energy metabolism due to chronic kidney disease using TH mice as a model.

### **Hypothesis**

Mitochondrial energy metabolism is impaired in kidneys of TH mice due to changes in mitochondrial translation components.

### **Methods**

Breeding of TH mice was established and described previously. C57BL/B6 (B6) and mice were used as control mice. Frozen kidney tissues were sliced and sonicated to obtain protein lysates. BCA assays were performed on the lysates to determine protein concentrations and assure equal loading of samples, which were used in Western blot analysis activity measurements.

### **Results**

We observed increased expression of mitochondrial translation elongation factor Tu and protein acetylation in TALLYHO mice by Western blot analysis.

### **Conclusion**

Changes observed in mitochondrial translation component(s) and acetylation may regulate energy metabolism and activities of oxidative phosphorylation complexes in this mouse model.

## **Thermal Imaging Reveals Temperature Retention in Hindlimbs of Mice up to 4 Hours after Targeted Intermittent Limb Heating**

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Department of Anatomy and Pathology

### **Background**

Our lab has previously demonstrated that daily unilateral limb heating permanently increases bone length in growing mice. The extent to which limb temperature remains elevated is unknown. In order to quantify temperature retention, we collected hourly and daily temperatures at scheduled time points throughout the trial with the goal of determining optimal conditions for recording temperature data in subsequent studies.

### **Hypothesis**

We hypothesize that limb temperature remains elevated on the treated side due to a heat-induced increase in vascular supply that accelerates bone lengthening.

### **Methods**

Weanling female mice (N=6) were treated daily at 7am for 2-weeks with 40C unilateral heat for 40 minutes per day. Infrared thermal images were captured at 320 X 240 resolution using a FLIR E8 infrared camera. Surface temperatures of the heat-treated and non-treated hindlimbs were obtained from calibrated images using FLIR tools software. Statistical comparisons were made using ANOVA and paired t-tests in SPSS. Data from multiple days were pooled at each time point since there were no significant differences among days analyzed.

### **Results**

Common trends in temperature differences between heat-treated and non-treated limbs were seen throughout the day. At 6am baseline prior to treatment, the heat-treated side was over 1% warmer than the non-treated side ( $t=1.84$ ,  $p=0.06$ ). After the treatment at 8am, limb temperatures were nearly equivalent ( $t=1.13$ , ns), suggesting a systemic post-anesthesia thermoregulatory response. By 11am, 4 hours after the treatment start, the heat-treated side was over 2% warmer than the non-treated side ( $t=8.06$ ,  $p<0.001$ ), indicating sustained heat retention. By 3pm, limb temperatures were again similar ( $t=0.13$ , ns), reflecting increased activity as mice approached the dark cycle.

### **Conclusion**

These pilot results support our hypothesis that limb temperature remains elevated on the heated side up to 4 hours after treatment. This study is an important step toward understanding the mechanisms by which heat enhances limb elongation.

**Determination of the Impact of Counseling on Smoking Cessation Rates in  
Urban and Rural Appalachians Taking Nicotine Replacement Therapy**

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Medicine

**Background**

Our research compares the differences in smoking characteristics and the effects of intensive counseling on smoking cessation in West Virginia's rural and urban populations. The goal of our project is to analyze smoking cessation rates among patients receiving repeated counseling in conjunction with Nicotine Replacement Therapy (NRT), in contrast to sole NRT use. Specifically, the project intends to identify patient beliefs, risk factors, and cigarette smoking rates in the urban and rural populations we serve. This will be accomplished by having student led clinics at both a rural family practice office and Marshall Medical Outreach, a student led mobile clinic which provides medical care to the local homeless and destitute in Huntington, WV. In order to accurately determine true smoking cessation we will use a Breath Carbon Monoxide test (BCO), along with self-reported cessation.

**Hypothesis**

Repetitive smoking counseling in conjunction with Nicotine Replacement Therapy increases the rate of smoking cessation in rural and urban populations in West Virginia.

**Methods**

An initial survey is given to assess risk factors and smoking habits. All participants receive one month supply of Nicotine Replacement Therapy and are divided into two groups – non-counseling and counseling. Monthly, participants return to receive the next month's supply of Nicotine Replacement Therapy and will remain in their perspective group, non-counseling and counseling. Participants will also complete monthly surveys to assess any changes in smoking habits.

**Results**

Research is in progress with 37 participants at our urban site, Marshall Medical Outreach and 5 participants at our rural site in Lavalette, to date.

**Conclusion**

Based on our data and results we hope to conclude that repetitive smoking counseling in conjunction with Nicotine Replacement Therapy increases the rate of smoking cessation in both rural and urban populations in West Virginia.

## **Improving Resident Knowledge and Awareness of Utilization of MDI Spacer Device in Asthma Management**

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### **Background**

In the management of asthma exacerbation, studies have shown that short acting beta agonists (SABA) via metered-dose inhaler with spacer (MDI-S) is equally or more effective than SABA via nebulizer. Using MDI-S in an asthma exacerbation in the emergency department is associated with better outcomes, decreased hospital length of stay, and decreased readmission rate. However, many barriers still exist in implementing MDI-S as a standard of care in the pediatric asthma patient. The largest barriers to MDI-S implementation include concerns about safety and cost, feasibility of providing spacers, and parental desire for nebulizers.

### **Hypothesis**

The purpose of this project was to educate residents about MDI-S to improve their knowledge as well as their confidence in teaching and demonstrating techniques of use.

### **Methods**

Residents were given a 12 question, pre-intervention self assessment survey which explored their overall knowledge and comfort with MDI-S use. Questions were answered on a 5 point Likert scale. Participants then received educational intervention via multimedia videos pertaining to MDI-S facts and maintenance, a live demonstration of common MDI-S techniques, and a question and answer session with our allergist / immunologist. Participants were then given a post-intervention, self assessment survey containing the same questions and 5 point Likert scale.

### **Results**

There was significant improvement ( $p < 0.05$ ) in all evaluated aspects of the project. Greatest improvement was noted in knowledge of using MDI-S, maintaining MDI-S, and awareness of economic convenience of MDI-S use. There was also significant improvement in resident comfort in demonstrating proper MDI-S technique.

### **Conclusion**

In this project, we successfully improved the ability of our residents to deliver quality care by improving their knowledge and confidence in demonstrating proper MDI-S use and maintenance.



## **Anti-Viral Medication Tenofovir Induces Oxidative Stress and Apoptosis in HK-2 Cells**

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### **Background**

Tenofovir disoproxil fumarate (Viread) is a highly effective HIV antiviral drug approved for treating Human Immunodeficiency Virus (HIV) and Hepatitis B. It is one of the first line drugs used to treat HIV and is efficacious in both novel and treatment-experienced HIV patients. Tenofovir is administered orally as the prodrug tenofovir disoproxil fumarate (TDF), which is deesterified to the active drug tenofovir. However, renal damage is a major adverse effect associated with its use. Tenofovir can induce decreased glomerular filtration rate (GFR), renal failure, and Fanconi Syndrome. The exact mechanism of this toxicity remains unknown, largely due to limited experimental models.

### **Hypothesis**

Our laboratory has established that clinically relevant concentrations of tenofovir are toxic within 72 h. The purpose of this study was to investigate the cellular mechanism of cytotoxicity in a human renal proximal tubular epithelial cell line (HK-2).

### **Methods**

Tenofovir (TFV) is the active form of Viread and was used for all studies. HK-2 cells were seeded and grown to confluency for 48h followed by a 72 h exposure to 0-30uM tenofovir. The vehicle was phosphate buffered saline (PBS). Cell viability was assessed using the MTT assay. Mitochondrial dysfunction was assessed by measuring ATP and ADP levels. Oxidative stress was assessed using OxyBlot.

### **Results**

Tenofovir induced a loss of cell viability when compared to vehicle within 48-72h but did not alter MTT following a 24h exposure. 72h exposure to tenofovir drastically reduces ATP levels compared to control. Increases in protein carbonylation are seen after 48-72h exposure. New studies indicate that tenofovir increases 4-HNE and 3-NT modifications on cellular proteins; additional experiments are needed. Caspase 3 and 9 cleavage was induced by tenofovir as measured by Western blot compared to vehicle.

### **Conclusion**

These studies suggest that mitochondrial stress and apoptosis occur in tenofovir treated HK-2 cells.

# Comparison of ExPRESS Miniature Glaucoma Shunt Insertion Alone or Combined with Phacoemulsification Surgery in Patients with Uncontrolled Glaucoma

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## Background

The purpose of this research is to compare the clinical outcomes of patients who have failed medical therapy for treatment of glaucoma undergoing insertion of ExPRESS miniature glaucoma shunt alone (EMGS) with patients undergoing combined surgery of phacoemulsification of cataract and insertion of shunt (p-EMGS).

## Hypothesis

We propose that there will be no difference in the clinical outcomes between the two groups.

## Methods

A chart review was completed identifying 73 patients who underwent insertion of the shunt. 46 patients were in the EMGS group while 27 were in p-EMGS. The parameters recorded for each group included intraocular pressure (IOP), number of glaucoma medications, complications, and success rate.

## Results

There was no difference in pre-operation IOP between the two groups with EMGS having an average IOP of 21.88  $\pm$  4.69 and p-EMGS having an IOP of 21.14  $\pm$  2.78. The average number of pre-operation glaucoma medications needed in each group was 2.79  $\pm$  .35 for EMGS and 2.62  $\pm$  .22 for p-EMGS. At 24 months post-operation, the groups had an average IOP of 11.46  $\pm$  2.22 for EMGS and 10.97  $\pm$  1.90 for p-EMGS. The average number of glaucoma medications at 24 months was 0.68  $\pm$  .48 for EMGS and .51  $\pm$  .29 for p-EMGS. The most common complication was hypotony with the EMGS groups experiencing it more frequently. 37.5% of patients in the EMGS group experienced hypotony while only 10.8% of patients in the p-EMGS group experienced this complication ( $p=0.013$ ). There was no difference in the rates of complete success (IOP  $\leq$  5 and  $\leq$  18 with no medications) between the groups with EMGS and p-EMGS having a complete success rate of 56.0% and 62.8% respectively ( $p=0.582$ ).

## Conclusion

The results of this study suggest that combining insertion of the ExPRESS miniature glaucoma shunt with phacoemulsification is a safe and effective method of treating patients who need surgical intervention for both cataracts and uncontrolled glaucoma.

## **Exploring the Mechanism by Which 2,3,7,8-tetrachlorodibenzodioxin (TCDD) Regulates Jagged-1 via the Aryl Hydrocarbon Receptor**

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### **Background**

Approximately 10-20% of breast cancer patients are diagnosed with triple negative breast cancer (TNBC). Jagged1 (JAG1) is a transmembrane receptor protein that has been proven to play a role in cancer biology and is normally over-expressed in TNBC. Studies show that JAG1 plays a key role in metastasis in various cancers. High JAG1 mRNA and protein expression levels are also indicators of poor prognosis. Silencing of JAG1 (siRNA) in cancer cells induced anti-metastatic effects. This makes it a potential chemotherapeutic target for hormonal therapy resistant cancers such as TNBC.

### **Hypothesis**

We hypothesize that JAG1 plays a functional role in metastasis. Decreased expression of JAG1 in the presence of TCDD suggests that the aryl hydrocarbon receptor (AHR) can potentially inhibit JAG1-dependant signaling and expression by ubiquinating the JAG1 intercellular domain (JICD) and inducing its proteasomal degradation.

### **Methods**

First, we will treat TNBC cells with AHR ligands or JAG1 siRNA in order to compare the levels of EMT regulators (SLUG, SNAIL, ZEB1, and uPA) and anti-metastatic effects to each other as well as their respective controls. Second, we will determine if AHR down-regulates JAG1-dependent signaling and expression in a proteasome-dependent manner.

### **Results**

Our lab showed that TCDD decreased the expression of JAG1 in TNBC cells at 12 and 24 hours via western blot. Our lab also showed that SNAIL expression was increased over the course of 24 hours in vehicle (DMSO) treated TNBC cells. However, in TCDD treated TNBC cells we observed similar SNAIL concentrations at 12 and 24 hours, with a slight decrease after 24 hours, indicating that TCDD may suppress SNAIL expression.

### **Conclusion**

These findings can identify a novel mechanism that can target JAG1-dependent signaling using non-carcinogenic AHR ligands in combination with other chemotherapy agents as a novel form of treatment for TNBC as well as potentially other types of cancer.

## **Late-Onset Bipolar Disorder: A Case Report and Literature Review**

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### **Background**

Bipolar disorder with onset after age 50 is commonly referred to as late-onset bipolar disorder. Approximately ten percent of cases of bipolar disorder have onset after age 50. Late-onset bipolar disorder may differ from earlier-onset bipolar disorder both in etiology and presentation. For example, there is evidence suggesting cerebrovascular pathology may play a role in etiology in late onset bipolar disorder. Presenting symptoms may be different in that patients with late-onset bipolar disorder are more likely to have cognitive impairment and less likely to experience hypersexuality, substance abuse, or anxiety. Furthermore, patients with late-onset bipolar disorder tend to have longer hospitalizations than those with early onset. Diagnosis requires a thorough work up to rule out secondary causes such as drugs, metabolic disturbances, infection, neoplasm, and other toxins.

### **Case Presentation**

A 67 year-old female was brought to the emergency department after a neighbor found her wandering outside and confused. In the emergency department, the patient was agitated and psychotic. Collateral information confirmed the patient had recently developed restlessness, excessive shopping, paranoia, and poor sleep. The son and a friend also reported the patient had a strong family history of bipolar disorder. She was described as having been a moody person throughout her life. There was no prior psychiatric history until a suicide attempt by overdose four years prior, in the setting of her husband's sudden death. Although she was admitted to a psychiatric unit at that time, she was discharged after one day and did not have any psychiatric follow-up. She had been living independently since that time without further mood episodes. During the current hospitalization, the patient walked excessively in the hallways, insisted on dancing, and frequently sang, making up songs about the medical staff.

### **Discussion**

She was diagnosed with late-onset bipolar disorder - mania with psychosis. Treatment with quetiapine was begun.

## **Common mechanisms and specializations in force detection and control in cockroaches, stick insects and Drosophila**

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### **Background**

Information from sense organs that detect forces may be particularly important in neural control of muscles as modular groups (synergists). We have performed comparative studies to characterize force detection in insects, using physiological studies in stick insects and cockroaches to gain insight into comparable mechanisms in fruit flies (*Drosophila*), in which new and powerful genetic tools have been developed. Campaniform sensilla are mechanoreceptors that encode forces as cuticular strains. Previous studies have shown they can reinforce muscle synergies.

### **Hypothesis**

Receptors fulfill similar functions in different species but the effects of individual groups are determined by the specific forces they encode.

### **Methods**

Whole mount and dissected preparations were studied using confocal, scanning electron and light microscopy. Sense organs and leg muscles were labeled using dil diffusion from the thorax. Physiological studies used extracellular recordings from peripheral nerves and muscles. .

### **Results**

Many receptors are homologous but the structure and responses of the femoral group (fCS) and mobility of the trochanter-femur joint (TrF) are species specific. In cockroaches, the TrF joint is mobile and movements are opposed by an elastic (resilin) band; the fCS are sensitive to posterior forces but insensitive to forces in the joint plane. In stick insects, the TrF joint is fused and fCS receptors discharge to both posterior forces and forces in the joint plane. Sensitivities to forces in the joint plane are, therefore, correlated with effects on muscle synergies. In *Drosophila*, the fCS are located on the ventral femur, suggesting that they should be sensitive to forces in the joint plane. We are currently testing motor effects using neurophysiological recordings from larger Calliphorid flies.

### **Conclusion**

There are clear homologies in some groups of force receptors. Legs of flies combine elements found in cockroaches and stick insects. Sensory feedback can have similar effects in activation of muscle synergies in flies.

## Neuropsychiatric Features of Urea Cycle Disorder

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### Background

Urea cycle disorders are inborn errors of metabolism that affect the body's ability to convert ammonia, a waste product of protein metabolism, to urea, which can be excreted by the kidneys. Individuals born with a non-functional or partially functional enzyme in this pathway are prone to multiple hyperammonemic crises that will have a variety of deleterious effects on the central nervous system, including cerebral edema, altered neurodevelopment, and NMDA-mediated excitotoxicity. These disorders are often detected in early childhood due to the severe repercussions of excess ammonia, but if an individual has partial (rather than total) urea cycle enzyme deficiencies, the disorder may go undetected until later in life. As a result of multiple hyperammonemic crises, these individuals typically develop a number of neurological and psychiatric symptoms, most prominently including seizure disorders, but also including a range of psychiatric sequelae including confusion, behavioral disturbances, or psychosis. The mechanism of CNS damage as well as the critical role played by the liver in the disease create a unique set of parameters for managing both the primary disorder and its neuropsychiatric consequences.

### Case Presentation

In this case report, we discuss a 31-year-old male patient with a history of carbamoyl phosphate synthetase I deficiency who had an initial onset of symptoms in his early teens and developed a seizure disorder as well as significant neurocognitive impairment. He was admitted to the medical floor with altered mental status, including aggressive and combative behaviors as well as hallucinations, and was seen by the psychiatric consult-liaison service.

### Discussion

The patient's hospital course and treatment are discussed, providing an opportunity to explore a review of the literature, the mechanisms of this rare disorder, and the unique constraints they impose on available pharmacological interventions.

# Teaching Interpersonal and Communication Skills: Results of a Parent-Directed Resident Education Program on Children and Youth with Special Health Care Needs (CYSHCN)

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## Background

Few educational programs address and implement the ACGME competencies of interpersonal skills communication.

## Hypothesis

To assess and compare resident and parent evaluations, including written comments, on the effectiveness a parent-taught program providing a family-based perspective on pediatric chronic disease to develop interpersonal and communication skills.

## Methods

Since 1998 pediatric residents on their behavioral/developmental rotation have met individually with parents of CYSHCN to participate in a curriculum developed nationally by Project DOCC (Delivery of Chronic Care). Two 3-hour sessions of a scripted parent interview (PI) followed by guided home visit (HV) were evaluated by residents using a Likert Scale from 1 (poor) to 5 (excellent). The percentages of the optimal response (rating #5) obtained were compared using chi-square and Fisher's exact tests. Unstructured resident and parent comments underwent qualitative analysis by two authors with similar statistical comparison.

## Results

The resident comment category describing the experience as "Eye-opening" (gained new insight or perspective) was noted in 75 (82%) for PI and in 57 (75%) for HV ( $p=0.08$ ). The parent comment category describing the resident as "Interested" was found in 174 (92%) for PI and 96 (98%) for HV ( $p=0.04$ ) while "Empathetic" was noted in 116 (61%) for PI and 60 (61%) for HV ( $p=0.98$ ).

## RESIDENT EVALUATION GIVEN OPTIMAL SCORE (#5)

	PI (n=125)	HV (n=115)	p value
Provided new information	71 (57%)	73 (63%)	0.29
Relevance	78 (62%)	74 (64%)	0.75
Met educational objectives	94 (75%)	90 (79%)	0.57
Depth of coverage	94 (75%)	89 (77%)	0.69
Amount of time spent	90 (72%)	89 (77%)	0.40

## Conclusion

Both PI and HV components of Project DOCC appear to facilitate the exchange of information and collaboration between families with CYSHCN and residents providing a unique opportunity for achieving competency in interpersonal and communication skills.

## **Superior Mesenteric Artery Syndrome in an athletic 22 year old female**

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### **Background**

Superior mesenteric artery syndrome (SMAS) is a rare condition that affects less than 4% of the population. It is duodenal obstruction due to decreased space between the superior mesenteric artery and abdominal aorta. Fat and lymphatic loss in the mesenteric fat pad are typically the cause, but many disease states predispose one to this condition. Patients present with symptoms associated with duodenal obstruction and diagnosis is with abdominal films, CT, endoscopy, or arteriography. Conservative management is usually successful, but surgery is sometimes required. We present a case of a female who presented with weight loss, vomiting, abdominal pain and CT findings consistent with SMAS.

### **Case Presentation**

A 22 year old female patient presented after being evaluated at multiple outside hospitals with 4-8 week history of abdominal pain, nausea, vomiting and 25lbs weight loss. CT abdomen showed collapsed distal small bowel with distended duodenal bulb and stomach. EGD showed severe narrowing of the third part of the duodenum. Due to intolerance to the Dobhoff tube, Gastrojejunostomy was required. Bowel function returned post-operatively and the immediate postoperative course was unremarkable.

### **Discussion**

SMAS is a rare condition that should be considered in any patient who presents with chronic vomiting and predisposing conditions such as rapid loss of retroperitoneal and mesenteric fat, trauma, and dietary disorders. There are only approximately 400 cases of SMAS described in the literature, but it is likely SMAS is underdiagnosed. SMAS should be on the differential diagnosis more frequently as misdiagnosis and delay in treatment can be fatal. Conservative management is usually sufficient but surgery can be an effective treatment option. Our patient required surgery, making her case a unique addition to the literature.



## **Mycoplasma Pneumonia Associated Mucositis: A Diagnostic Challenge**

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Pediatrics, Marshall University School Of Medicine

### **Background**

Mycoplasma pneumoniae causes pulmonary and extra pulmonary complications. In children less than five years, M. pneumoniae is the leading infectious cause of community acquired pneumonia. Mycoplasma associated mucositis is one of the rare extra pulmonary complications of M. pneumoniae infection. In literature, this condition has been reported as "Mycoplasma pneumoniae-associated mucositis" or MPAM, "Atypical SJS", "SJS spectrum".

### **Case Presentation**

We report a case of 12 year old boy presented to Emergency Room with 3 days of fever, cough, and fatigue. He was diagnosed with right middle lobe pneumonia by Chest X-Ray at Urgent Care 3 days ago, prescribed azithromycin and oral steroids. His prescriptions were not filled and did not take any medication. One day prior to Emergency Room presentation he developed swelling of the lips, swelling of eyes with photosensitivity and painful oral blisters. On physical examination, he had fever, severe mucositis extending from inner lips to posterior pharynx, conjunctivitis, right middle lobe crackles, erythematous swelling around penile meatus. Laboratory tests revealed M. pneumoniae with viral respiratory PCR. The patient was treated successfully with Azithromycin, Steroids, Benadryl, and Ibuprofen.

### **Discussion**

As infection rates from M. pneumoniae seem to be increasing, this atypical presentation will likely become more prevalent. Hence, it is critical for physicians to understand and recognize this atypical presentation, for early intervention and management. Increased awareness is needed among primary care physicians in order not to miss this atypical presentation of M. pneumoniae. Eventually, this can decrease duration of illness, hospital length of stay, expenditure, and prevent further lab testing.

## **Interstitial Microduplication of 16p13.3 – A case report**

Hilary Cornell, Dr. Kalpana Miriyala

Department of Psychiatry, JCESOM

### **Background**

Chromosomal imbalances are often the cause of syndromic phenotypes, however karyotyping can only identify a limited number of these causes. Microarray technology is a far superior technique for the assessment of copy number of millions of loci across the human genome. It helps identify etiological diagnosis of patients with previously idiopathic congenital abnormalities, mental retardation (MR) and/or psychiatric problems. Microduplication of the 16p13.3 region that includes the CREBPP is associated with many variable phenotypic traits such as intellectual disability, dysmorphic facial features, arthrogryposis, small and proximally implanted thumbs.

### **Case Presentation**

We describe a 6 year old female who presented for evaluation of disruptive behavior. Her birth history was remarkable for possible maternal substance use and a nuchal cord. She was diagnosed with developmental dysplasia of the hip at age 6 months, elevated TSH, and vitiligo. Family history was significant for juvenile diabetes mellitus in sister and bipolar disorder in the mother. Physical exam revealed dysmorphic facies but a normal philtrum. Her hands were noted to have mild clinodactyly. Psychiatric diagnoses given were ADHD and post traumatic stress disorder. Chromosomal Microarray was ordered to evaluate for possible causes of the idiopathic congenital anomalies. This analysis revealed duplication of a 596 KB region of 16p13.3, encompassing 9 OMIM genes, including CREB binding protein which is implicated in the phenotype.

### **Discussion**

The purpose of reporting this case is: 1. To highlight the importance of using easily available higher sensitivity methods to screen patients with idiopathic multiple congenital anomalies, Intellectual disability and autism. 2. The description of this phenotype continues to evolve with only 30 reported cases over the last 10 years and this case report will add to it. 3. Identifying the cause of congenital anomalies can help provide appropriate counseling and guidance to the family.

**The Removal of Zolpidem from Standardized Order Sets and its Effect on the  
Rate of Inpatient Falls in a Community Teaching Hospital**

Casey Summers, Crystal D. Heise, Derek Grimm, Paul Ferguson

Marshall Health Neuroscience Department, Marshall University School of Pharmacy,  
Marshall University, Joan C. Edwards School of Medicine, Cabell Huntington  
Hospital, Huntington, West Virginia

**Background**

Falls are the leading cause of hospitalized accidents. Recent studies have found zolpidem use to be an independent, potentially modifiable risk factor for inpatient falls.

In March 2015, the hospital administration elected to remove zolpidem from all standardized order sets in an attempt to improve patient safety and decrease fall rates.

**Hypothesis**

The primary objective of this study was to evaluate the effect of zolpidem removal would have on fall rates.

**Methods**

This retrospective, quality improvement evaluation was completed utilizing previously existing data. A retrospective review of all inpatient falls from November 2014 to May 2015 was performed. Fall rates 3 months prior to and 3 months after zolpidem removal were compared.

**Results**

A total of 201 patients met inclusion criteria for this study, which accounted for 242 inpatient falls. Of the 242 falls, only 8 patient falls had received zolpidem prior to the fall. The overall fall rate during the entire study period was 4.26 falls per 1000 patient bed days. The fall rate during the three month period before removing zolpidem from standardized order sets was 3.8 falls per 1000 patient bed days and 4.7 falls per 1000 patient bed days the 3 months following removal. A notable trend in a decreased number of zolpidem orders was observed after zolpidem removal.

**Conclusion**

This study demonstrated that removal of zolpidem from standard order sets at this institution did not directly decrease the inpatient fall rate; however, a trend in decreased zolpidem utilization was observed. Future study of decreased zolpidem utilization and fall rate should be repeated to determine if adequate time was as given to detect a significant change.

**Pro224-Ala mutation of the Rat Na/K-ATPase  $\alpha$ 1 Subunit Prevents Na/K-ATPase Signaling Without Affecting Ouabain-Sensitive Ion-Exchange Function**

Yanling Yan, Zi-jian Xie, Joseph I. Shapiro and Jiang Liu

Pharmacology, MIIR

**Background**

Carbonylation modification of the Na/K-ATPase  $\alpha$ 1 subunit regulates Na/K-ATPase signaling and subsequent transepithelial sodium transport in renal proximal tubules.

**Methods**

Mutation of Pro224 of rat  $\alpha$ 1 subunit. Assays for ouabain-sensitive enzymatic and ion-exchange activities of the Na/K-ATPase, as well as ouabain-stimulated Na/K-ATPase signaling function.

**Results**

Cardiotonic steroids (CTS, such as ouabain) amplifies reactive oxygen species (ROS) through Na/K-ATPase signaling. Direct carbonylation modification of pig Pro222 in the Na/K-ATPase  $\alpha$ 1 subunit was required to initiate ouabain-stimulated Na/K-ATPase/c-Src signaling and subsequent regulation of active transepithelial  $22\text{Na}^+$  transport. A single mutation of rat Pro224 (corresponding to pig Pro222) to Ala has no significant effect on the ouabain-sensitive enzymatic activity and ion-exchange activity of the Na/K-ATPase as an ion pump, but abolishes ouabain-stimulated Na/K-ATPase signaling and inhibition of active transepithelial  $22\text{Na}^+$  transport. Computerized docking analysis suggests a change of the binding of the Pro222 to pig c-Src SH2 and Kinase domain, before and after carbonylation. Taking our previous findings, the data indicates that carbonylation modification of Pro224 in rat  $\alpha$ 1 subunit of the Na/K-ATPase  $\alpha$ 1 subunit dictates ouabain-mediated Na/K-ATPase signal transduction and subsequent sodium transport.

**Conclusion**

Direct carbonylation of Pro224 prevents ouabain-mediated Na/K-ATPase signaling and related sodium handling in renal proximal tubules.

## **Excess Catalase modulates hypothalamic appetite regulation**

Deborah L. Amos<sup>1</sup>, Logan Efaw<sup>1</sup>, Carla Cook<sup>1</sup>, Melissa B. Massie<sup>1</sup>, Noah S. Mitchell<sup>2</sup>, Akhil M. Gudivada<sup>1</sup>, Nalini Santanam<sup>1</sup>  
2College of Arts and Sciences, Bluefield State College, Bluefield, WV; 1Department of Pharmacology, Physiology and Toxicology, Joan C. Edwards School of Medicine, Marshall University, Huntington, WV

### **Background**

Obesity is a global health threat. Under the influence of adipose derived leptin signaling, appetite is tightly regulated by orexigenic and anorexigenic pathways within the hypothalamus. It is implicated that oxidative stress impacts obesogenic signaling. The endogenous antioxidant, Catalase (CAT), is known to be involved in metabolic diseases. However, its role in obesity is still unclear.

### **Hypothesis**

We hypothesized that excess CAT would deter oxidative stress mediated appetite dysregulation.

### **Methods**

We tested our hypothesis in studying appetite regulation and obesogenic changes in Catalase transgenic (Cat-tg) mice, that expressed 3-4 fold excess human catalase, as well as the newly engineered Bob-Cat mice (hybrid of Cat-tg and leptin-resistant obese, Ob-Ob mice). Leptin-deficient, Ob-Ob mice and C57Bl6 mice were control groups (n=4/group). Body fat composition and metabolic parameters were measured using ECHO-MRI and CLAMS (Comprehensive Laboratory Animal Monitoring System). Hypothalamic appetite regulation was determined using a microarray of appetite regulating genes (Qiagen). Changes in adipokine gene expression, catalase activity, and oxidative stress levels were measured in the adipose tissue. GraphPad PRISM and SPSS were used for statistical analysis.

### **Results**

ECHO-MRI showed a lower fat to lean mass ratio in Cat-tg and Bob-Cat mice compared to Ob-Ob mice. CLAMS showed no differences in energy expenditure (RER) or food intake, but a higher heat production in Cat-tg and Bob-Cat mice compared to C57Bl6. In the hypothalamus, Cat-tg showed an induction in the anorexigenic POMC (>2.5 fold) and a decrease in orexigenic Npy (<0.5 fold), while Bob-Cat mice showed a reduction in both these genes, compared to the C57Bl6 mice. Adiponectin, Leptin, and MCP-1 were differentially modulated between the genotypes.

### **Conclusion**

These findings indicated that excess CAT, as in the case of Bob-Cat mice, can modulate fat mass and hypothalamic appetite regulation. The mechanism by which excess CAT regulates metabolic pathways in obesity is under investigation.

## **MB5, an Analogue of Ouabain, Ameliorated PNx-Mediated Cardiac Fibrosis and Function**

Preeya T. Shah, Xiaoliang Wang, Muhammad A. Chaudhry, Yanling Yan, Rebecca Martin, Kyle Maxwell, Zi-jian Xie, Joseph I. Shapiro, and Jiang Liu  
Pharmacology, MIIR

### **Background**

We have shown that the Na/K-ATPase signaling regulates cardiac and renal fibrosis. Here we report that blockade of Na/K-ATPase signaling by MB5 (3,4,5-Trihydroxyxanthone, C<sub>13</sub>H<sub>8</sub>O<sub>5</sub>) ameliorated 5/6 renal partial nephrectomy (PNx) mediated cardiac function in C57BL/6 mice. MB5 is a xanthone derivative that can inhibit Na/K-ATPase with an IC<sub>50</sub> of ~10  $\mu$ M. Most interestingly, unlike ouabain, MB5 is unable to activate the signaling function of the Na/K-ATPase.

### **Methods**

The C57BL mice were randomly divided into experimental groups and processed for Sham surgery (Sham) or PNx surgery (PNx). The Sham and PNx groups were further treated with MB5 to investigate its preventive and reversible effect on cardiac fibrosis and function. MB5 was dissolved in 70%DMSO/30%EtOH, and delivered by minipumps for 4 weeks (the minipumps were implanted in the same time when the 2nd PNx surgery removing right kidney).

### **Results**

Comparing with sham, PNx surgery significantly stimulates type 1 collagen expression in heart left ventricles and remnant kidney. Administration of MB5 significantly ameliorated PNx-mediated fibrosis in both heart and remnant kidney. Transthoracic Echocardiography analysis demonstrated that treatment with MB5 also ameliorated PNx-induced changes in relatively wall thickness (RWT), myocardial performance index (MPI), left ventricular mass (LVM) and LVM indexed to body surface area (LVMI).

### **Conclusion**

MB5, as a Na/K-ATPase inhibitor but unable to activate Na/K-ATPase signaling, can function as an antagonist of Na/K-ATPase signaling to ameliorated PNx-mediated cardiac function.

## **Response of Family Medicine Residents to An Educational Intervention About Patient-Physician Communication**

Harsh M., Mays A., Cousins RF, Barker SB, Nair D.

Department of Family Medicine, Marshall University Joan C. Edwards School of Medicine, Huntington, WV

### **Background**

Studies indicate that patients misunderstand the majority of information provided during appointments. The Teach-Back Method (TBM) is meant to assess patients' recall and comprehension.

### **Hypothesis**

We aimed to characterize Family Medicine Residents' attitudes, knowledge, and perceptions of their use of TBM in patient communication.

### **Methods**

We developed an educational intervention consisting of a Grand Rounds lecture and discussion, followed by role playing. We surveyed residents pre- and post intervention eliciting both Likert scale and narrative responses. A total of 20 residents completed both surveys, with 12 participating in the intervention.

### **Results**

Both before and after intervention, residents strongly felt that TBM was effective in increasing patient retention of physician instructions. They also maintained a high level of confidence in current communication practices and a high frequency of assessing patient understanding.

Prior to the study, 6 participants were able to define TBM, this increased to 15 participants after intervention ( $p=.004$ ). After intervention, residents were less inclined to learn more about TBM, citing time as a major constraint in utilizing TBM. Further, the reported utilization of TBM did not change from baseline.

However, the residents, including those who did not attend the intervention, assessed patient understanding more frequently than prior to participation in the study ( $p=0.021$ ).

### **Conclusion**

Though there was a high receptivity to learning about patient-physician communication, the residents were reluctant to adopt TBM in their practices. Notably, however, the residents reported they were assessing their patient understanding more frequently.

This pilot study demonstrates that conducting an educational intervention can result in identifiable improvements in physicians' communication. These promising results suggest that continued educational interventions in patient-physician communication are worthwhile in residency programs.

## **Prospective, open-label study of Andexanet Alfa in patients receiving a Factor Xa inhibitor who have acute major bleeding: A case report and clinical trial review**

Victoria Watson, Alyssa Zirille, R.N., Robin Ashford, Pharm. D., John Cornell, M.D.  
Department of Neuroscience, Marshall University

### **Background**

Increasing numbers of patients are started on Factor Xa inhibitors such as apixaban (Eliquis) and rivaroxaban (Xarelto) for treatment and prevention of DVT/PE, but these novel anticoagulants have no approved reversal agent for patients that experience life threatening bleeding while on the medications. Marshall is one of the few institutions participating in the ANNEXA-4 clinical trial for andexanet alfa, a factor Xa inhibitor reversal agent, and we recruited the first ever patient for the trial. The drug is produced by Portola Pharmaceuticals and is currently undergoing fast track FDA approval. The company is also submitting for BLA, and Marshall has enrolled 20% of these BLA patients.

### **Hypothesis**

Andexanet alfa, in phase 3b/4 clinical trials, is proposed to effectively and safely reverse the anticoagulant effect produced by Factor Xa inhibitors.

### **Methods**

Patients taking a Factor Xa reversal agent that present with an episode of acute major bleeding are screened with inclusion and exclusion criteria. If qualified for the study, they receive a bolus followed by an infusion of andexanet alfa. Labs are checked at 1, 4, 8, and 12 hours post-infusion, and follow up continues until day 30. The study is discontinued at any time if the patient is determined to require another form of life saving treatment, or according to patient wishes.

### **Results**

The first ANNEXA-4 patient suffered intracranial hemorrhage while on apixaban for atrial fibrillation and was transferred to CHH from an outlying facility. She received andexanet alfa, and her life threatening intracranial bleeding was stopped, enabling her to obtain full recovery.

### **Conclusion**

Andexanet alfa appears to be a safe and effective reversal agent for the Factor Xa inhibitors, but more patients are needed for phase 3b/4 of the ANNEXA-4 trial.

### **Case Presentation**

The first patient ever to be enrolled in the ANNEXA-4 trial was an 85 year old female transferred from an outlying facility to Cabell Huntington Hospital due to acute intracranial hemorrhage while on apixaban. As she had taken the medication within the past 18 hours and had no contraindications to participation, she was enrolled in the ANNEXA-4 trial. She then received a bolus of andexanet alfa, followed by infusion of the drug according to protocol. Labs and clinical status were monitored, and repeat head imaging did not demonstrate expansion of the intracranial hemorrhage. A complete recovery was made by the patient.

### **Discussion**

Novel factor Xa are gaining popularity due to ease of administration and no need for routine monitoring, but this picture is complicated by the fact that there is no approved reversal agent for patients suffering from acute life threatening bleeding while taking these medications. Andexanet alfa, produced by Portola Pharmaceuticals, appears to be safe and effective in reversing acute symptomatic bleeding in patients taking factor Xa inhibitors, but more patients are needed for this phase 3b/4 clinical trial before the FDA can approve the drug.





**POSTER SESSION II • 2:30 PM – 3:15 PM**

# 28TH ANNUAL RESEARCH DAY ORAL SESSION

## **Development of Direct Oral Anticoagulant Order Sets to Ensure Appropriate Use and Attenuate Risk**

Crystal D. Heise, Derek Grimm, Justin Nolte, and Paul Ferguson

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Marshall University Joan C. Edwards School of Medicine, and Cabell Huntington  
Hospital, Huntington, West Virginia

### **Background**

Direct oral anticoagulants (DOACs) have been marketed to offer the benefits of standardized dosing without the need for regular monitoring and fewer drug interactions. With anticoagulants being identified as one of the top five 'highest risk medications' associated with patient safety incidents in the U.S., careful considerations in medication administration, appropriate patient selection, and dose optimization is essential to assure safety and efficacy of DOAC use.

### **Hypothesis**

It was the goal of this study to evaluate the use of DOACs within our institution to identify areas for improvement in its prescribing, dispensing, and administration.

### **Methods**

This retrospective, quality improvement evaluation was completed utilizing previously existing data. A chart review of all patients ordered and administered a DOAC (apixaban, rivaroxaban, or dabigatran) during an inpatient stay during November 1, 2013 to March 30, 2015 was performed.

### **Results**

DOACs were administered during 175 individual patient admissions during the study time period, with 82% (n=144) being continuation of home medication and 18% (n=31) new DOAC starts. Atrial fibrillation was the most common indication for use (81% of home medication continuation and 58% of new starts). Evaluation of patient-specific dosing based on indication, renal function, and interacting medication found DOAC dosing to be appropriate in 73.1% (n=128). Further analysis of those with inappropriate dosing (26.9%, n=47) for which an identifiable contributing factor was identified (n=39) found 41% (n=16) of doses were too high (increasing bleeding risk) and 59% (n=23) of doses were too low (increasing risk of thrombosis).

### **Conclusion**

Accuracy of DOAC dosing was found to be less than optimal. Complicated dosing recommendations and varying renal function may lead to confusion and inappropriate dosing resulting in significant risk/adverse patient events. Recommendations for optimizing use have been identified such as indication-specific order sets/protocols, standard administration times minimizing preventable drug interactions, and timing administration with meals when appropriate.

## **An Update on Pediatric All-Terrain Vehicle Trauma: A Two-Decade Statewide Experience**

Johnson Walker, Matthew Snyder, Bonnie Beaver, David Denning

Department of Surgery, Joan C. Edwards School of Medicine

### **Background**

Over the past two decades, the use of all-terrain vehicles has become ever more popular, affordable and mainstream, especially in rural areas. Research published in the *Journal of Pediatric Surgery* in 1998, examining pediatric ATV trauma in West Virginia (Lister et al.), revealed the majority of pediatric ATV trauma patients were unhelmeted, leading to more significant morbidity and mortality. As a result, West Virginia created legislation in 2004 regulating the use of all-terrain vehicles, including a law mandating the use of helmets in the pediatric population.

### **Hypothesis**

Passage of legislation will lead to increased helmet use and reduced injury severity.

### **Methods**

Data were compiled from the West Virginia State Trauma Registry and analyzed retrospectively. Included were all patients younger than 17 years, with ATV-related injuries, who presented to one of the trauma centers in West Virginia, between January 2008 and December 2012 (n = 1199). Age, gender, helmet status, length of hospitalization, Glasgow Coma Score, Injury Severity Score, and mortality were analyzed and compared to those obtained during the pre-legislation period, as described by Lister.

### **Results**

The majority of patients were unhelmeted at the time of their injuries (66.2%). Both helmeted and unhelmeted riders were most likely to suffer orthopedic injuries, followed by head injuries. Significantly more riders were wearing helmets in the post-legislation study, compared to the pre-legislation data. Additionally, presenting Injury Severity Score, length of hospitalization, and overall mortality were all significantly improved post-legislation.

### **Conclusion**

There has been a significant increase in helmet use in pediatric ATV riders in West Virginia, leading to reduced severity of injury, shortened hospitalizations and improved mortality. The data show progress in West Virginia in regards rider safety; however, there is room for improvement. More education is needed to ensure that ATV riders always wear helmets and to further encourage safe operation of these vehicles.

## **Reduced iron intake protects mitochondrial energy metabolism in ethanol consumption**

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Marshall University Joan C. Edwards School of Medicine, Huntington WV

### **Background**

Understanding the role of iron in ethanol-derived hepatic stress could help to elucidate the efficacy of dietary or clinical interventions designed to minimize liver damage from chronic alcohol consumption. It is well-known that ethanol consumption causes iron accumulation and damage in liver.

### **Hypothesis**

We hypothesized that reduced levels of iron intake would alleviate ethanol-derived liver damage.

### **Methods**

To determine the impact of normal (55mg/kg) and low (5mg/kg) dietary iron levels, male C57BL/6 J mice were fed isocaloric Lieber-DeCarli liquid ethanol diets for 22 weeks where 30% of kcals were derived from ethanol in a pair-fed design. We performed Western blot analysis, electron transport chain complex assays, and measured NAD/NADH levels to further determine mitochondrial metabolism in these animals.

### **Results**

Chronic ethanol exposure led to mild hepatic stress possibly characteristic of early stage alcoholic liver disease, seen as increases in liver to body weight ratios, hepatic transferrin receptor expression, and whole cell protein acetylation. Dietary iron reduction led to decreased hepatic ferritin and increased transferrin receptor expression, and decrease in NAD<sup>+</sup> and NADH levels in ethanol consumption. The dietary iron reduction in ethanol-treated mice resulted in increased complex II of the oxidative phosphorylation process, succinate dehydrogenase, possibly to compensate for reduction in NAD<sup>+</sup> levels. In addition, processes involved in mitochondrial biogenesis were protected under low iron conditions.

### **Conclusion**

Our results indicate that reduction of iron intake could be a preventative measure in chronic drinkers.

**Initial Treatment Outcomes for Types 1 and 2 Trigeminal Neuralgia following Stereotactic Radiosurgery: A Retrospective Analysis**

Raj Singh, Sanjeev Sharma

Department of Radiation Oncology, Joan C. Edwards School of Medicine, Marshall University, Huntington, WV

**Background**

Trigeminal neuralgia (TN) is a chronic facial pain condition, and stereotactic radiosurgery (SRS) is often turned as a local treatment option for TN.

**Hypothesis**

The purposes of this study were to assess the effectiveness of SRS in providing pain relief and examine side effects stemming from treatment.

**Methods**

We screened the RSSearch® Patient Registry, a national SRS database, for type 1 and 2 TN cases from July 2007 to June 2015. An analysis of initial pain as measured by the Visual Analog Scale (VAS), treatment planning, decline in VAS scores following SRS, and post-treatment side effects was performed.

**Results**

Our analysis included 163 patients; 125 patients with type 1 TN and 38 patients with type 2. For type 1 and 2 cases, the median prescribed doses were 60 Gy (range: 41.25 Gy - 80 Gy) and 75 Gy (range: 17.78 Gy - 75.3 Gy), respectively, but were not significantly different (p-value = 0.38). Initial mean VAS pain scores were 7.47 (95% CI: 7.00 - 7.94) for type 1 cases and 6.89 (95% CI: 5.93 - 7.86) for type 2 cases. Following SRS, average VAS scores were found to be significantly lower for both type 1 TN (1.86; 95% CI: 1.33 - 2.38) and type 2 TN (1.84; 95% CI: 0.82 - 2.87) following paired t-tests (p-value = 0.000). The vast majority of both type 1 TN patients (87.2%) and type 2 TN patients (86.8%) experienced pain relief following SRS. The percentage of types 1 and 2 patients experiencing side effects after SRS were 18.3% and 10%, respectively, with the most common being neuropathy.

**Conclusion**

This study demonstrates the effectiveness of SRS in providing pain relief for both types 1 and 2 TN patients with side effects observed in less than 20% of all patients.

**Clinical utility of methicillin-resistant Staphylococcus aureus nasal polymerase chain reaction (PCR) in intensive care unit patients with pneumonia**

Binh Le, Omar Ahmed, Cat Higgins, Stephanie Giancola, Ai Thi Nguyen, James Aaron Sizemore  
Marshall University School of Pharmacy

**Background**

Nasal colonization with methicillin-resistant Staphylococcus aureus (MRSA) occurs in 8% of patients in the intensive care unit (ICU) and is related to greater risk of infections. Limited studies are available to assess the value of a negative MRSA nasal PCR. Previous studies have shown that a negative MRSA nasal PCR test is associated with a 97-100% negative predictive value for ruling out clinically confirmed MRSA pneumonia.

**Hypothesis**

We expect the MRSA nasal PCR test to have a high negative predictive value that would be clinically useful to guide rapid de-escalation of antibiotic therapy for pneumonia in patients with MRSA risk factors.

**Methods**

This study is a single-center, retrospective chart review. Adult patients admitted to the ICU at St. Mary's Medical Center (SMMC) with an admitting diagnosis of pneumonia, respiratory failure, or sepsis were identified from the electronic health database and screened for inclusion in the study. Patients were then evaluated for confirmed or possible pneumonia according to pre-defined criteria based on radiographic evidence and presence of two or more symptoms of pneumonia. Overall predictive values were calculated and a subgroup analysis was conducted to examine the predictive values for each subtype of pneumonia.

**Results**

In all patients, the MRSA nasal PCR test was determined to have a sensitivity of 81.0%, specificity of 79.4%, positive predictive value of 30.4%, and negative predictive value of 97.4%.

**Conclusion**

Of the 210 patients included in the study, 10% had clinically confirmed MRSA pneumonia. A high negative predictive value of 97.4% can be a clinically reliable tool to guide early de-escalation of anti-MRSA antibiotics. The addition of MRSA nasal PCR testing to standard pneumonia protocol may be beneficial to reduce anti-MRSA antibiotic use. Further studies to confirm the clinical usefulness of MRSA nasal PCR outside of the ICU/IMCU setting and for other types of infections is warranted.

## Measurement of Protein Carbonylation of the Na/K-ATPase $\alpha$ 1 Subunit by Gel-Filtration HPLC

Yanling Yan, Yun-hui Xu, Zi-jian Xie, Joseph I. Shapiro and Jiang Liu  
Pharmacology, MIIR

### Background

Measurement of protein carbonylation by western blot analysis is time-consuming and semi-quantitative. Given the limitation of western blot analysis, we explore the possibility of using HPLC coupling gel-filtration method with whole cell lysate

### Methods

The DNPH derivatives were prepared as we previously described for western blot. Several approaches of afterward preparation of sample were compared. Purified pig Na/K-ATPase (with and without DNPH derivation) was used as positive control. A Shimadzu HPLC system (Shimadzu LC-20AP coupling a SPD-M20A diode array detector) and a TSKgel QC-PAK GFC200 column (TOSOH) were used. Mobile phase was 0.05M PBS buffer with 0.5% acetonitrile. Protein concentration and carbonylated proteins were measured at absorbances at  $276\pm 4$ nm and  $370\pm 4$ nm, respectively.

### Results

We treated LLC-PK1 cells with antioxidant NAC (50mM for 1h, to "minimize" carbonylation and serve as control of 0 percent carbonylation) and H<sub>2</sub>O<sub>2</sub> (10mM for 1h, to "maximize" carbonylation and serve as 100 percent carbonylation). The testing samples were prepared as the following: (1) NAC alone 100  $\mu$ g, (2) NAC 25  $\mu$ g + H<sub>2</sub>O<sub>2</sub> 75 $\mu$ g, (3) NAC 50  $\mu$ g + H<sub>2</sub>O<sub>2</sub> 50 $\mu$ g, (4) NAC 75  $\mu$ g + H<sub>2</sub>O<sub>2</sub> 25 $\mu$ g, and (5) H<sub>2</sub>O<sub>2</sub> alone 100 $\mu$ g. We assume that these samples represent 0%, 25%, 50%, 75% and 100% of carbonylation levels respectively, based on the ratio of H<sub>2</sub>O<sub>2</sub>-treated sample vs. total protein. The same samples were also analyzed and compared with western blot methods.

### Conclusion

With further optimization, the gel-filtration HPLC method might be an alternative approach for carbonylation measurement for a larger number of samples.

**diagnostic value of cardiac computed tomography angiography in patients with  
left bundle branch block and abnormal single photon emission computed  
tomography**

Ahmed fahala\_fatima alwusbai  
internal\_medicine

**Background**

The presence of septal perfusion defect on myocardial perfusion single-photon computed tomography (SPECT) in patients with known left bundle branch block (LBBB) can present a major diagnostic dilemma.

**Hypothesis**

The prevalence of anteroseptal perfusion abnormalities in patients with complete left bundle branch (LBBB) is variable and not well known. We thought to study the prevalence of myocardial perfusion single-photon computed tomography (SPECT) abnormalities in patients with LBBB and correlation with conventional coronary angiography (CCC).

**Methods**

Over the last 3 years, 96 patients with known LBBB on surface electrocardiogram referred for SPECT to exclude coronary artery disease. Only pharmacological stress tests with adenosine or dipyridamole were included in this study. Same day or two days rest stress-gated Technetium (99mTc) tetrofosmin or sestamibi (SPECT). The perfusion abnormalities were reported as fixed or reversible only in septum or anteroseptal wall. CCC was performed on 10 patients only.

**Results**

Total study population was 96, 57 (59%) male and 39 (41%) female, mean age was 63 ± 12, 40 (43%) diabetics, 44 (46%) hypercholesterolemic, 59 (62%) hypertensive. 57 (59%) patients had normal SPECT, and 38 (40%) had abnormal SPECT, two out of patients with abnormal SPECT had fixed defects and the remaining had reversible defect. CCC was performed on 10 patients only, 8 patients had normal CCC and only 2 patients had left anterior descending coronary artery disease (LAD).

**Conclusion**

The presence of abnormal SPECT in a patient with LBBB did not necessarily indicate the presence of CAD. Approximately 70% of patients with LBBB and abnormal SPECT had normal CCTA. The authors strongly believe CCTA must be considered the first noninvasive test in patients without history of CAD and LBBB. Normal CCTA excludes CAD, but patients with obstructive CAD more than 50% on CCTA will benefit from conventional coronary angiography.



## **Orthopaedic Surgeon Density in West Virginia**

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Department of Orthopaedic Surgery, Joan C. Edwards School of Medicine,  
Huntington, WV

### **Background**

According to the American Academy of Orthopaedic Surgeons (AAOS), West Virginia has among the lowest density of orthopaedic surgeons in the country, between 6 and 7 surgeons per 100,000 people. The purpose of this study is to determine the distribution and density of orthopaedic surgeons in the state and to highlight underserved areas within the state in need of improved orthopaedic care.

### **Hypothesis**

With a purported deficit of orthopaedic surgeons compared to the national average as described by the AAOS, the authors hypothesize that West Virginia suffers from a low density of orthopaedic surgeons relative to its population. Furthermore, we theorize residents of West Virginia are at a disadvantage compared to the average American with regards to orthopaedic care as a result of this below average density.

### **Methods**

Records from the West Virginia Board of Medicine were cross referenced with those of the AAOS and with West Virginia hospital websites to form a comprehensive and current list of orthopaedic surgeons in the state. This data was then juxtaposed to national census data for the state of West Virginia.

### **Results**

The study found that West Virginia has a density of orthopaedic surgeons equivalent to that of the national average at 8 per 100,000 and that these surgeons are most concentrated in Monongalia and Cabell counties (>20 per 100,000). Thirty counties in the state do not have an orthopaedic surgeon, although in every case one can be found in a neighboring county with minimal travel distance.

### **Conclusion**

The authors conclude that the density of orthopaedic surgeons in West Virginia is equal to the national average. This information can help in determining resource allocation for the treatment of orthopaedic maladies in addition to serving as a tool to assist regional physicians in directing patients seeking orthopaedic treatment.

## **Retrospective analysis of outcomes from use of a novel carbon fiber implant for oncologic and fracture outcomes**

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### **Background**

Traditionally, metal implants are the standard-of-care when repairing pathologic fractures. They are cost-effective, have high tensile strength, and provide adequate support. However, they are radio-opaque and cause artifacts on MRI imaging, which limits the surveillance of bone healing and tumor activity in cancer patients. Recently, carbon fiber composite implants, which aim to avoid these problems, have been used as a treatment modality. Carbon-fiber-reinforced polyetheretherketone (CFR-PEEK) have minimal artifacts on MRI and complete radiolucency on radiographic imaging. Additional advantages include a Young's modulus of elasticity closer to that of bone, thus promoting bone healing and delivering higher fatigue strength.

### **Hypothesis**

This study analyzes the significance of using CFR-PEEK implants in orthopedic fracture repairs and oncologic patients.

### **Methods**

A retrospective analysis of 27 patients with carbon fiber implants was done. 21 of the 27 patients were oncologic. Cost, fluoroscopy time, and implant related complications were recorded. These factors were then compared to reported rates for traditional metal implants.

### **Results**

There was one implant-related failure, resulting in hypertrophic nonunion over the fibula. 5 patients had wound complications, mainly failed wound flaps possibly influenced by previous cancer treatment. Average cost for a CarboFix implant is 53% greater than a traditional Synthes implant. Carbon fiber implants had slightly longer fluoroscopy times. Average time for a femur nail CarboFix implant was 129.5 seconds, versus 106.2 seconds for the metal implant. Average tibial nail fluoroscopy time was 99.58 seconds for carbon fiber, and 71 seconds for the metal.

### **Conclusion**

Based on the results of this analysis, carbon fiber may have advantages when treating oncologic patients, given its radiolucency and low modulus of elasticity. Despite being more expensive than Synthes implants, and having slightly increased perioperative fluoroscopy times, Carbon fiber implants offer valuable prospect as an alternative to metal; however, further studies need to be made to determine their true potential.

**pNaKtide, an antagonist of Na/K-ATPase Signaling, Ameliorated PNx-Mediated Cardiac Function**

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**Background**

We have shown that the Na/K-ATPase signaling regulates cardiac and renal fibrosis. Attenuating oxidative stress and blocking Na/K-ATPase signaling is capable of restoring PNx-mediated cardiac and renal fibrosis. Here we report that blockade of Na/K-ATPase signaling by pNaKtide ameliorated 5/6 renal partial nephrectomy (PNx) mediated cardiac function in C57BL/6 mice.

**Methods**

The C57BL mice were randomly divided into experimental groups and processed for Sham surgery (Sham) or PNx surgery (PNx). The Sham and PNx groups were further treated with pNaKtide to investigate its preventive and reversible effect on cardiac fibrosis and function.

In "preventive" set, pNaKtide (25mg/KG BW, ip) was given weekly 7days after surgery. In "reversible" set, pNaKtide was give every other day for 7 days, beginning at 4 weeks after PNx surgery.

**Results**

Comparing with sham, PNx surgery significantly stimulates type 1 collagen expression in heart left ventricles assayed by western blot and histology analyses. Administration of pNaKtide significantly ameliorated PNx-mediated collagen production and protein carbonylation. Transthoracic Echocardiography analysis demonstrated that "preventive" treatment with pNaKtide prevented PNx-induced changes in relatively wall thickness (RWT) and myocardial performance index (MPI), and the "reversible" pNaKtide treatment improved RWT but not MPI.

**Conclusion**

pNaKtide, an antagonist of Na/K-ATPase signaling, ameliorated PNx-mediated cardiac function

## **Distance to care is associated with lower healthcare maintenance and survival in patients with gynecologic malignancies**

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### **Background**

Women with gynecologic malignancies in rural regions may have limited access to the highly specialized care they need, and often travel long distances for treatment. Prior reports have suggested that distance to treatment facility is a barrier to appropriate healthcare maintenance and treatment. We previously reported on the effect of the distance traveled by patients with gynecologic malignancies to a university hospital on the disease presentation as well as short and long term outcomes. We sought to investigate the effect of this distance on healthcare maintenance.

### **Hypothesis**

Patients living in rural areas might have poor follow up records for maintenance of care.

### **Methods**

Patients with gynecological malignancies treated at the ECCC, and MU between 2006 and 2014 were identified using the cancer registry database. Clinical and demographic data is collected utilizing American College of Surgeons/Commission on Cancer data elements and met National and State quality edits. The dates of last pap smear and mammogram in relation to the gynecological malignancy diagnosis were collected to be evaluated with the outcome.

### **Results**

810 patients with gynecologic malignancies, ovarian (n=127), uterine (n=489), cervical (n=88), vulvar (n=52), peritoneal (n=22) other (n=32) cancers were identified during the study period and the clinical data was subject to a multivariable analysis. When taking the median DTC as a cutoff, short DTC was found to be significantly associated with a more than 4 years interval since the last pap smear and more 5 years since the last mammogram. Patients with a poor healthcare maintenance records were found to have a worse prognosis.

### **Conclusion**

Geographic proximity to a university hospital appears to significantly influence healthcare maintenance record and survival in patients with gynecologic malignancies. These findings highlight the importance of access to care to improve the outcome for our patients. Further studies may help identify areas of geographic disparity and potential outreach programs.

## **Buprenorphine modulates angiogenesis**

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### **Background**

Opioid abuse is a significant problem in the West Virginian population especially during pregnancy. This results in 14% of neonates being born addicted to opioids. Buprenorphine has recently gained popularity in treating opioid addicts by way of opioid maintenance therapy. In several studies, buprenorphine has been shown to result in less neonatal abstinence syndrome rates than methadone treated pregnant women. However, there are areas of functioning that can't be tested at birth since they have not developed yet. Some studies indicate that babies prenatally exposed to buprenorphine might have cognitive deficits such as executive functioning, short term memory, inhibition and selective visual attention. Studies in rats have shown cognitive deficits, social behavior deficits, and increased anxiety behavior in rats that were prenatally exposed to buprenorphine.

### **Hypothesis**

Our aim in this study is to determine the role that the blood brain barrier might play in leading to some or all of the deficits seen in babies who were prenatally exposed to buprenorphine.

### **Methods**

We used rat brain micro vascular endothelial cells in cell culture to test for protein differences and functional differences between treated and untreated samples. We used western blot analysis, scratch assay, and matrigel assays.

### **Results**

We have shown an alteration in the levels of phospho erk1/2 and p38 map kinases, as well as a difference in the level of VEGF receptor and neuropilin 1, which suggest a change in angiogenesis potential in these cells. Preliminary data indicates that Buprenorphine modulates angiogenesis in the scratch assay system.

### **Conclusion**

This data indicates that buprenorphine can regulate angiogenesis. Angiogenesis plays a key role in brain development, and changes in this process could lead to a difference in delivery of either nourishing materials, toxic materials, or both to the developing brain.

**Giant Cell Interstitial Pneumonia is a rare manifestation of chronic  
Nitrofurantoin lung toxicity**  
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Internal Medicine

**Background**

Nitrofurantoin, can cause interstitial pneumonitis mimicking cryptogenic organizing pneumonia (COP) or pulmonary fibrosis. Rarely, it may cause giant cell interstitial pneumonia (GIP), which is a form of chronic interstitial pneumonitis commonly found in workers exposed to hard metals.

**Case Presentation**

A 66 year old male presented with progressive dyspnea on exertion. He had no smoking history and his prior occupation was as a phone technician in a company. He did not have any exposure to asbestos, silica or coal dust. Spirometry showed a vital capacity of 3.3 L (87% of predicted), FEV1 2.6 L (90%) and FEV1/FVC ratio of 80%. Lung volume measurements showed total lung capacity of 5.3 L (91%) and residual volume of 85%. Diffusion capacity was reduced at 19.34 mL/mm/m (62% of predicted.)

A high-resolution computed tomography (HRCT) scan showed bilateral ground glass opacities with lower lobe predominance. In addition, his past medical history included recurrent urinary tract infections treated with nitrofurantoin for several months. Further blood chemistry analysis revealed no abnormalities; in particular, there was no eosinophilia.

Bronchoalveolar lavage fluid (BAL) showed a predominance of lymphocytes (70%), eosinophils (3%) and a decreased CD4/CD8 ratio of 0.40. Video assisted thoracoscopy with biopsy was diagnostic for giant cell interstitial pneumonia, with many intra-alveolar giant cells and non-polarization. Nitrofurantoin was discontinued the patient's status and pulmonary function tests improved .

**Discussion**

GIP is very rarely attributed to drug toxicity such as with nitrofurantoin. Most often related to heavy metal pneumoconiosis,. In this case the lack of exposure history and the lack of polarization in the foreign material biopsied would argue against these particular diagnostic entities Which suggest chronic Nitrofurantoin toxicity is the causative agent in this case

**CONCLUSION:**

GIP as a rare manifestation of chronic nitrofurantoin lung toxicity.

## **Geriatric trauma: are the elderly undertriaged?**

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### **Background**

Geriatric patients often sustain life threatening injuries from minor trauma, and a growing body of research suggests that these patients are often undertriaged in the emergency setting. This research evaluates the emergency response to geriatric trauma patients who presented to Cabell Huntington Hospital over the last 5 years, and determine if these patients were undertriaged. This research also aims to identify factors associated with undertriage, and if necessary, establish a new criterion in the hospital's Trauma Team Activation (TTA) policy to improve the care of this vulnerable population.

### **Hypothesis**

Geriatric patients are undertriaged and an age specific criterion is warranted.

### **Methods**

Data on 1434 trauma patients over 65 presenting from 2010-2015 was retrospectively collected from the CHH trauma registry. Undertriage was determined using the Cribari method, and was defined as having an ISS =16 without a full TTA. CHH goals are set for <5% undertriage and <50% overtriage. Average ISS and mortality rate was calculated for the most common diagnoses.

### **Results**

A substantial number of geriatric trauma patients at CHH are undertriaged (9.5%), and the majority of undertriaged patients have sustained head trauma and developed an intracranial hemorrhage. Intracranial hemorrhage occurred in 10% of all cases and was associated with the highest average ISS ( $17.4\pm 1.3$ ) and highest mortality rate (16.1%). Furthermore, 77% of patients who were undertriaged had suffered head trauma, and 58% suffered an intracranial hemorrhage. Of all patients with head trauma, a GCS =12 was associated with an ISS of  $21.5\pm 2.9$  and 60.0% mortality.

### **Conclusion**

The authors recommend that a new geriatric criterion be added to the priority 1 (full) TTA criteria: individuals over the age of 65 suffering head trauma with a GCS =12 OR suspicion of intracranial hemorrhage. Elevating the emergency response to these potentially life threatening injuries may significantly improve the quality of care delivered to these vulnerable patients.

## **PanColitis with ileitis caused by Methicillin-Resistant Staphylococcus Aureus (MRSA).**

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### **Background**

Methicillin-resistant Staphylococcus aureus (MRSA) is responsible for numerous infectious processes. Gastrointestinal tract involvement is rather rare and only a handful of cases of MRSA colitis have been reported in North America.

### **Case Presentation**

A 75 year old male patient with past medical history of Psoriasis and diverticulosis presented with 2 days history of constant dull lower abdominal pain, 2/10 in severity, without increasing/relieving factors, not radiating, associated with moderate amount of non-offensive sticky diarrhea of 4-5 times per day, associated with subjective fever, chills and occasional hematochezia. He denied nausea, vomiting, oral ulcers, odynophagia, dysphagia, jaundice, recent antibiotics use, or travel/out of home food intake. Vital signs showed hypotension and tachycardia that resolved with IV fluids. Labs showed mild leucocytosis, ESR 53 mm/hr, positive stool culture for MRSA and fecal leucocytes. He had negative blood cultures, stool work up for other infectious causes including Clostridium difficile, fecal occult blood testing, and autoimmune work up. Abdominal Computed tomography (CT) scan showed pancolitis with diverticulosis. Colonoscopy showed diverticulosis, ileitis, moderate superficial pancolitis with relative sparing of the rectum without visible pseudomembranes. All biopsies showed findings consistent with an infectious process as opposed to inflammatory bowel disease. Immunohistochemistry for Cytomegalovirus was negative. The patient was treated oral vancomycin and fluoroquinolones and his abdominal pain and diarrhea improved.

### **Discussion**

Acute diarrhea can be caused infectious and non-infectious causes. The most common pathogens identified in patients with bloody diarrhea are Shigella, Campylobacter, Salmonella, and E.coli O157:H7. MRSA is responsible for numerous infectious processes. Gastrointestinal tract involvement is rather rare and only a handful of cases of MRSA colitis have been reported in North America. We present a rare case of MRSA colitis with ileitis in an adult that was proven by stool culture and histological findings and improved with antibiotics.



## Morphine-mediated neuroprotection from hemin using an in vitro model of intracerebral hemorrhage

S. Mohan Ph.D., J. T. Robinson

### Background

Intracerebral hemorrhage (ICH) stroke is defined by the rupture of intracranial artery that leads to the formation of a hematoma. Neuronal damage is associated with the lysis of red blood cells, which releases hemoglobin. Hemoglobin and its breakdown product hemin are neurotoxic. The role of opioids and their cognate receptors in hemin-induced neurotoxicity remains unclear.

### Hypothesis

We hypothesized that morphine may exacerbate and naltrexone may protect against hemin-induced toxicity.

### Methods

Using neuronal cultures, we investigated hemin-induced toxicity and the role of mu-opioid receptors. SK-N-SH cells were used to model neurons. Cell viability following hemin (10.0 – 100 $\mu$ M) treatment for 18h was measured using LDH and Calcein AM assays (n=n-6). To measure the role of the mu-opioid receptor in these cell types against hemin toxicity, receptor selective agonist, morphine (1 – 100 $\mu$ M) and antagonist, naltrexone (1 – 100 $\mu$ M) were used

### Results

Contrary to our hypothesis, co-treatment with morphine-protected neurons from hemin toxicity. Hemin (75 $\mu$ M) treatment alone significantly increased levels of LDH compared to vehicle alone ( $p < 0.05$ ) and co-treatment with morphine (10 $\mu$ M) significantly decreased levels of LDH compared to hemin treatment alone ( $p < 0.05$ ). Using the live-cell, Calcein-AM assay, morphine also decreased the number of dead-cells compared to hemin treatment alone

### Conclusion

Current recommendations for the management of pain following ICH are the use of opioid analgesics. For example, morphine is titrated to minimize pain and increases in ICP. However, data shown here may also support a neuroprotective property of opioids that could improve outcomes following ICH. Further studies are warranted to elucidate the mechanisms involved in morphine-mediated neuroprotection.

## **Intra-operative total knee arthroplasty distraction significantly reduces visible particulate debris**

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Department of Orthopaedics

### **Background**

Third body wear contributes to failure in total knee arthroplasty (TKA). The authors propose a technique using a lamina spreader to distract the tibial and femoral components, enhancing debridement of potential third body particles remaining after traditional pulsatile lavage.

### **Hypothesis**

The authors hypothesize that this distraction technique will reduce potential sources of third body wear.

### **Methods**

Cement and bone/soft tissue debris was recovered in fifty one consecutive primary TKA patients using distraction of cemented femoral and tibial components with a lamina spreader prior to final polyethylene placement.

### **Results**

Distraction allowed for removal of previously hidden cement and bone/soft tissue fragments in 80% of patients (41/51). A total of 133 fragments were debrided: 85 cement fragments and 48 bone/soft tissue fragments with an average size of 158 mm<sup>3</sup>, larger than a standard pencil eraser.

### **Conclusion**

The authors conclude that this technique reduces potential third body particles in total knee arthroplasty.

## **MRSA Pyomyositis Mistaken for Septic Hip Arthritis in a Pediatric Patient**

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### **Background**

Septic arthritis of the hip is a commonly encountered orthopaedic problem among pediatric patients. It is often diagnosed by refusal to bear weight on the affected limb, fever, and elevated ESR and WBC. Septic arthritis of the hip is typically treated with antibiotics and emergent irrigation and debridement of the hip joint. Primary pyomyositis is a rare bacterial infection of the muscle that can have a very similar presentation to septic arthritis of the hip. In this case, we present a pediatric patient with primary pyomyositis who was mistakenly diagnosed as having septic arthritis of the hip and underwent unnecessary irrigation and debridement of the hip joint.

### **Case Presentation**

A 13 year old nonverbal autistic male presented with a two day history of fevers and refusal to bear weight on the right lower extremity. Physical exam was remarkable for pain with weight bearing and restricted range of motion of the right lower extremity. Inflammatory markers including WBC, ESR, and CRP were elevated, indicative of an infectious process. The patient was diagnosed with septic arthritis of the hip and underwent emergent irrigation and debridement of the hip joint. Cultures of the hip were negative and the patient did not improve clinically. An MRI of the right thigh was performed and revealed an abscess involving the rectus femoris. The patient subsequently underwent multiple irrigation and debridements for MRSA pyomyositis of the right thigh.

### **Discussion**

This case highlights the need for clinical suspicion for pyomyositis in pediatric patients suspected of having septic arthritis. Although rare, primary pyomyositis can be difficult to distinguish from septic arthritis, and careful diagnosis can guide appropriate treatment and prevent unnecessary procedures.

## **Inhalation drug abuse induced cryptococcal Meningococcalencephalitis**

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### **Background**

Cryptococcal encephal meningitis is a serious fungal infection that is most commonly seen in immunocompromised patients. It is an acquired infection that enters the respiratory tract. Only 30% of patients infected with cryptococcal encephal meningitis are immunocompetent and so far there is limited evidence of a prior patient case study with reported infection by inhalation drug use.

### **Case Presentation**

A 29 year-old male with past medical history of intravenous and inhalation drug abuse and hepatitis C presented with headache accompanied by photophobia, blurry vision, nausea and vomiting, or other related symptoms. Initial CT scan was negative, but MRI of brain revealed edema and suspected atypical posterior reversible encephalopathy syndrome of unknown etiology. Repeat CT indicated increased intracranial pressure with cerebellar tonsillar herniation through foramen magnum. During hospitalization, the patient was noted to have preferential leftward gaze. Neurosurgery consulted and ventriculostomy tube was placed with cerebral spinal fluid drain. Cerebral spinal fluid was sent for culture and cytology. Initial CSF studies showed lymphocytic pleiocytosis suggestive of a viral etiology. Patient was empirically started on Acyclovir for coverage of herpes simplex virus and varicella zoster. His viral workup was all negative, as were all bacterial studies. MRI showed unusual enhancement of the cerebellum and a working diagnosis of vasculitis ensued. During hospitalization, the patient developed slit ventricles on CT and the ventriculostomy tube was clamped shut. Patient quickly deteriorated requiring intubation and neurosurgery was consulted to retrieve cerebellar biopsy as all viral, bacterial, vasculitic, and fungal workup were negative. Biopsy was performed and specimen was sent to Johns Hopkins resulted in a positive stain for Cryptococcus. Patient was started on amphotericin B. Patient improved vastly with normalization of his gaze.

### **Discussion**

This case illustrates the potential for cryptococcal infection with inhalation drug use in an immunocompetent patient with negative CSF cryptococcal studies .

## Homicidal Ideation in Psychiatric Emergency Room

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### Background

Background: Homicidal ideation (HI) is a serious symptom that is routinely assessed, usually along with suicidal ideation (SI) during psychiatric evaluations. Although HI has been found to be less common than SI, there is very limited study of HI in psychiatric settings. To our knowledge, there is little study examining HI and associated psychiatric comorbidities in the psychiatric emergency room (ER).

### Hypothesis

Study Hypothesis: psychiatric symptoms are correlated and certain correlations are statistically and clinically more significant than others. HI is significantly correlated with certain concomitant psychiatric symptoms.

### Methods

Methods: 226 consecutive psychiatric ER patients from an academic medical center were examined by retrospective chart review. Three patients did not have data regarding HI and were excluded from the study, leaving 223 subjects. Data collected included demographics, clinical variables, past history of HI, current HI, psychiatric diagnoses, substance use, and family history. Data was entered into SPSS and analyzed.

### Results

Results: Homicidal ideation was present in 6.3% (N=14) of patients presenting to a psychiatric ER. Of these, 79% (N=11) had a prior history of HI, and 79% (N=11) also had SI. The majority (62%, N=8) also had illicit substance use. Variables that were significantly associated with having HI included having remote ( $p=0.001$ ) or recent ( $p=0.031$ ) history of HI, current SI ( $p=0.006$ ), having SI with a plan ( $p=0.013$ ), and current illicit substance use ( $P=0.027$ ).

### Conclusion

Conclusion: Although not common in the psychiatric ER, presence of HI is significantly associated with illicit substance use disorder, suicidal ideation and history of HI. While SI is associated with mood disorders, HI is not, likely reflecting a more heterogeneous population that presents with HI.

## **Introductory Performance Improvement Evaluation to Optimize Door to Needle Time for IV Thrombolysis Therapy in Acute Ischemic Stroke**

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### **Background**

Acute ischemic stroke is a serious medical emergency requiring rapid evaluation and treatment. Patients experiencing acute ischemic stroke quickly and efficiently to maximize clinical outcomes. Door to Needle Time (DNT) for IV tPA administration in acute stroke, has become an important quality metric. Literature has shown that earlier administration of IV tPA improves patient outcomes with a primary goal of DNT of less than 60 min.

### **Hypothesis**

The goal of this performance improvement study to assess current trends in DNT time and investigate any opportunities for quality improvement in current tPA ordering, supply, and administration.

### **Methods**

A retrospective chart review of all ischemic stroke patients who received IV tPA during March 2014 to March 2015 was performed.

### **Results**

Ten patients received tPA during the study period. Average time from order entry to tPA administration was  $25.6 \pm 11.2$  minutes (Range: 9–49 min). Order-to-administration times were similar for events occurring during day ( $22.5 \pm 8.3$  min, n=4) and evening shift ( $27.7 \pm 4.2$  min, n=6). Times were also comparable for events occurring on weekends versus weekdays.

### **Conclusion**

With the recent implementation of the Joint Commission's "Target Stroke" campaign, an effort to increase rapid tPA use in acute stroke, it is becoming standard practice to monitor DNT. One area in which tPA process could be streamlined is rapid medication order entry and reconstitution within the pharmacy to allow more prompt tPA administration. Our facility implemented a "Stroke Alert: tPA" procedure within the pharmacy to further improve order-to-administration time. Other performance improvement considerations have been identified, such as a formal multidisciplinary stroke protocol, standardization of documentation of time of arrival, and rapid communication of patient weight to expedite dosing calculations in anticipation of tPA order. Future study and continued quality improvement assessment is needed to build upon current data and optimize processes as the stroke program continues to grow.

## **Robotic Partial Nephrectomy in 119 Consecutive Cases**

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### **Background**

Partial Nephrectomy improves all-cause mortality in patients with renal cell cancer (RCCA) without compromising oncological results, and Robotic Assisted Laparoscopic Partial Nephrectomy (RALPN) is the Standard of Care in this technique. We report our results of RALPN in 119 consecutive cases.

### **Hypothesis**

RALPN does not significantly reduce renal function compared to baseline.

### **Methods**

All patients with renal masses seen at our institution since September 2006 have been offered potential RALPN providing a) no significant tumor thrombus; b) > 50% of the affected kidney by CT/MRI was potentially salvageable; c) no limiting nodal metastases; and d) no specific contraindications to surgery. MDRD calculated GFR was measured at baseline and at >1 month post operatively. Statistical analysis was performed in Excel using Students t-Test, and the Chi-squared analysis, as appropriate.

### **Results**

119 patients underwent RALPN for apparent RCCA between October 2006 and December 2015. Of these, 59 were men and 60 were women. The average age, size, and Nephrometry Score was 59.3 years, 4.3 cm (Range: 1-10cm), and 6 (Range: 4-12), respectively. Follow-up GFR one or more months following surgery compared to Baseline was not significantly different ( $p = 0.09$ ). Baseline GFR/Follow-up GFR was tested for significance in the following comparisons: baseline GFR  $\leq 60$  versus baseline GFR  $> 60$  ( $p = 0.10$ ), size  $\leq 4$ cm versus size  $> 4$ cm ( $p = 0.14$ ); and Nephrometry Score  $\leq 6$  versus Nephrometry Score  $> 6$  ( $p = 0.36$ ).

### **Conclusion**

Within our study, RALPN did not degrade GFR compared to baseline. Furthermore, size  $> 4$ cm, baseline GFR  $\leq 60$ , and Nephrometry Score  $> 6$  were not associated with lower GFR post operatively. Our study suggests that RALPN results in desirable renal functional outcomes and might be considered when more than 50% of the affected kidney can be spared regardless of renal mass size.

## Cost of Care for the Surviving Periviable Neonate

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### Background

Preterm births impose a heavy financial burden on the U.S. health care system, costing more than \$26 billion in 2005. Only 6% of preterm infants are born <28 weeks gestation; however, this population accounts for 1/3 of the total cost. Mortality is high in the extreme premature infant with rates of 74%, 45%, and 28% at 23, 24 and 25 weeks gestation respectively. In addition, severe disabilities are evident in 1/3 of the survivors at 6 years of age. Very little is known regarding the current costs of caring for these periviable infants during their initial hospitalization.

### Hypothesis

Objective:

To perform an analysis of financial charges and costs for the initial hospital care of the surviving periviable neonate (23-25 weeks gestation) admitted in a 42 month period at a single tertiary care NICU.

### Methods

Retrospective chart analysis of the medical records and financial data for neonates who survived of 23-25 weeks gestational age cared for in a single tertiary NICU from 1/1/2012-7/1/2015.

### Results

Gestational age	23 weeks (n=12)	24 weeks (n=17)	25 weeks (n=22)
Survivors	7 (58%)	11 (65%)	22 (100%)
Avg. Length of stay (days)	114 +/-11	111 +/-13	91 +/-23
Avg. Birthweight (grams)	551 +/- 106	679 +/- 78	741 +/- 132
Total Charges	\$895,000+/-101,758	\$822,000+/- 120,262	\$694,000+/-200,293
Direct Hospital Cost	\$226,000+/-25,700	\$199,900+/-34,450	\$168,550+/-54,550

### Conclusion

This study defines the hospital cost and distribution of charges for the periviable neonate during their initial hospitalization providing essential information for administrators in this new era of value-based population management and guides clinicians in using economic information for quality improvement and building a foundation for future cost management.



## **Tumor-to-Tumor Metastasis (TTM) Occurring in the Penis**

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### **Background**

Isolated tumor metastases to the penis are usually associated with bladder or prostate cancer primaries, although rectal cancer ranks third overall in frequency of origin. In most cases, this clinical situation portends a poor prognosis. Local excision of the lesion with penile preservation is usually recommended if feasible, in order to spare the patient further indignity in the final stages of advanced disease. The phenomenon of tumor-to-tumor metastasis (TTM) has been described for metastatic lesions involving a variety of tumor types; the common denominator appears to be spread of a primary to a richly-vascularized recipient tumor bed. We present a case of an isolated prostate cancer metastasis to a myointimoma occurring on the patient's glans penis.

### **Case Presentation**

A 69-year-old man with a diabetic neuropathic bladder was treated with external beam radiotherapy for localized prostate cancer. He was dependent upon intermittent catheterization for bladder emptying, and subsequently developed radiation cystitis, manifested by recurrent bouts of hematuria, which gradually cleared within a year, and his PSA remained low. His clinical course was further complicated four years later, when he developed a 1 cm fleshy lesion on his glans penis, which was locally excised, along with a circumcision. Pathology showed this lesion to be a myointimoma, a type of benign fibroepithelial tumor; however, the base of the lesion contained metastatic prostate cancer. A radiological evaluation, including bone scan and CT, showed no other evidence of tumor spread, and his PSA remained stable; thus, hormonal therapy was deferred. He has had no evidence of tumor recurrence after one year.

### **Discussion**

The above is an example of TTM occurring in the penis. Although TTM usually involves two different malignant tumors, in this case, the recipient tumor was benign. Conceivably, chronic irritation of the penis from repeated catheterizations may have promoted both the myointimoma and metastatic prostate cancer.

## **A Quality Improvement Project: Improving Patient Safety by Standardizing the Handoff Process**

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### **Background**

Handoffs involve transfer of patient information from one person to another. This point of transition is a source of adverse events and medical errors. It has been shown that a standardized handoff reduces the rate of medical errors. The ACGME requires institutions to have training in patient handoff skills.

### **Hypothesis**

Implement a standardized handoff that increases use of key elements of a good handoff.

### **Methods**

Before implementation of the IPASS handoff, surveys evaluating the current handoff system were given to resident and attending physicians. Baseline data regarding medical errors and adverse events was obtained. Check offs were done regarding current inclusion of key elements included in IPASS. Resident and attending physicians attended three hours of teaching focusing on team communication and use of the IPASS system. Handoffs were observed post-training to assess how frequently the key elements were included.

### **Results**

Resident and attending physicians were not satisfied with the current handoff system. Both groups believed we would benefit from directly observed handoffs with feedback by the attending physicians. Attending physicians favored the quality of the current printed handoff tool but it was found to be of poor quality by resident physicians. Both groups felt that there have been adverse events as a direct result of the handoff system. We were able to show improvement in all areas of the standardized handoff. There was a slight increase in length of handoffs. We found a total of 62 adverse events reported over 4 years.

### **Conclusion**

Implementing a standardized handoff curriculum increases the inclusion of key elements of a safe patient handoff. While the amount of time for each handoff increased slightly, this is likely due to the increase of synthesis by receiver, which was absent prior to implementation of the IPASS system. Our study was performed in a rural setting and was driven by a resident.

## **Pregnancy After Endometrial Ablation Complicated by Placenta Accrete**

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### **Background**

Pregnancy after endometrial ablation is a rare event, occurring in approximately 0.7% of cases. Placenta accreta occurs in 0.2% of all pregnancies. The incidence of placenta accreta after endometrial ablation has not been estimated. Several poor pregnancy complications may be anticipated for a pregnancy occurring after endometrial ablation, including abnormal placentation.

### **Case Presentation**

In this case, a 37-year-old Gravida 4, Para 3-1-0-3 presented for prenatal care 8 years after endometrial ablation. This patient had 3 previous uncomplicated vaginal deliveries at 37 to 38 weeks, and one stillbirth at 29 weeks due to placental abruption, all prior to her endometrial ablation. The patient's current pregnancy was complicated by buprenorphine maintenance for opiate dependence, tobacco use, and hypothyroidism. No definite evidence for placenta accreta was found on any ultrasound. A planned cesarean was performed at 36 weeks and 4 days for breech presentation and suspected placenta accrete despite the lack of ultrasonographic evidence. At the time of surgery, the decision was made to perform a cesarean hysterectomy with the placenta left in situ after attempted and failed removal of the placenta.

### **Discussion**

Endometrial ablation has become increasingly popular for the treatment of dysfunctional uterine bleeding, but it also predisposes patients to pregnancy complications, including abnormal placentation. Physicians should be aware of these pregnancy complications and risks in order to properly manage the patient. Physicians should also provide appropriate counseling about the risks and likelihood of adverse outcomes of pregnancy after endometrial ablation and the necessity of contraception.

## **Prevalence of Ideal Cardiovascular Health Metrics in Children & Adolescents: A Systematic Review**

Justin M. Pacor, Adnan Younos, Rehan Malik, Muhammad Aziz, Rameez Ahmad, Shozab Ali, Oluseye Ogunmoroti, Chukwuemeka Osondu, Lara Roberson, Muhammad A. Younos, Erica S Spatz, Salim Virani, Khurram Nasir  
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### **Background**

Several emerging studies have examined the prevalence and trends of the American Heart Association's ideal cardiovascular health (ICVH) metrics in children. In this systematic review of CVH metrics in children and adolescents, we aggregated available evidence amongst published reports to examine prevalence of these metrics across studies.

### **Hypothesis**

N/A

### **Methods**

A MEDLINE database search was conducted for studies published between January 2010 and July 2015. To be included in the review, studies had to report prevalence data on at least four of the seven metrics included in the ideal cardiovascular health concept.

### **Results**

BMI and diet were the only metrics for which all studies reported prevalence of ICVH. Definitions for blood pressure (<90th percentile), total cholesterol (<170 mg/dL), glucose (<100 mg/dL) and BMI (<85th percentile) were largely consistent across studies. Definitions for smoking status, physical activity and diet were more variable. The prevalence of ideal blood pressure was the highest of all the 7 CVH metrics/factors. Both blood pressure and BMI reported a prevalence of ideal >50% uniformly across all studies. By contrast, the healthy diet has the lowest prevalence of ideal CVH metrics. Prevalence of ideal physical activity was also low, but the most variable.

### **Conclusion**

Overall few studies have assessed ideal CVH status in children and adolescents (n=6). Ideal diet and physical activity had the lowest prevalence among CVH metrics. Our study findings suggest focused efforts on standardizing assessment of these metrics as well delineating strategies to achieving ICVH among children and adolescents.

## **Effects of Maternal Polydrug Exposure on Fetal Neonatal Abstinence Syndrome Severity**

Brooke Andrews, Sean Loudin

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### **Background**

Approximately 14% of neonates born at Cabell Huntington hospital have Neonatal Abstinence Syndrome (NAS), due to withdrawal from substances they were exposed to during gestation. This study's purpose is to determine how polydrug exposure of opioids and other substances of abuse affect hospital length of stay (LOS) and treatment.

### **Hypothesis**

The hypothesis is that LOS and the necessity of administration of second-line pharmacological therapy, Clonidine, for NAS will be dependent on combinations of drugs used during pregnancy.

### **Methods**

A retrospective chart review was performed on patients treated for NAS at CHH between January and June of 2014. Drug exposure was determined from reported maternal drugs and umbilical cord blood screens. LOS, Finnegan scores, and the use of Clonidine, were recorded.

### **Results**

Results found that of the 90 babies that displayed NAS during this time, 83% were treated with methadone. Of this population, 27% were reported to have only a single opioid drug exposure, while the other 73% were exposed to polydrug combinations including multiple opioids, (32%), and opioids plus one or more of the following, Benzodiazepines 8.0%, Cocaine 6.7%, Cannabinoids 27%, and Tobacco 41.3%. Average LOS was 32.8 days for all treated babies; LOS was not affected by the type or number of opioids, or tobacco use. Cannabis use during pregnancy resulted in a lower LOS 29.2  $\pm$ 7.0 days, while both cocaine (50.4  $\pm$ 13.7 days) and benzodiazepines (39.7  $\pm$ 13.2 days) increased LOS. Adjunct clonidine treatment was required in 14.6% of all NAS neonates. Clonidine administration was required more often to treat NAS with either cocaine (60%) or benzodiazepines (33%) exposed neonates.

### **Conclusion**

These results show in conclusion that babies exposed to polydrug combinations, particularly when exposed to Cocaine and Benzodiazepines, can be expected to have a significantly longer LOS as well as a higher likelihood of requiring second-line pharmacological therapy.

# **Characterization of Renal Cytotoxicity and Oxidative Stress Induced by the Radiocontrast Agent Diatrizoate (DA) in a Human Kidney Cell Line**

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## **Background**

Contrast-induced nephropathy (CIN) is the third most common cause of acute renal failure in hospitalized patients. CIN is the result of exposure to iodinated contrast media which are required for many diagnostic procedures including: computed tomography, angiography, and cardiac catheterization. Approximately half of CIN cases occur in patients undergoing percutaneous coronary intervention and cardiac catheterization. The likelihood of acute renal injury greatly increases (40%) in patients with preexisting diminished renal impairment. Although the exact mechanism of toxicity of CIN has not been fully elucidated, three potential mechanisms have been supported: oxidative stress, changes in renal hemodynamics, and direct cytotoxicity.

## **Hypothesis**

This project tested the hypothesis that the radiocontrast agent diatrizoic acid (DA) will induce cellular cytotoxicity and oxidative stress in the absence of hemodynamic influence.

## **Methods**

Immortalized human adult proximal tubular epithelial (HK-2) cells (ATCC) were incubated with clinically relevant concentrations (0-111.0 mg l/mL) of DA for 24 or 48 hours. All treatment groups have a minimum n of 5. Viability was assessed using the conversion of (3-(4,5-Dimethylthiazol-2-yl)-2,5-Diphenyltetrazolium Bromide) (MTT) to formazan. Oxidative stress was quantitated using Western blot analysis for 4-hydroxynonenal (4-HNE), a byproduct of lipid peroxidation.

## **Results**

Toxicity was evident in HK-2 cells exposed to 27.5-110.0 mg l/ml relative to vehicle control ( $p < 0.05$ ) at 24 and 48 hour treatment groups as measured by the MTT assay. A statistically significant ( $p < 0.05$ ) increase in 4-HNE was observed in HK-2 cells exposed to 55.5 and 111.0 mg l/mL DA at 24 hours when compared to vehicle control.

## **Conclusion**

This study established that HK-2 cells can be used as a model to examine DA renal cytotoxicity. HK-2 cells were sensitive to clinically relevant concentrations of DA and undergo oxidative stress as part of cell toxicity. (Supported partially by NIH Grant P20GM103434 to the West Virginia IDeA Network for Biomedical Research Excellence).

**Observational Study of the Structured and Monitored Management of Chronic  
Non-Malignant Pain with Opiates in a Rural Primary Care Office in a High Opiate  
Abuse Region**

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Family and Community Health, Joan C. Edwards School of Medicine

**Background**

The use of opioid medication for non-malignant chronic pain (NMCP) and unintentional overdose deaths increased dramatically over the last twenty years. There have been regulatory changes implemented to reduce overdose death and opioid misuse. Included in these changes are several best practice guidelines regarding opioid prescribing in NMCP. Compliance with these guidelines has been poor.

**Hypothesis**

A new care delivery method is associated with a portion of patients choosing to stop opioids for NMCP.

**Methods**

A retrospective observational study was conducted on all patients of a single civilian rural provider exposed to a new care delivery method over the first 18 months of delivery. The method was applied to all patients treated for NMCP with opioid medication. The method involved establishing a clinic within a practice to address NMCP. Patients had to attend the clinic once every three months. Self-reported questionnaires were used to generate standardized data for the medical history, perceived pain, functional status, mood and the risk of diversion. A template guided note incorporated this data in order to form treatment goals and to monitor drug screens, controlled substance databases and pain contract compliance. Standardized educational materials were given at each visit.

**Results**

A total of 36 patients were observed. There were 32 at the start of observation and 4 that were added. Of the 32 patients at the start 37.5% elected to wean off opioids, 53.1% engaged the new method and 9.4% transferred care. Mean morphine equivalents mg/day was lowest in the group that stopped and highest in the group that transferred (range 17 to 36).

**Conclusion**

A large portion of patients exposed to this care delivery method chose to change to non-opioid forms of treatment. This method can reduce the number of people requiring opioids and improve compliance with opioid prescribing guidelines.

## **Phenotypic Plasticity associated with Hsp90 inhibition**

Abdalla Lawag and Vincent Sollars

Biochemistry and Microbiology

### **Background**

The process of canalization whereby phenotypic traits are buffered against stochastic fluctuations to preserve the evolutionarily advantageous “normal” level can be potentially exploited during cancer progression. Release of canalization through pharmacologic or genetic down-regulation of Hsp90 removes this buffer and increases variation, allowing for rapid changes in traits as evidenced in *Drosophila*, *Arabidopsis*, and maize. If cancer is viewed as a Darwinian struggle of the premalignant cell to acquire the hallmarks of a fully malignant cell or be extinguished, then increasing variation or heterogeneity has a beneficial effect on the fitness of the premalignant cell. It is the goal of this work to test the hypothesis that Hsp90-derived canalization, though its ability to buffer phenotypic variance and thus reduce cell plasticity, is involved in hematopoietic cell differentiation. Furthermore, we wish to determine if the canalization mechanism has an epigenetic component. We are currently using a murine hematopoietic stem cell culture system, EML cells, to investigate this hypothesis. EML cells have been induced to differentiate into macrophage and granulocyte lineages with and without pharmacologic inhibition of HSP90 through 17-AAG.

### **Hypothesis**

Hsp90-derived canalization, though its ability to buffer phenotypic variance and thus reduce cell plasticity, is an important mechanism controlling cellular differentiation in the hematopoietic system.

### **Methods**

Methods employed in this study include immunophenotyping using flow cytometry, protein assays such as western blotting, and cellular stress assays. All studies were employed using the in vitro hematopoietic stem cell model system of EML cells.

### **Results**

Phenotypic plasticity is induced by inhibition Hsp90 and various forms of cellular stress suggesting that cellular stress may aid in cancer progression through this mechanism.

### **Conclusion**

Loss of canalization could be a potentially powerful mechanism driving cancer progression. Fully understanding the mechanism involved would allow for new therapeutic insights and provide vital information regarding the use of HSP90 inhibitors.



## **A Pilot Time-Motion Study of Academic Family Physician's Patient Care Activity**

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Family and Community Health

### **Background**

Time-motion studies were initially developed for improving the efficiency of industrial processes through continuous and independent observation of the subjects. Time-motion studies have been performed in order to determine the efficiency of physicians. They have also been used in academic clinical setting to assess the work of both residents and teaching physicians.

### **Hypothesis**

This study aims to examine how family physicians utilize their time during a patient care block in their academic practices. This study provides a unique perspective for a pre-clinical medical student into the daily activities of various family physicians because the student directed and conducted the data collection.

### **Methods**

I followed 7 Family Medicine attending physicians over a four-hour time block using a Microsoft Access time-motion program developed by the Department of Health and Human Services. As a physician changed his or her activities, the predominant activity and the time spent were recorded. There were a total of forty-two activities possible, including physical exam, talking to patient, and record entry.

### **Results**

The data showed the both individually and combined, Family Medicine physicians spent the most activity-specific time in patient conversation, EMR documentation, and conversation with colleagues/staff. The data is currently being analyzed to determine time spent in activity areas (computer, paper, patient, other).

### **Conclusion**

Despite the significant proportion of time spent on the computer, family physicians spent more time on direct patient interaction. This method was a successful way to provide this medical student a realistic look at the daily patient care activities of Family Medicine physicians and could be easily replicated in a variety of other settings and specialties.

## **Achieving Complete Response on Post-Therapy PET Scan Might Inversely Correlate with Survival in Small Cell Lung Cancer.**

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### **Background**

In most lymphomas, improving patient outcome rely on the assessment of response to therapy. Functional imaging with 18-fluoro-deoxyglucose (FDG) positron emission tomography (PET) increases sensitivity and specificity of disease assessment, predicts outcome and directs future management. Lately, PET-scan is more utilized in small cell lung cancer (SCLC) both for initial staging and to assess response to therapy. However, there are very few data in the literature that evaluate the prognostic value of post-therapy response on PET-scan in SCLC.

### **Hypothesis**

This study aimed to assess whether achieving complete response (CR) on post-therapy PET-scan can predict outcome in SCLC patients.

### **Methods**

This is a retrospective chart review of SCLC patients who received their first-line chemotherapy between January-2007 and December-2013 at Edwards Comprehensive Cancer Center in Huntington, West Virginia. Complete data on age, sex, race, cancer stage, histologic grade, pre- and post-therapy PET-scans, chemotherapy, and radiotherapy were available. CR was defined as either 100% drop in FDG uptake or no detected FDG uptake on post-therapy PET-scan.

### **Results**

Out of 178 reviewed charts, fifty patients met the inclusion criteria. Among them, 46% had Limited Stage Small Cell Lung Cancer (LS-SCLC), and 54% had Extensive stage small cell lung cancer (ES-SCLC). All Patients were treated with platinum-based chemotherapy in addition to concurrently radiation therapy for LS-SCLC group. Eleven patients (22%) achieved CR.

Using COX regression model, we evaluated the correlation between achieving CR and survival outcome. Achieving CR was significantly correlated with worse outcome in ES-SCLC group (HR =2.70; 95%CI:1.26-5.81; p=0.01).

### **Conclusion**

Unlike lymphomas, achieving CR on post-therapy PET-scan in SCLC was associated with worse survival outcome. This might indicate that in aggressive SCLC, despite excellent response to first-line therapy, the prognosis is still dismal. These results suggest that further prospective studies are warranted to identify the clinical rule and evaluate the cost effectiveness of post-therapy PET-scan in SCLC.

## **Tobacco Use and Associated Factors Among Patients Presenting to a Psychiatric ER**

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### **Background**

According to the CDC, 17.8% of US adults smoke cigarettes; however, 31% of all cigarettes are smoked by adults with mental illness. Previous studies have examined the elevated rates of tobacco use among different psychiatric diagnoses and in specific populations and treatment settings. However, there has been little study of tobacco use in patients in the psychiatric (ER) setting. In this study, we examined the prevalence of tobacco use and associated factors among patients presenting to a psychiatric ER.

### **Hypothesis**

Tobacco use may be associated with particular psychiatric diagnoses, including depression and anxiety disorders.

### **Methods**

226 consecutive psychiatric ER patients from an academic medical center were examined by retrospective chart review. Tobacco use data was missing for 23 subjects, which resulted in 203 subjects. Data included demographics, clinical variables, tobacco use, other substance use, psychiatric diagnoses, medications, and family history. Data was entered into SPSS and analyzed, using student t tests and Fisher exact tests to compare groups as appropriate.

### **Results**

Of the 203 patients, 49.8% (n=101) reported using tobacco. Among these, alcohol use was reported in 32.8% (n=66), and illicit substance use in 25.1% (n=51). Active suicidal ideation (SI) was reported by 11.8% (n=24). Tobacco use was significantly associated with any other substance abuse ( $p<0.001$ ) as well as a family history of alcoholism ( $p=0.006$ ), prior psychiatric hospitalization ( $p=0.023$ ), having active SI ( $p=0.009$ ), and dementia ( $p=0.014$ ). There was no association between tobacco use and age, gender, race, marital status, employment or living situation.

### **Conclusion**

Tobacco use among psychiatric ER patients is much higher than that of the general population. There is a very high association of substance use disorders with tobacco use. The associated variables of active SI, prior psychiatric admissions and other substance use disorders suggests the tobacco users may be a more psychiatrically ill group.

## **Reciprocal regulation of IL-17 and IL-22 secretion by CD4 T cells through the Aryl Hydrocarbon Receptor**

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### **Background**

CD4 T cells are critical for host defense against microorganisms and direct immune responses by differentiating into specialized subsets. While Th17 cells secreting IL-17 and IL-22 contribute to vaccine immunity, they have also been implicated in autoimmune inflammation. Our goal is to understand how endogenous factors regulate Th17 cell cytokine secretion. Murine models have demonstrated that the aryl hydrocarbon receptor (AhR) can promote Th17 differentiation; however, it also has anti-inflammatory effects during systemic immune responses, suggesting that pleiotropic effects of AhR are dependent on the ligand and/or cell type. Tryptophan metabolites have recently been identified as endogenous AhR agonists that can modulate T cell immunity. Here, we examined a potential link between tryptophan metabolism and the AhR on cytokine secretion by human CD4 T cells.

### **Hypothesis**

Tryptophan metabolism inhibits Th17 cell differentiation in an AhR-dependent manner.

### **Methods**

Naïve human CD4 T cells were purified from peripheral blood of healthy volunteers, and cultured under Th17 conditions (anti-CD3, anti-CD28, IL-6, TGF-beta, +/- IL-1beta, +/- IL-23) with excess L-tryptophan (25ug/mL), the tryptophan metabolite L-kynurenine (25ug/mL), or an AhR inhibitor. CD4 T cell cytokine production and transcription factors were measured by ELISA and PCR, respectively.

### **Results**

Tryptophan and kynurenine significantly decreased IL-17 secretion by CD4 T cells, correlating with decreased expression of ROR-gamma t in T cells. The AhR antagonist did not modulate IL-17, suggesting that kynurenine was functioning independently of the AhR. In contrast, the AhR antagonist potently decreased IL-22 secretion, suggesting the AhR is required for optimal IL-22 production in human CD4 T cells.

### **Conclusion**

These data suggest that IL-17 and IL-22 production are reciprocally regulated in human CD4 T cells by the AhR, and have implications for treating chronic inflammatory diseases.

## **How Safe is Healthcare? Patient and Family Exposure and Perceptions**

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### **Background**

Complexity of health care is progressively increasing and with that the number of medical errors and adverse events are increasing to an alarming level. The purpose of this study is to assess the public perception of healthcare safety and quality of care and examine the association between the perception regarding healthcare safety and the prior exposure to medical errors and adverse events.

### **Hypothesis**

The exposure to medical errors negatively impacts the perception regarding the safety of the healthcare system.

### **Methods**

The study is a cross-sectional online survey. The online survey included basic demographics and a series of questions related to the knowledge and perception about healthcare safety and personal healthcare experience. To reduce the possible selection bias during the survey process, a random sample (50%) was used for the regression analysis for the predictive factors that healthcare is safe,

### **Results**

504 respondent completed the survey. 424 respondents (84%) reported one or more exposure to medical errors or adverse events. 52.9% knew somebody who died or suffered permanent damage because of a medical error. 70.7% of the respondents thought that medical errors are occurring less frequently than 10 years ago. 89.6% of the respondents thought that healthcare is a safe industry. Looking at Factors Predicting the Perception that Healthcare is Safe, there was no clear correlation with the exposure to medical errors except for surgical complications exposure (p-value=0.013, OR 21.4)

### **Conclusion**

The study showed that respondents felt that healthcare is safe, regardless of their exposure to medical errors or adverse events. There is a need to educate the public and healthcare workers regarding the medical error rate and the healthcare safety to help make patients and their families become partners in their care and to help healthcare workers better understand the limitations of healthcare processes that may affect patient safety and outcomes.

## **Effects of Opioid Abuse Potentially Mediated by Epigenetic Histone Modifications**

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### **Background**

Opioid abuse is increasing throughout the country, but the state of West Virginia has seen a particularly serious rise in addiction and its complications. Of particular concern is the incidence of opioid abuse during pregnancy, and the deleterious effects of these drugs on fetal development. Initial studies suggest a potential relationship between epigenetic modifications and symptoms of drug withdrawal in neonates, known as Neonatal Abstinence Syndrome (NAS). Buprenorphine is an agent used for treatment of withdrawal symptoms in neonates suffering from NAS, as well as a maintenance therapy for pregnant women addicted to other opioids. This agent is a mixed partial opioid agonist-antagonist: an agonist at the mu-opioid receptor (MOR), and an antagonist at the kappa-opioid and d-opioid receptors (KOR, DOR). Opioid receptors are widely distributed in the human body, and thus, opioid agents and withdrawal impact multiple systems.

### **Hypothesis**

The purpose of this project is to identify potential epigenetic regulatory mechanisms induced by opioid exposure, and the subsequent effects on the nervous system and associated structures.

### **Methods**

Our epigenetic profiling focuses on histone post-translational modifications (PTMs) and chromatin composition. We treated rat brain micro-vascular epithelial cells (RBMVEC) with 50 ng/mL of buprenorphine, a dose based on levels found in umbilical blood of neonates who developed NAS in Southern West Virginia, and collected proteins at varying treatment times. We used Western blot analysis to check for the presence of a subset of histone PTMs.

### **Results**

Our results suggest that opioids exposure alters the cell's epigenetic profile, and demonstrate a potential relationship between histone PTMs, chromatin-associated proteins and prolonged opioid exposure.

### **Conclusion**

As the long-term effects of opioids on chromatin structure/composition remain understudied, these results are the first step towards understanding the epigenetic mechanism of action of buprenorphine and how it can affect human development.

**IMPROVING HEALTH CARE OUTCOMES FOR HOMELESS APALACHIAN CHILDREN: Care Coordination by Parents of Children with Special Health Care Needs. A West Virginia CARES (Coordination Access to Resource and Emergency Services) Project from the Healthy Tomorrows Partnership for Children Program.**

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Department of Pediatrics, Joan C. Edwards School of Medicine at Marshall University

**Background**

Homeless children are a complex and vulnerable subset of children with special health care needs (CSHCN) who are at increased risk for behavioral and academic problems and fragmented medical care.

**Hypothesis**

The project will determine if care coordination provided by parents of CSHCN can improve health care outcomes, including ADHD, for homeless children entering the City Mission.

**Methods**

From July 2007 through November 2011, all homeless children who entered the City Mission met with a care coordinator (CC) who assisted parents to complete a visit survey documenting recent healthcare needs, improvement measures and ADHD status and treatment.

**Results**

The information was then provided to a pediatric resident and attending physician in Continuity Clinic. The data comparing the first and second time periods of the project were analyzed with chi square (or Fisher's exact when appropriate).

A total of 203 encounters were recorded from 2007-2008(24 months), and 217 from 2009-2011 (28 months), representing of 327 children.

Table 1. Comparison of Positive Responses from WV CARES Visit Survey

	2007-2008	2009-2011	P Value	
1. ER visit in last 3 months	21%	17%	0.23	
2. Hospital admission in last 3 months	10%	2%	0.08	
3. Illness causing school or work absence in last 3 months		40%		25%
				0.006
4. Inability to find work due to child's illness in last 3 months	16%	2%	<0.001	

During the five year period, 37 of 115 (32%) school aged children were identified by parents with ADHD, but only 12 (32%) received medication

**Conclusion**

During the last 28 months of the program there was a significant decrease in reported illnesses causing school or work absence and inability to find work due to the illness in the child. A trend toward decreasing hospital utilization was also noted. ADHD is a common, often untreated, condition in homeless school-age children.

## **Abstract: Evaluation of Therapy Dog Visits on Healthcare Worker Stress**

Dr. Rebecca Wolfer, Maria Espiridon, Ryan Clagg

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### **Background**

Therapy dogs and their volunteer owners have roamed the hallways of hospitals since 1976. The healthcare benefits resulting from therapy dog visits in a hospital setting have been well studied. The purpose of this project is to evaluate healthcare workers' perceptions of therapy dogs in the workplace and the dogs' effects on the healthcare employees' stress levels through a brief and anonymous online survey following the dogs' visits.

### **Hypothesis**

We hypothesize that having the therapy dog program at Cabell Huntington Hospital improves healthcare worker stress and employees will wish to continue the therapy dog program. This may help to improve employee satisfaction leading to improved quality of work and patient care at Cabell Huntington Hospital.

### **Methods**

Five therapy dogs and their owners visited all floors and offices of Cabell Huntington Hospital at regular intervals throughout the month. Will contact all Cabell Huntington Hospital employees by email and asked for their voluntary completion of a 14 item survey. The survey was distributed to 2675 employees via SurveyMonkey.

### **Results**

The survey was released to 2675 employees of Cabell Huntington Hospital and 228 (8.52%) responses were completed and returned online. The majority of employees (n=112, 52.34%) reported that they were satisfied with the amount of time they had with the therapy dog. Most responses (n=106, 48.18%) strongly agreed with the statement "I find the therapy dog program at Cabell Huntington Hospital beneficial to myself, the staff, the patients and their family members." Largely positive responses were provided in the 15 item survey, including five free-response sections.

### **Conclusion**

The Cabell Huntington Hospital therapy dog program has been met with largely positive responses from employees. Hospital staff benefited from the therapy dogs through stress reduction and increased productivity. Employees also shared several additional scenarios that would benefit from therapy dogs that we can incorporate into future therapy dog visits.



## **Body mass index as a predictor of tibial component size in unicompartmental knee arthroplasty**

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### **Background**

Unicompartmental knee arthroplasty (UKA) is an increasingly popular alternative to total knee arthroplasty (TKA). Obesity has classically been regarded as a contraindication to UKA. However, more recent evidence is unclear regarding the contribution of obesity to poor outcome in UKA, and a number of studies have found that obesity has no effect on UKA outcome. Polyethylene wear is a critical mechanism of failure, for which the design and size of the prosthesis has been shown to be an important determinant. Studies in TKA prostheses have shown that an increased body mass index (BMI) to tibial component size ratio is associated with increased polyethylene wear. Currently, little is known about the relationship between BMI and implant size in UKA. The proposed study aims to determine if BMI correlates with tibial component size in UKA.

### **Hypothesis**

The authors hypothesize that height, weight, and BMI positively correlate with tibial component size.

### **Methods**

Height, weight, BMI, and tibial component size was recorded from the charts of 80 patients who underwent unicompartmental knee arthroplasty by a single surgeon (FC) from 2011 to 2015. Regression analysis was performed to determine if there was a correlation between height, weight, or BMI and tibial component size.

### **Results**

Tibial component size was positively correlated with height ( $R^2=0.7373$ ) but not weight ( $R^2=0.2484$ ) or BMI ( $R^2=0.0059$ ).

### **Conclusion**

Larger tibial components are typically used in taller patients; therefore the risk of having a high BMI:component size ratio is mitigated in taller patients. These patients may be at a lower risk of developing polyethylene wear.

## **Role of antioxidants in kinase-dependent regulation of mitochondrial energy metabolism**

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### **Background**

Metabolic syndrome, which leads to other disorders such as obesity, cancer, and type 2 diabetes, is quickly becoming a world-wide pandemic. Metabolic syndrome can be attributed to increased oxidative stress generated during mitochondrial dysfunction. One of the non-receptor Src family tyrosine kinases, Fyn, has been shown to play a significant role in metabolic syndrome and is activated by oxidative stress. The mitochondrion is not only important in energy production, but it also plays a major role in the production of reactive oxygen species (ROS), as a byproduct of oxidative phosphorylation (OXPHOS). Fyn kinase overstimulates OXPHOS by Tyr phosphorylation of the subunits.

### **Hypothesis**

Mitochondrial translation machinery plays an essential role in the synthesis of 13 subunits of OXPHOS complexes; therefore, Fyn-dependent stimulation of mitochondrial translation results in increased ROS generation and ultimately the progression of mitochondrial dysfunction.

### **Methods**

Human hepatocellular carcinoma cell lines, HEP3B and HEPG2, were used to determine the effects of Fyn kinase on mitochondrial translation and OXPHOS at varying nutritional conditions. Fyn-dependent generation of ROS measured in cells treated with natural antioxidants and Src kinase inhibitor, SU6656.

### **Results**

The Fyn-dependent overstimulation of OXPHOS results in overproduction of ROS and ultimately can result in mitochondrial dysfunction. Natural antioxidants and Src kinase inhibitor treatments of cells reversed the effects of OXPHOS overstimulation and ROS production.

### **Conclusion**

The overstimulation of OXPHOS can eventually lead to mitochondrial dysfunction and to the development of diseases, such as metabolic syndrome. Antioxidant treatments help to reduce the effects of Fyn kinase on OXPHOS; therefore, reducing the amount of ROS released and decreasing the probability of mitochondrial dysfunction and the development of diseases.

## **A Survey of African American Men in Chicago Barbershops: Implications for the Effectiveness of the Barbershop Model in the Health Promotion of African American Men**

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### **Background**

Barbershops have been used to target African American (AA) men for health screenings, interventions, and research. Few studies explore the sociodemographic characteristics of clients and barbers, and few have evaluated the clients' comfort in receiving health information and screenings. Additionally, barbers' perceived ability to influence the health decisions of AA men is unknown.

### **Hypothesis**

Barbershops have a limited reach to segments of AA men.

### **Methods**

AA male clients and barbers were surveyed in barbershops within AA neighborhoods throughout Chicago, Illinois. We assessed sociodemographic characteristics and attitudes towards receiving physical and mental health education and screenings in non-clinical settings. Barbers were surveyed regarding their perceived ability to influence the decision-making of AA males by age group.

### **Results**

The mean age for respondents was 39.5 years (range 23.5-70). The 127 participants had similar high school completion, poverty and unemployment rates as AA residents in their neighborhoods. 62.7% of subjects had received physical health education or screening within the past year. Notably, only 13.5% received mental health education or screening within the past year.

Overall, 89.8% preferred receiving physical health services at a medical doctor's office, while 79.4% preferred receiving mental health services at a mental health professional's office. Nevertheless, the next preferred locations were barbershops and churches.

Barbers most often serve males ages 18-39, and 66.7% stated men over 65 years old were the least served age group. Overall, barbers did not believe they could influence the decision-making of AA men. At best, 33% felt they could influence 18-29-year-old men.

### **Conclusion**

Barbershops serve AA men representative of the neighborhood demographic. Barbers reach a small population of older men and largely feel they are incapable of influencing the decisions of AA men. Future studies must consider other locales for accessing older AA men and evaluate the feasibility of physical and mental health interventions and screenings within barbershops.







