



**THE 34<sup>TH</sup> ANNUAL RUSH UNIVERSITY  
FORUM FOR RESEARCH AND  
CLINICAL INVESTIGATION**

**March 1 and 2, 2017**

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**WELCOME TO THE 34<sup>TH</sup> ANNUAL RUSH UNIVERSITY FORUM FOR RESEARCH  
AND CLINICAL INVESTIGATION**

The Forum showcases the diversity and strength of basic science, clinical and community based research performed by faculty, staff, fellows, and students from the four colleges of Rush University. All sessions will highlight facets of research from each College.

## FORUM HIGHLIGHTS

## WEDNESDAY, MARCH 1

- **31<sup>st</sup> Annual Frederic A. dePeyster Memorial Lecture for the Rush Surgical Society**
- **SIGMA Xi Poster Competition** poster presentations by Graduate Students, Fellows and Residents.
- **Social Event** for Poster Session

**THURSDAY, MARCH 2.** Podium Presentations and Award Presentations will be held in the Field Auditorium, Room 160, Cohn Building.

- **Research Update at Rush** by Joshua J. Jacobs, MD the Associate Provost for Research.
- **Keynote Speaker**, Diana J. Wilkie, PhD, RN, FAAN, Professor, Prairieview Trust – Earl and Margo Powers Endowed Professor and Director, Center of Excellence in Palliative Care Research, Department of Biobehavioral Nursing Science, College of Nursing, University of Florida
- **Rush University Student Presentations** top abstracts are selected within each College by an internal Reviewing Committee.

**CHS:** Samantha Eugenio, BS

**GC:** Allison Nipper, BS

**CON:** Angela Moss, PhDc, MSN, APN-BC, RN

**RMC:** Kevin King, BS

- The **Denis A. Evans Lectureship**, sponsored by the Scientific Leadership Council, featuring David A. Bennett, MD, Director, Rush Alzheimer's Disease Center, Robert C. Borwell Professor of Neurological Sciences, RUMC

- **Research Presentation by Faculty Members** selected by each College.

**CHS:** George Fitchett, DMin, PhD

**GC:** Kalipada Pahan, PhD

**CON:** Masako Mayahara, RN, PhD, FPCN

**RUMC:** Eunsil Hahm, PhD

- **Rush University College Awards** will be presented by the Dean of each College and awardees will present their research.

**CHS:** Ilana Nurko, BS

**GC:** Michael Ohene-Nyako, BSc, MHS

**CON:** Melissa Halverson, DNP, RN

**RMC:** Ashley Heilingoetter, BA, MPH

- **Award Presentations** will be held at 3:30 p.m.

All faculty members are encouraged to judge the poster presentations during the Sigma Xi Poster Competition. This is an excellent opportunity for our students and fellows to gain experience in describing their research to reviewers and will be an excellent experience in support of advancing their research careers.

All posters will be open for viewing during the both days. See Table of Contents for listing of poster numbers by primary author and presenter.

The Annual Research Forum is an exciting and stimulating platform for everyone at Rush University Medical Center to both celebrate and become familiar with the novel research being investigated and pioneered at Rush!

Rush Forum Committee



Thomas A. Deutsch, MD  
Provost, Rush University



To: Faculty, Staff and Students  
From: Thomas A. Deutsch, MD, Provost, Rush University  
Re: 34<sup>th</sup> Annual Rush University Forum for Research and Clinical Investigation  
Date: February 27, 2017

Welcome to the 34<sup>th</sup> Annual Rush University Forum for Research and Clinical Investigation, sponsored by Rush University, Rush University Medical Center, the Rush University Chapter of Sigma Xi and the John H. Stroger, Jr. Hospital of Cook County. Let's embrace this opportunity for to celebrate and learn about the breadth of compelling research being conducted by Rush and its partners.

In addition, faculty, fellows and students at Rush University who are engaged in basic, clinical or applied research in various disciplines have the chance to share their work and explore collaborative opportunities as they get to know one another in a collegial social environment.

Plan to participate in several of the stimulating activities representing the four colleges of Rush University:

- Attend the keynote address and lectureship event. This year there are two exceptional keynote lectures:
  1. The keynote speech will be in charge of Dr. D. Wilkie, Prairieview Trust-Earl and Margo Powers Endowed Professor at the University of Florida, is an internationally known pain specialist with a special emphasis on palliative and end-of-life care in cancer and other life-threatening illnesses. She has been continuously funded since 1986 from numerous organizations such as the National Institutes of Health, the National Cancer Institute and the Robert Wood Johnson Foundation totaling more than \$37 million. She is a member of the Institute of Medicine and a fellow in the American Academy of Nursing.
  2. The second year of the Denis Evans Lectureship, which has been bestowed upon one of Dr. Evans' trainees, Dr. David Bennett, Director of the RADC. The Denis Evans Lectureship was established to honor the many scientific contributions that Dr. Evans has made to the field of aging and Alzheimer's disease, and to his prominent role in the successful development of so many careers. Dr. Bennett is one of Dr. Evans' more famous students who has himself contributed much to the field of Alzheimer's disease and research mentorship.
- Attend research presentations at the inaugural session of Research and Diversity from students and trainees of Rush on Diversity and inclusion sponsored by the Rush Initiative to Maximize Student Development program.
- Attend the Rush University Sigma Xi poster session. This poster session provides investigators the opportunity to share with the Rush community research posters that have been presented at national meetings during the past year. Additionally, it offers students and junior faculty the opportunity to showcase their research and gain valuable feedback prior to submission to a broader audience.
- Attend the Awards Ceremony for the Sigma Xi Poster Competition. Awards for posters of excellence by a student in each of the four colleges are granted, as well as a poster of excellence by a postdoctoral fellow (or resident) in either the basic or clinical sciences. Three additional award categories are granted through the Rush Graduate Student Council, the Irwin Press Patient Experience Research Award and the Clinical Research and Scholarship Award.

Please note that this year's event will be held in multiple locations, including the Searle Conference Center, Armour Academic Center and the Cohn Research Building.

I look forward to seeing everyone at this year's forum as we celebrate our scientific achievements and scholarly activities.

## **ACKNOWLEDGMENTS**

### **34TH ANNUAL RUSH UNIVERSITY FORUM FOR RESEARCH AND CLINICAL INVESTIGATION FORUM PLANNING COMMITTEE 2017**

Alejandro Espinoza Orias, PhD

**Chair**

Norma Sandoval

**Administrative Manager**

#### **Committee Members:**

- The Graduate College: Gabriella Cs-Szabo, PhD and Thomas Schmid, PhD
- College of Health Sciences: Christy Tangney, PhD
- Rush Medical College: Maureen Richardson, PhD and Raj Shah, MD
- College of Nursing: Joellen Wilbur, PhD, APN, FAAN & Mary Heitschmidt RN, PhD, APN, CCRN
- Office of the Associate Provost for Research: Joshua J. Jacobs, MD
- Sigma Xi: Carl Maki, PhD and Animesh Barua, PhD
- University Affairs: Michelle Michael

#### **Funding Support:**

- Office of Associate Provost for Research

#### **Award Support:**

- Center for Clinical Research and Scholarship Award
- Graduate College Student Council
- Irwin Press Award for Research on the Patient Experience
- Rush University Chapter of Sigma Xi

#### **Many thanks to the following:**

- Kevin Le, Information Services for the REDCap support.
- Bill Richert & the Photo Group Team for documenting the Rush Research Forum.
- Bill Richardson & Team, Media Services for providing AV support.
- Billy Dishuk, Vivian Lee, Krystyna Houston and the entire Room 500/Searle Conference Center staff for excellent services.
- Chris Kanakis, General Education Resources for assistance with the poster displays.
- Vanessa Perez and Thi Tran for organizing the Annual Frederic A. dePeyster Memorial Lecture.
- Tom Schmid and Students for assembling the poster boards.

# 34<sup>TH</sup> ANNUAL RUSH FORUM FOR RESEARCH & CLINICAL INVESTIGATION PROGRAM

**March 1 & 2, 2017**

**Posters Display:** Claude H. Searle Conference Center, Professional Building, 5<sup>th</sup> Floor

**Podium Presentations:** Field Auditorium, Room 160 Cohn  
Rush University Medical Center

<b>WEDNESDAY, MARCH 1</b>	
<b>12 - 5 p.m.</b>	<b>POSTER SESSION – OPEN VIEWING</b>
<b>7 - 8:30 a.m.</b> Rm. 539 AcFac	<b>SESSION I: 31ST ANNUAL FREDERIC A. DEPEYSTER MEMORIAL LECTURE FOR THE RUSH SURGICAL SOCIETY</b> Surgical Services and Sciences Resident Research Competition
	<i>"Clinical and Personal Comparative Effectiveness"</i> <b>Julie A. Freischlag, MD</b> Vice Chancellor for Human Health Sciences & Dean of the School of Medicine at UC Davis
<b>1 - 2:40 p.m.</b> Field Auditorium Presentations (15 min.) Q&A (5 min.)	<b>SESSION II: RESEARCH AND DIVERSITY</b> Sponsored by the Rush IMSD Program <b>Moderators:</b> Lena Al-Harhi, PhD, Professor & Associate Chair, Department of Immunology, RMC and Director of Rush-IMSD Gabriella Cs-Szabo, PhD, Associate Dean and Professor, GC Department of Orthopedic Surgery, RMC
1 - 1:15 p.m.	<i>"The Relation between Physical Activity and Cognitive Change in Older Latinos"</i> <b>Shannon Halloway, PhD, RN</b>
1:20 - 1:35 p.m.	<i>"Determining the role of PRCP/PREP in Triple Negative Breast Cancer"</i> <b>Ricardo Perez, BS</b>
1:40 - 1:55 p.m.	<i>"Proprotein-Convertase Subtilisin-Kexin Type 9 (PCSK9) and Low Density Lipoprotein Receptor (LDLR) Genotype Distribution and Association with Statins in Filipino American Women"</i> <b>Joanne Michelle Gomez, MD</b>
2 - 2:15 p.m.	<i>"The Concept of Caring in the Recruitment of African Americans with Chronic Health Disease: An Integrative Review"</i> <b>Charlene Gamboa, MPH, PhD Student</b>
2:20 - 2:35 p.m.	<i>"Salud Comunitaria y la Escuela: Using Classroom Modules and a Community Garden to Encourage Wellness in Students"</i> <b>Mallory Davis, BS, MD Candidate</b>
<b>3 - 5 p.m.</b> SCC	<b>SESSION III: JUDGING OF POSTERS</b>
<p>Poster oral presentations by students and fellows/residents (basic/clinical) will be judged by Rush faculty for Sigma Xi. Announcement for awards and certificates of recognition will be made on Thursday at 3:30 p.m.</p> <p>Presenters must be present according to the following schedule.</p> <ul style="list-style-type: none"> <li>– 3 p.m. Odd Numbered Posters</li> <li>– 4 p.m. Even Numbered Posters</li> </ul>	
<b>3 - 5 p.m.</b> SCC	<b>SESSION IV: SOCIAL EVENT FOR POSTER SESSION</b>

## THURSDAY, MARCH 2

<b>8 a.m. - 5 p.m.</b> SCC	<b>POSTER SESSION – OPEN VIEWING</b>
<b>8:15 – 8:20 a.m.</b> Field Auditorium	<b>SESSION V: WELCOME &amp; RESEARCH UPDATE</b> <b>Moderator:</b> Alejandro Espinoza Orías, PhD Assistant Professor, Department of Orthopedic Surgery and Chair, Research Forum
8:20 - 8:35 a.m.	<i>"Research Update at Rush"</i> <b>Joshua J. Jacobs, MD</b> Associate Provost for Research, Rush University
8:40 - 8:45 a.m.	<b>SESSION VI: KEYNOTE SPEAKER</b> <b>Moderator:</b> Joellen Wilbur, PhD, APN, FAAN, Professor and Endowed Independence Foundation Chair in Nursing, Rush University, College of Nursing
8:45 – 9:15 am	<i>"Technology to Facilitate Patient-centered Care across Settings: Pain Management Exemplar"</i> <b>Diana J. Wilkie, PhD, RN, FAAN</b> Professor, Prairieview Trust – Earl and Margo Powers Endowed Professor and Director, Center of Excellence in Palliative Care Research Department of Biobehavioral Nursing Science College of Nursing, University of Florida
<b>9:25 – 10:45 a.m.</b> Field Auditorium Presentations (15 min.) Q&A (5 min.)	<b>SESSION VII: FACULTY PRESENTATIONS</b> <b>Moderator:</b> Alejandro Espinoza Orías, PhD
9:25 -9:40 a.m. CHS	<i>"The Effect of Chaplain Spiritual Care on TBI Rehabilitation Outcomes"</i> <b>George Fitchett, DMin, PhD</b> Professor, Director of Research, Department of Religion Health and Human Values
9:45 – 10 a.m. CON	<i>"E-Pain Reporter: A Digital Pain and Analgesic Diary for Home Hospice Care"</i> <b>Masako Mayahara, RN, PhD, FPCN</b> Assistant Professor, Department of Community, Systems and Mental Health
10:05 - 10:20 a.m. GC	<i>"Novel Drugs from the Brain for Brain Disorders"</i> <b>Kalipada Pahan, PhD</b> The Floyd A. Davis, M.D., Endowed Chair in Neurology Professor, Departments of Neurological Sciences, Biochemistry and Pharmacology
10:25 - 10:40 a.m. RMC	<i>"Role of suPAR in Kidney Disease"</i> <b>Eunsil Hahm, PhD</b> Assistant Professor, Internal Medicine
<b>10:50 – 11:35 a.m.</b> Field Auditorium	<b>SESSION VIII: DENIS A. EVANS, MD LECTURESHIP</b> <b>THE SCIENTIFIC LEADERSHIP COUNCIL</b> <b>Moderator:</b> Denis A. Evans, MD, Rush Institute for Healthy Aging, RUMC & Jesmer Professor of Internal Medicine, RMC
10:55 – 11:25 a.m.	<i>"Risk Factors, Pathology, and the Clinical Expression of AD"</i> <b>David A. Bennett, MD</b> Director, Rush Alzheimer's Disease Center Robert C. Borwell Professor of Neurological Sciences, RUMC
<b>11:40–12:25 p.m.</b>	<b>BREAK</b>

<b>12:30 – 1:50 p.m.</b> Field Auditorium Presentations (15 min.) Q&A (5 min.)	<b>SESSION IX: STUDENT PRESENTATIONS</b> <b>Moderator:</b> Christy C. Tangney, PhD, FACN, CNS, Professor, Department of Clinical Nutrition & Associate Dean for Research, CHS
12:30 - 12:45 p.m. CHS	<i>“Changes in FGM Concentrations and Behavior in Response to Construction in African Wild Dogs”</i> Samantha Eugenio, BS
12:50 - 1:05 p.m. CON	<i>“Worksite Access to Primary Care Services: Health-seeking Behaviors and Health Outcomes Among Low-Income Foodservice Workers.”</i> Angela Moss, PhDc, MSN, APN-BC, RN
1:10- 1:25 p.m. GC	<i>“B Cell Immunoaging”</i> Allison Nipper, BS
1:30 - 1:45 p.m. RMC	<i>“Fractionated Stereotactic Radiotherapy and Stereotactic Radiosurgery as Salvage Treatment for Recurrent Malignant High-Grade Glioma”</i> Kevin King, BS
<b>1:55 – 3:30 p.m.</b> Field Auditorium Presentations (15 min.) Q&A (5 min.)	<b>SESSION X: DEANS’ AWARDS PRESENTATIONS</b> <b>Moderator:</b> Maureen H. Richards, PhD Assistant Professor, Department of Internal Medicine, RMC
1:55 - 2:10 p.m. CHS	<i>“Modified Ketogenic Diet: Impact on Seizure Activity, Anthropometrics, and Gastrointestinal Symptoms in Adults with Epilepsy”</i> Ilana Nurko, BS
2:15 - 2:30 p.m. CON	<i>“Initiative to Address the Psychological Needs of IBD Patients”</i> Melissa Halverson, DNP, RN
2:40 - 2:55 p.m. GC	<i>“Alteration in Markers of Neuronal Activity and Plasticity in the Limbic Brain of HIV-1 Tg Rats Revealed by Methamphetamine Self-Administration”</i> Michael Ohene-Nyako, BSc, MHS
3 - 3:15 p.m. RMC	<i>“Histopathology in chronic rhinosinusitis varies with sinus culture”</i> Ashley Heilingoetter, BA, MPH
<b>3:30 – 4 p.m.</b> Field Auditorium	<b>SESSION XI: AWARDS CEREMONY</b> <b>Moderator:</b> Carl Maki, PhD President, Rush Chapter of Sigma Xi
Awards and certificates of recognition will be presented by: <ul style="list-style-type: none"> <li>– Center for Clinical Research and Scholarship Award</li> <li>– Graduate Student Council Awards</li> <li>– The Irwin Press Patient Experience Research Award</li> <li>– Sigma Xi</li> </ul>	



## SIGMA XI POSTER SESSION

The Rush University Chapter of Sigma Xi is a local chapter of the parent international Sigma Xi Organization, an honor society of research scientists and engineers that recognizes and promotes scientific achievement. Founded in 1886, Sigma Xi is dedicated to the advancement of science and engineering through outstanding programs and services delivered in a collegial and supportive environment. The mission of Sigma Xi is to enhance the health of the research enterprise, foster integrity in science and engineering, and promote the public's understanding of science for the purpose of improving the human condition. In this spirit, the Rush Chapter annually hosts this poster session and competition during the Rush University Forum to recognize excellence in the sciences. This 2017 forum will be held on March 1 and 2. Membership in the Society by faculty, postdoctoral trainees, and students provides the critical support for chapter activities and therefore, is always welcome. For more information, visit [www.sigmaksi.org](http://www.sigmaksi.org). You can also communicate with your Rush chapter officers (listed below).

This year, the Rush Chapter offers awards for posters of excellence by a graduate student of each of the 4 colleges, as well as poster of excellence by a postdoctoral fellow (or resident) in either the basic or clinical sciences. The Chapter also offers additional award categories through support of the Rush Graduate Student Council, the Irwin Press Award for Research on the Patient Experience and the Clinical Research and Scholarship Award. On Wednesday (3:00 – 5:00 p.m.), the competing posters are judged by Rush faculty for excellence in presentation, scientific merit, and visual aesthetics of the poster itself. As always, we appreciate the participation of Faculty members as judges. Please come and help us evaluate the work of students and fellows in your area of expertise. Click [here](#) to register.

***You must be present at your poster to be judged!!!***

Announcement and presentation of monetary prizes and certificates will be made on Thursday (3:30- 4 p.m.).

Posters will be located for viewing throughout the Searle Conference during the 2 days. They are posted by abstract numbers indicated on the poster boards. Look for abstract directories posted outside the rooms to locate posters.

### Officers, Rush Chapter of Sigma Xi

Carl Maki, PhD	President	Department of Anatomy and Cell Biology
Animesh Barua, PhD	Treasurer	Department of Pharmacology

## **Pediatric B cell Acute Lymphoblastic Leukemia Patient Refractory to Lumbar Puncture at the Time of Diagnosis: A Diagnostic and Management Dilemma**

**Primary Author:** Nidhi Bhatt, MD

**Contributors:** Nitin Sane, B.S. (Rush University Medical Center, UIC) Paul Kent, MD (Rush University Medical Center)

**Introduction:** Leukemic brain masses are well described in Burkitts leukemia, but not in precursor B Cell ALL (B-ALL). We describe what we believe to be a unique case of CNS leukemia mass found on MRI after repeated failure to obtain CSF on multiple lumbar punctures (LP) at diagnosis. Current including Children's Oncology Group (COG) protocols do not recommend brain imaging in B-ALL.

**Objective:** To describe a rare case of CNS leukemia mass in B-ALL and management

**Methods:** We conducted an extensive search on PubMed, Google Scholar, also reviewed COG and COG precursor group protocols from 2006 to 2015 for recommendations to perform brain imaging at diagnosis or when LP failed to obtain CSF.

**Results:** 10-year-old male presented with 2-week history of fever and hip pain thought to septic arthritis was found to have B-ALL after a suspicious CBC lead to bone marrow examination. His exam was otherwise unremarkable except for mild hepatosplenomegaly and with a completely normal CNS exam. B- ALL was confirmed by us and COG and Burritt's rule out due to presence of TdT, lack of C-myc rearrangement, dim CD 45, and negativity for other mature B cell markers. Diagnostic LP failed after more than 20 attempts with 2 pediatric oncologists and 2 anesthesiologists. The patient was under general anesthesia, thin and had no spinal abnormalities. All physicians felt a characteristic 'pop' but without CSF flow, suggesting the possibility of CSF flow obstruction. MRI of Brain/Spine showed extra axial left frontal parafalcine enhancing lesion measuring 3.9X1.3x0.5cm. Spinal MRI was normal except for multiple tiny CSF leaks at the LP sites. The patient was given 48 hours of Decadron with complete resolution of the mass on imaging. Subsequent LP took one attempt to obtain free flowing CSF and revealed CSF blasts. The patient continues on standard COG chemotherapy per protocol, classified as high risk CNS (+).

**Conclusion:** Patient did not have cranial nerve palsy or any neurological deficits, the only abnormal finding was being refractory to lumbar puncture. We conclude that if experienced clinician is having difficulty obtaining CSF think about proximal blockage of CSF and obtain Imaging

## **Lung SBRT for Early-stage NSCLC in the Very Elderly ( $\geq 80$ years old): Extremely Safe and Effective**

**Primary Author:** Paul Kreinbrink, BS

**Contributors:** Philip Blumenfeld, MD (Rush); George Tolkedis, CMD (Rush); Neilayan Sen, MD (Rush); David Sher, MD MPH (UT Southwestern); Gaurav Marwaha MD (Rush)

**Introduction:** Stereotactic body radiotherapy (SBRT) for early-stage non-small-cell lung cancer (NSCLC) is the accepted standard of care in medically inoperable patients, with local control rates comparable to surgery. In very elderly patients, previous studies have shown SBRT to offer excellent local control, though with higher toxicities than in younger populations.

**Objective:** We report our institutional experience using SBRT in the definitive management of NSCLC in patients  $\geq 80$  years old and compare our results to other published data.

**Methods:** Using an IRB-approved registry of 157 patients treated with definitive-intent, linear accelerator-based lung SBRT for early-stage NSCLC at our institution between 2010 and 2016, patients  $\geq 80$  years of age were identified. CTCAEv4 scales were prospectively recorded during follow-ups and utilized for toxicity assessments. Kaplan-Meier estimates were utilized for survival analyses.

**Results:** For the 30 patients and 33 lesions included, median age was 83, (Range (R) 80-93), median ECOG performance status was 1.5 (R 0-3), and median length of follow-up was 14.4 months (R 2-42.1). Median PTV size was 24.0cc (R 5.83-62.1cc). Prescription dose median was 54Gy in 3 fractions (R 50-60Gy in 3-8 fractions). Local control was 100% at 3 years. Median survival was 25.4 months. There were no grade 2-5 toxicities. Grade 1 toxicities included: fatigue in 5 patients (16.7%), pneumonitis in 12 (40%), and dyspnea in 2 (6.7%).

**Conclusion:** Lung SBRT with a BED of  $\geq 100\text{Gy}_{10}$  for very elderly patients with NSCLC was extremely safe and effective, with low toxicity rates (zero grade 2-5 toxicities). With stringent dosimetric parameters and planning guidelines, very elderly patients remain excellent candidates for full-dose SBRT.

## Role of DNA damage in mucosal vs classical melanoma tumorigenesis

**Primary Author:** Tyler Kloweit, BS

**Contributors:** Paolo Gattuso, MD/Department of Pathology/Rush University Medical Center Nicholas Gattuso/University of Illinois Lela Buckingham/Department of Pathology/Rush University Medical Center

**Introduction:** Classic melanoma and mucosal melanoma are aggressive cancers involving uncontrolled proliferation of melanocytes. Classic melanoma is known to develop due to over exposure of UV radiation. UV radiation will cause extensive damage to DNA which can overwhelm the cell's repair processes and thus contribute to the development of the cancer. Mucosal melanomas develop in mucosal tissues such as the colon, urogenital tract, and in the nose and throat, areas less exposed to UV radiation.

**Objective:** Evidence supports the hypothesis that classic and mucosal melanomas each have a distinct pathogenesis and distinct molecular profiles, e.g. previous research showed a significant difference in the methylation of apoptosis gene promoters between the two types of melanoma. The objective of this study was to assess DNA damage in mucosal compared to classic melanomas.

**Methods:** For this study we used 19 mucosal melanomas and 19 classical melanomas. Enzyme-linked immunoassay for a known marker of DNA damage, 8-OHdG, was used to measure genomic DNA damage in classic melanoma and mucosal melanoma tumors and matched normal tissue. Parametric and non-parametric statistical analysis was performed using SPSS.

**Results:** By Wilcoxon analysis of paired samples, tumor DNA displayed significantly more damage than normal tissue in both groups ( $p=0.011<0.05$ ). Comparison of the tumor groups, however showed no significant difference in damage between the classic and mucosal melanomas ( $t(8)=0.925$ ,  $p=0.382>0.05$ ).

**Conclusion:** There is significantly increased DNA damage in tumor tissue compared to non-malignant tissue in both classic and mucosal melanoma. Contrary to our original hypothesis, DNA damage levels as measured by immunosorbent assay were similar in both mucosal and classic tumor types.

**Significance:** Unlike classic melanoma which has a known risk factor in UV sun exposure, mucosal melanoma develops in the absence of this risk factor. This results of this study will apply to the nature of development of mucosal melanoma. Based on the similar levels of DNA damage in the mucosal and classical melanoma observed here, the role of DNA repair will next be assessed by measuring expression of a DNA repair gene, XRCC3 and a repair-related transcription factor gene, EGR4. These studies will determine if development of mucosal tumors is a result of failure of DNA repair rather than equal levels of DNA damage.

## The effect of *G.gallus* and *C.aethiops* normal fibroblasts on human cancer cell line growth

**Primary Author:** Lydia Usha, MD

**Contributors:** Seby Edassery MS (Rush), Oleksandra Klapko MD (Rush)

**Introduction:** Tumor fibroblasts is an integral part of carcinogenesis and development of metastases. They can be modified by the tumor cells to become cancer-associated fibroblasts (CAF) which in turn, affect the tumor growth. Xenogeneic fibroblasts as well as syngeneic and allogeneic fibroblasts home to the tumor and affect its growth. In addition, they can trigger host immune anti-tumor response in vivo.

**Objective:** To investigate the effect of two primary fibroblast cell lines, Embryonic fibroblast (CRL12203) from *Gallus gallus* (East Lansing Line hen) and Kidney fibroblast (CCL70) from *Cercopithecus aethiops* (African green monkey), on five human cancer cell lines with co-culture technique

**Methods:** Cancer cells were co-cultured with fibroblast cell lines using trans-well systems for 5 days. Growth of cancer cells in the tissue culture wells was measured using MTT (tetrazole) cell proliferation assay and repeated thrice. The data was analyzed using Student's t-test

**Results:** Co-culturing with *C.aethiops* fibroblasts increased significantly ( $p < 0.05$ ) proliferation of the majority of cancer cell lines: brain cancer (HTB14) by 12%, ovarian cancer OVACR3 (HTB161) by 13.5% and fibrosarcoma cell line (CCL121) by 11%. Co-culturing with *G.gallus* embryonic fibroblasts showed mixed effect on cancer cell lines; increased the growth of brain cancer cells by 16% and reduced the growth of breast cancer MCF7 (HTB22) by 25% and OvCar3 by 14% compared to the control ( $p < 0.05$ ). Pancreatic cancer cell line (HPAF II, CRL1997) growth showed no significant change in the co-culture with the fibroblast cell lines

**Conclusion:** Previous studies demonstrated that cancer cells can interact with syngeneic and allogeneic fibroblasts directly and indirectly. This is the first study to show that xenogeneic fibroblasts can also affect the growth of human cancer cells in vitro. Further investigation is required to identify the possible mechanism(s) and may potentially lead to the development of novel anti-neoplastic therapeutics.

## **Dietary Ashwagandha supplementation decreases ovarian tumor progression by reducing tumor induced IL-16 expression**

**Primary Author:** Aparna Yellapa, PhD

**Contributors:** Janice M Bahr, PhD (UIUC); Pincas Bitterman, MD (Rush); Sanjib Basu, PhD (Rush); William P Hanafin, PhD (UIUC) and Animesh Barua, PhD (Rush)

**Introduction:** Long standing unresolved inflammation is a risk factor for cancer and ovulation is an inflammatory process, risk factor for ovarian cancer (OVCA). IL-16 is a pro-inflammatory and pro-angiogenic cytokine associated with OVCA development and progression. Unresolved inflammation may be prevented by dietary supplementation of Ashwagandha (ASH), an anti-inflammatory, anti-angiogenic and anti-tumor in nature and may reduce inflammatory associated increase in IL-16 expression and inhibit tumor progression.

**Objective:** The goal of this study was to examine whether ASH treatment decreases IL-16 expression and also the frequency of microvessels associated with ovarian tumor-associated IL-16 expression in the laying hen.

**Methods:** 3-4 years old White Leghorn laying hens were fed with ASH root powder for 45 days (control, 1% and 2% treatment). Serum samples were collected, hens were euthanized and ovarian tissues were processed for routine histological and protein studies. Expression of IL-16 by ovarian malignant cells and smooth muscle actin (SMA) by microvessels was determined by IHC and were confirmed by proteomic studies. Normal human ovarian surface epithelial cells (HOSE) were treated with IL-16 protein (50ng/mL & 100ng/mL at 24 and 48 hours) to observe the secretion of IL-8 (angiogenic cytokine).

**Results:** Frequencies of IL-16 expression and SMA expressing microvessels was significantly ( $p < 0.001$ ) reduced in 2% Ash treated hens as compared with untreated. Similar pattern was observed for serum IL-16 expression in ASH treated and untreated hens. A band of approximately 50-55kDa was observed for IL-16 and expression was similar to that of IHC. HOSE treated with IL-16 protein showed increased IL-8 expression at 24 hours treatment of 100ng/mL indicating proangiogenic role of IL-16. This study suggests that ASH treatment decreases IL-16 expression and also tumor associated microvessel expression in comparison with untreated hens

**Conclusion:** ASH dietary supplementation may be considered as an alternative therapy along with the current chemotherapeutic agents.

## **SIMULTANEOUS BILATERAL OPEN THORACOTOMIES FOR PULMONARY METASTASES IN OSTEOSARCOMA TO REDUCE DELAY IN SYSTEMIC THERAPY**

**Primary Author:** Caroline Kelmis, student

**Contributors:** Antonio Logan, BS (RMC); Caleb Oh, (RMC); Graham Zolkowski, (RMC); Michelle March, BS (RMC); Paul Kent, MD (RMC)

**Introduction:** Osteosarcoma (OST) is the most common type of primary bone malignancy in children and young adults. Approximately 10-15% of patients will have primary metastases, and 66% will have recurrence with 90% involving the lungs (JCO 2002; 20(3):776-90, COG Can 2009; 115(22):5339-48). Aggressive surgical resection of all metastatic sites has a known survival advantage (J Ped Surg 2006; 41(1):194-9).

**Objective:** Preference for staged versus simultaneous open thoracotomies for bilateral metastases has not yet been studied. Although Chen et al. describes 8 of 12 OST patients with bilateral disease who underwent simultaneous thoracotomies, no data on delays in chemotherapy was available (Eur J Card thor Surg 2008; 34(6):1235-39). In a retrospective analysis of 10 children who underwent simultaneous bilateral thoracotomies, H  cker et al. reported no increased risk (Eur J Ped Surg 2007; 17(2):84-9). Simultaneous bilateral open thoracotomies in pediatrics have not been described in detail. Our goal is to report our experience with simultaneous bilateral open thoracotomies in young OST patients.

**Methods:** We reviewed all patients with bilateral OST lung metastases at our institution in the last 20 years. Delay time was calculated by subtracting pre-surgery from post-surgery cycle start dates.

**Results:** Among the 9 patients reviewed, 44% (n= 4) received simultaneous versus staged bilateral thoracotomies. Age ranged from 8-29 years with 6 males and 3 females. Of the patients who underwent simultaneous thoracotomies there were 1, 10, 21 and 23-day delays (Mean: 13.75 days, Standard Deviation (SD): 10.24). Of the patients who underwent staged thoracotomies, there were 16, 62, 75, and 121-day delays (Mean: 81.00 days, SD: 48.23). An independent t-test comparing simultaneous versus staged bilateral thoracotomy was computed (t= 2.70, p-value= 0.030).

**Conclusion:** Simultaneous bilateral open thoracotomies appear to be a safe approach for resection of metastatic OST lung disease with a potential benefit of decreased delay in chemotherapy in young patients.

## The Efficacy of The Chest X-Ray for T1 Renal Cell Carcinoma Surveillance

**Primary Author:** Alyssa Kahan, BA

**Contributors:** Alexander Chow (Rush), Christopher Coogan (Rush), Kalyan Latchamsetty (Rush)

**Introduction:** Pulmonary metastasis is seen in less than 5% of patients with T1 (< 7 cm) renal cell carcinoma (RCC). Despite this low incidence, the National Comprehensive Cancer Network (NCCN) recommends an annual chest x-ray (CXR) for three years post-nephrectomy. A recent single institution study determined that the CXR may be a low yield diagnostic tool in this population (Canvasser et al, Journal of Urology, 2016). We further expanded this investigation using a large multi-institutional Urology database.

**Objective:** This study aims to evaluate the utility of the CXR in detection of asymptomatic metastases in T1 RCC.

**Methods:** We performed a retrospective review of the UroPartners database of patients treated surgically for T1 RCC from 2000-2015. Charts were examined for patient demographics, tumor pathology, and duration of postoperative pulmonary surveillance. The primary outcome measured was the incidence of asymptomatic pulmonary lesion concerning for pulmonary metastasis as detected with a CXR. A secondary outcome was comparing incidence of metastases between partial versus total nephrectomy.

**Results:** 215 patients met criteria for our study. Mean duration of follow up for T1a and T1b was 63.86 months and 44.26 months, respectively. A mean of 3.27 and 3.0 CXRs were done for T1a and T1b. 97 patients had CXR surveillance for greater than 3 years. 3 patients developed pulmonary metastases detected by CXR. Two individuals had T1a disease and one individual had T1b disease with metastases discovered at 25.9, 44.9, and 51.6 months postoperatively. 1 patient developed metastases that were only discovered by CT. When assessed by treatment modality, there was no significant difference in the rate of pulmonary metastases for patients undergoing partial nephrectomy (2/108) or radical nephrectomy (1/105) ( $p=1.00$ ).

**Conclusion:** The chest x-ray is a low yield screening method for surveillance of pulmonary metastases in patients with T1 RCC regardless of treatment by partial or radical nephrectomy.

**Significance:** Our multi-institutional study with mean follow up of 4.5 years illustrates that the standard annual CXR for 3 years postoperatively in patients with T1 RCC has a low diagnostic yield for pulmonary metastases. Furthermore, there is no difference in detection of pulmonary metastases based on selection of surgical treatment. A surprising result in our review is that two of the three patients with pulmonary metastases were diagnosed greater than 3 years out from initial surgery. This finding is alarming given that the current NCCN surveillance protocol advocates for annual CXR up to 3 years. Future work needs to determine the optimal postoperative surveillance protocol for T1 RCC.



## Determining the role of PRCP/PREP in Triple Negative Breast Cancer

**Primary Author:** Ricardo Perez, BS

**Introduction:** Triple negative breast cancer (TNBC) accounts for 15-20% of all breast cancer cases. Currently, the only effective treatment for TNBC is chemotherapy agents. A well-established characteristic of TNBC is the ability of these cells to become metastatic following chemotherapy treatment resulting in increased mortality. New forms of treatment which target TNBC are urgently needed. Insulin receptor substrate 1 (IRS1) has been extensively study in the regulation of the insulin and insulin-like growth factor receptor signaling cascades, specifically in the induction of the intracellular PI3K/AKT/mTORC1 and MAP kinase pathways. The roles of such pathways in cancer are currently being studied and considered for therapeutic targeting.

**Objective:** Our hypothesis is that PRCP/PREP are potential therapeutic targets in TNBC. Specifically, we hypothesize that blocking the expression or reducing the activity of PRCP/PREP will inhibit the PI3K/AKT/mTORC1 pathway in TNBC cells and, in turn, reduce growth, survival, and metastasis in these cells.

**Methods:** N/A

**Results:** N/A

**Conclusion:** To test this, we will be treating a number of TNBC cell lines with a PRCP/PREP inhibitor and determining IRS1/2 protein levels, AKT/mTORC1 signaling, and growth, survival, and metastatic potential.

## Bisphosphonate as Maintenance in Very High Risk Osteosarcomas

**Primary Author:** Lizette Leanos, BS

**Contributors:** Christopher Kuo, Medical Student (Rush); Stephen J. Dvorak, MFA (Rush); Antonio Logan, BS (Rush); Karen Tamulonis, RN (Rush); Amina Rafique, MD (Tulane University); Paul Kent, MD (Rush)

**Introduction:** Children, adolescents and young adults (AYA) with osteosarcoma and a poor response have a 50% 5-year survival. Those with metastasis at diagnosis or relapse (except for an isolated resected pulmonary nodule) have a 5-year survival of 0-20% (C Janeway K et al, Ped Blood & Can 2013). There is currently no standard of care or accepted second line therapy for such high-risk patients. Over the last 11.5 years high-risk OST patients treated by us were offered a bisphosphonate as a 'maintenance' drug after completion of standard chemotherapy. Zoledronic acid (ZA), and other bisphosphonates, are indicated for primary bone diseases, including osteoporosis, OI, cancer-induced bone pain and bone metastasis.

**Objective:** We report our experience using bisphosphonates as maintenance in poor prognosis osteosarcoma (OST) patients.

**Methods:** We defined 'High Risk OST (HRO)' as: Poor Responder (Group A), First Relapse Resected (Group B) - excluding late isolated resected lung nodule which has a relatively good prognosis, and (Group C) Primary Metastatic, Multiple Relapses or Unresectable Disease. We searched for all HRO patients from 04/01/05 to 10/01/2016 less than 50 to see who received a bisphosphonate after completion of chemotherapy.

**Results:** During this 11.5 year period 16 of the 23 HRO patients received a bisphosphonate (15 ZA, 1 aldrionate), with a median age of 17 (7-29). The monthly ZA dose was 2.3mg/m<sup>2</sup> (4mg max) as in the COG safety study. The aldrionate dose was 70mg weekly. Group A (n=6) received a median of 6.5 doses of ZA (4-26), Group B (n=5) a median of 12 (4-24), and Group C (n=5) median 23 (7-32). Four of 5 Group C patients also got bevacizumab median 9 doses (0-20).

**Conclusion:** Our single institution, retrospective preliminary study suggests that bisphosphonates may offer a survival advantage in high risk OST patients. We are planning on opening a prospective pilot study to explore this hypothesis.

## **Dosimetric Predictors of PEG Dependence Following IMRT with Concomitant Chemotherapy for Oropharyngeal Cancer**

**Primary Author:** Andrew Cook, BA

**Contributors:** Philip Blumenfeld, MD MPH (RUMC); Heming Zhen, PhD (RUMC); Jessica Zhou, MD (RUMC); David Sher, MD MPH (UT Southwestern)

**Introduction:** Despite modern intensity-modulated radiation therapy (IMRT) planning, many patients still require percutaneous endoscopic gastrostomy (PEG) tube insertion to maintain adequate nutritional intake. It is important to identify predictors of prolonged PEG tube dependence in order to refine planning techniques and intensify rehabilitation efforts for patients at highest risk of chronic dysphagia.

**Objective:** The purpose of this study is to identify dosimetric predictors of PEG dependence in the treatment of patients with oropharyngeal cancer.

**Methods:** All patients with oropharyngeal cancer treated with IMRT and concomitant chemotherapy from Feb 2007 to March 2013 were included in this single-institution retrospective study. To obtain dosimetric data, the following structures were retrospectively contoured from patients' simulation scans: masseter receiving higher/lower dose (HMass and LMass), total masseter (TMass), epiglottis (Epi), superior constrictor muscles (SC), post-cricoid and arytenoid space (PACS), cervical esophagus (Esoph), base of tongue (BOT), floor of mouth musculature (FOM), oral cavity (OC), and larynx. In terms of clinical data, TNM and AJCC staging were determined as well as the primary cancer subsite. PEG removal time was determined using time from last radiotherapy treatment (XRT) to removal. Logistic univariate analyses (UVA) were performed for 4-, 6-, and 12-month endpoints as well as Cox regression to model time to PEG removal. Those with statistical significance from univariate analysis ( $p$ -value  $<0.1$ ) were then included in a forward stepwise multivariate analysis (MVA). The continuous variables were also dichotomized at the median using the same analyses as previously described.

**Results:** Seventy-nine patients were identified. Independent predictors of PEG dependence at 4 months were: T Stage III ( $p<0.004$ ), OC mean dose (OR 1.001 per unit increase [PUI],  $p=0.05$ ), SC mean dose (OR 1.002 PUI,  $p<0.03$ ), and HMass V40 (OR 1.030 PUI,  $p<0.05$ ). Independent predictors of PEG dependence at 6 months were: SC V65 (OR 1.041 PUI,  $p<0.02$ ) and OC mean dose (OR 1.001 PUI,  $p<0.04$ ). Independent predictors of PEG dependence at 12 months were: LMass V20 (OR 1.071 PUI,  $p=0.05$ ). Time to PEG removal was independently associated with the following variables: T Stage III ( $p<0.003$ ), SC mean dose (OR 0.999 PUI,  $p<0.006$ ), LMass V20 (OR 0.967 PUI,  $p<0.001$ ), OC max dose to 1cc (OR 0.999 PUI,  $p<0.001$ ), and Epi V40 (OR 0.957 PUI,  $p<0.03$ ). Regarding the dichotomized data, independent predictors at 4 months were T stage, FOM V60 (median=37.7%), OC V40 (49.1 %), and mean dose to larynx (4689 cGy). Independent predictors at 6 months were OC V20 (99.1%), OC V70 (1.27%), and larynx V50 (48.4%). Independent predictors at 12 months were OC V20, PACS V60 (1.15%), and Tmass V40 (39.2%).

**Conclusion:** PEG dependence at several time points following treatment was associated with a variety of structures important throughout the swallowing process, including the masseters, superior constrictors,

oral cavity, and epiglottis. Whether or not these variables reflect different pathophysiology across the recovery period, it is important to consider all of them in the optimization process. Further research is necessary to better understand the associations between dose to these structures and chronic dysphagia.

## Discovery of the Mechanism Underlying Apoptotic Compensatory Proliferation Signaling and its Implication in Cancer Therapeutics

**Primary Author:** Kajal Gupta, PhD

**Contributors:** Josef W. Goldufsky PhD, Stephen J. Wood PhD, Sasha Shafikhani PhD

**Introduction:** Apoptosis has been implicated in Compensatory Proliferation Signaling (CPS) where by dying cells induce proliferation in neighboring cells as a mean to restore homeostasis. Here we show in vitro and in vivo that apoptotic cells produce and release Crkl-containing microvesicles (ACPSVs), which induce proliferation in neighboring cells upon contact. We further show that Crkl inactivation by ExoT bacterial toxin from Gram-negative bacteria *Pseudomonas aeruginosa* and mutagenesis inhibits vesicle formation. c-Jun amino-terminal Kinase (JNK) plays a pivotal role in mediating vesicle induced CPS in recipient cells.

**Objective:** The main objective of the research is to further characterize and dissect the role Crkl-containing vesicles in CPS.

**Methods:** We have used differential centrifugation to purify ACPSVs and Immunofluorescent (IF) time-lapse videomicroscopy and scanning electron microscopy to show how ACPSVs are generated and released from apoptotic cells and how they induce proliferation in both normal and transformed cells upon contact.

**Results:** Our preliminary data strongly suggest that C10 regulator kinase I (Crkl) adaptor protein is required for the ACPSVs vesicle biogenesis and for CPS. ExoT by inhibiting Crkl-prevents dying cells from producing and releasing ACPSVs production, while causing massive apoptosis in epithelial cells. These data indicate that apoptotic; program cell death (PCD) and CPS are distinct processes, which can be uncoupled from each other by targeting Crkl. We also show that c-Jun amino-terminal kinase (JNK) plays a pivotal role in mediating vesicle-induced CPS in recipient cells.

**Conclusion:** We provides compelling evidence to demonstrate that Crkl containing microvesicles mediates CPS and importance of JNK activity in mediating CPS in recipient cells.

**Significance:** A critical gap in cell biology is our limited knowledge of compensatory proliferation signaling (CPS). This phenomenon has been described for nearly two decades but the molecular components, the nature of signaling, and the mechanisms underlying CPS have remained largely unknown. Our research will directly address these critical gaps. Many microbial pathogens induce apoptosis in their target cells as a mean to advance their infections. CPS could play an important role in host defenses in innate immunity against these pathogens in vivo.

## **Fractionated Stereotactic Radiotherapy and Stereotactic Radiosurgery as Salvage Treatment for Recurrent Malignant High-Grade Gliomas**

**Primary Author:** Kevin King, BS

**Contributors:** Philip Blumenfeld, MD MPH; Jacob Shin, MD; George Tolekidis MS; Aidnag Diaz, MD

**Introduction:** High-grade gliomas (HGG) are the most common and aggressive primary brain malignancies in adults. Local recurrence remains the predominant pattern of failure with a median survival after recurrence of 8 months for Glioblastoma (GBM), the most common HGG. Fractionated Stereotactic Radiotherapy (fSRT) and Stereotactic Radiotherapy (SRS) have emerged as a novel technique to deliver high doses of RT in the recurrent setting with aim for durable local control and potential overall survival benefit.

**Objective:** This study evaluated the patterns of recurrence, prognostic indicators as well as the efficacy of treatment in patients with recurrent HGG treated by fSRT or SRS.

**Methods:** A retrospective chart review was conducted of patients with recurrent HGG from 2006 to 2016 treated with SRS or fSRT at a single institution.

**Results:** Thirty-one patients with GBM (71.0%) or HGG (29.0%) were identified. Of those receiving SRS, the median overall survival (OS) from date of initial recurrence was 14 months. Of those receiving fSRT, the median OS from date of initial recurrence was 8 months. The main pattern of failure after RT at time of recurrence remained in-field.

**Conclusion:** Favorable outcomes were observed in patients treated with fSRT and SRS as salvage therapy. There was a suggestion of improved OS for patients with smaller PTVs, but this was not statistically significant. The predominant mode of failure post salvage SRS and FSRT remains in-field. Prospective trials are required to better define patient selection, tumor recurrence size, and effective dose regimen.

## **Pediatric Cancer Patients' Attitudes and Expectations for Fertility Preservation as Compared to those of their Parent/Guardian**

**Primary Author:** Vanessa Cutler, MD

**Contributors:** Stephen Dvorak MFA (Rush) Antonio DC Logan BA (Rush) Caroline Kelmis (Northwestern) Thomas Holland MD (Rush) Paul Kent MD (Rush)

**Introduction:** Five-year survival rates for pediatric cancer continue to rise, now exceeding 80%. However, current data suggests a lag between the progress of five-year survival rates and that of the preservation of fertility in these patients. As the right of refusal ultimately lies with the parents, conversations and consensus about fertility preservation between providers, parents, and patients is principally important. Few decisions are more personal than reproductive health and few rights more central.

**Objective:** Our goal is to assess pediatric cancer patients' expectations and attitudes towards fertility preservation options and future fertility capacity as compared to those of their parents or guardians.

**Methods:** We surveyed 21 pediatric oncology patients and their corresponding parent or guardian regarding the patients' and parents' attitudes toward fertility and reproduction in 4 questions on a four-point Likert scale ranging from 'No, not at all [important]' to 'Yes, very [important]' and one question on a three-point Likert scale from 'Not interested at all' to 'Absolutely'. The survey also questioned which member(s) of the healthcare team discussed options with them, which preservation methods were selected (if any), and whether the patient was treated with chemotherapy. Data were stratified by age, sex, ethnicity, and type of neoplasm.

**Results:** On a 4-point Likert scale, this preliminary data shows average responses for parents/guardians were 3.5, 2.6, 1.8, and 1.8, respectively [n=21]. For patients, average responses were 3.3, 3.7, 3.1, and 2.2, respectively [n=21]. Patients scored significantly higher on Q2-Q4 than their corresponding parent or guardian.

**Conclusion:** Both groups felt overall that they were well informed regarding their options for fertility preservation. Patients, however, reported higher on average than their parents that the preservation of their future fertility was important to them, and that they would be more apt to delay chemotherapy if fertility preservation was assured.

**Significance:** In a review of the literature, what little data is reported on this topic suggests that pediatric cancer patients historically have not been well informed about risks to their fertility, presumably due to the less favorable outcomes of the past. Consequentially, there is now an impasse in terms of what types of procedures are effective for preserving fertility in these patients, and what is covered by insurance. Prospective studies of this nature are in some sense a spearhead toward bringing about a new standard of care in which pediatric cancer patients receive more information from their providers regarding risks to their fertility and options for preservation, and having procedures that provide the patients with adequate protection where the costs can be met by insurance.

## **IMPROVING ACCRUAL OF ADOLESCENTS AND YOUNG ADULTS (AYAs) AND UNDERREPRESENTED MINORITIES WITH LEUKEMIA TO CHILDREN'S ONCOLOGY GROUP CLINICAL TRIALS: A NOVEL COLLABORATIVE APPROACH TO ADDRESS DISPARITIES IN LEUKEMIA**

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**Introduction:** The dramatic decrease in mortality from ALL and AML in children is related to improved participation in COG clinical trials. African-American (AA) and Hispanic children and AYAs 15-39 years are under-represented in clinical trials. AA and Hispanic children with leukemia have worse survival than white children. Access to chemotherapy, socio-economic and insurance status, differences in disease biology play a role in these disparities. Insufficient cancer clinical trial accrual and treatment with adult vs 'pediatric' inspired protocols is associated with inferior AYA survival. In 2008, to improve access to a largely underserved population, two COG institutions (UIC and Rush University) and a non-member hospital (Stroger Hospital) created a unified COG program utilizing one research team.

**Objective:** To assess the impact that UIC-Rush-Stroger COG program had on clinical trial enrollment for minority underserved and AYA patients with leukemia.

**Methods:** A retrospective comparative analyses of COG enrollment data from 2002-2008 and 2008-2014 for patients with leukemia by race/ethnicity, age, insurance status, clinical trial type and primary oncologists of enrollees' was performed.

**Results:** There was a three-fold increase in number of therapeutic leukemia trials open to enrollment and a 108% increase in total and 121% increase in therapeutic leukemia trial enrollments post-merger. There was a 370% in Hispanic and 220% increase in AA patients enrolled. There was a 610% increase in AYAs enrolled post-merger. 40 enrolments occurred at Stroger Hospital, 39% of which were uninsured, 75% were for AYAs. Nine Pediatric /six Medical Oncologists were engaged in post-merger COG enrollments compared to 6 Pediatric/ 1 Medical Oncologist engaged pre-merger.

**Conclusion:** Significant increase in COG leukemia trial enrollment especially for under-represented minorities and AYAs was a direct result of the creation of the novel UIC/Rush/Stroger COG Clinical-Trials program. The UIC-Rush-Stroger COG Program serves as a model for improved collaboration between institutions to address disparities in leukemia survival.



## Identification of a meta-gene network associated with metformin sensitivity and recurrence in double hit and double expressor lymphomas

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**Contributors:** Annesha Basu, Jeffrey Borgia, L Gordon, P. Venugopal, C.A. Frankenberger

**Introduction:** The 'double hit' (DH) lymphomas that harbor a c-myc mutation and BCL2 translocation, or 'double protein expressor' (DP) lymphomas that overexpress c-myc and BCL2 proteins in the absence of a detectable mutation, have amongst the worst clinical outcomes as compared to patients with diffuse large B-cell lymphomas (DLBCL) that lack upregulation of the c-myc oncogene. Metformin can down-regulate translation of c-myc, making it an appropriate anti-cancer drug to explore in c-myc+ lymphomas. Furthermore, a method to identify DH/DP patients most likely to benefit from metformin treatment has clinical relevance.

**Objective:** Aim 1: We will evaluate the impact of cachexia measured longitudinally on clinical outcomes in aggressive B-Cell non-Hodgkin Lymphoma (B-NHL) treated with standard chemo-immunotherapy. Aim 2: We will study associations between selected serum biomarkers, muscle and adipose index values, and survival in aggressive B-NHL treated with standard chemo-immunotherapy.

**Methods:** Within a publicly available gene expression array data set of R-CHOP treated DLBCL (n=232; GSE10846), a subset of DH/DP patients were defined as having above median expression of myc and BCL2 and below median expression of BCL6 as previously published by Horn et al. Survival analysis, significance analysis of microarrays (SAM) and gene set analysis (GSA) were performed characterizing the clinical, individual gene and biological ontology differences between DH/DP and non-DH/DP populations. Expression array data from a study testing metformin effects on THP-1 monocyte cells was reanalyzed using SAM and GSA as well. Changes in individual gene expression and overlapping ontological themes common to both GSA analyses of metformin effects on THP-1 cells and DH/DP characterization were identified. Genes with differential expression (DE) in both groups were evaluated topologically using a protein-protein interaction database to determine if any gene products had previously observed direct interactions. Network community detection identified tightly coupled signaling modules linking co-expression to mechanism. The resulting metformin-DH/DP network metagene was evaluated by k-means, clustering tumor samples into two groups over the metagene members in an independent data set of R-CHOP treated DLBCL patients (n=249; GSE32918) with differences in overall survival (OS) determined by log-rank.

**Results:** Of the 232 DLBCL patients treated with R-CHOP, 26 fit the criteria for DH/DP and had significantly lower OS (HR = 2.96;  $p < 0.001$ ). In DH/DP tumors, 2780 genes had DE (2208 up-regulated; 572 down-regulated), enriched for biological processes related to transcription, metabolism and cytokine production and down-regulated for processes related to immune response, cell signaling, vascular development and proliferation (Fig. 1A). Analysis of metformin treated THP-1 cells relative to control identified 7123 genes with DE. Biological themes common to metformin treatment and DH/DP specific biology were identified including mitochondrial biogenesis, alternate splicing, and hormone secretion (Fig. 1A-B; highlighted in red). The intersection of genes with DE in metformin treated and

DH/DP data sets identified 102 genes with direct interaction within a protein interaction network. Of the 19 communities detected by analyzing the resulting network topology, 3 showed significant correlation to survival in the GSE10846 data set (Fig. 2A, in red), forming a metformin-DH/DP metagene (Met-DH/DP-MG;  $n = 29$  genes total). This metagene was validated by applying it to an independent cohort of R-CHOP treated DLBCL patients ( $n = 249$ ), demonstrating 2 cluster groups (cluster 1,  $n=178$ ; cluster 2,  $n=71$ ; Fig. 2B) with differences in OS (HR = 1.61;  $p < 0.001$ ; Fig. 2C).

**Conclusion:** We have identified a metagene of interacting proteins associated with both metformin therapeutic effect and OS in DH/DP patients. This offers a potential method for selecting patients most likely to benefit from metformin therapy and identifies mechanistic avenues by which metformin treatment may specifically benefit DH/DP patients. As such, in vitro studies using DH cell lines and a phase I/II clinical trial exploring chemo-immunotherapy with metformin as an adjunct in DH/DP lymphomas are underway.

## **Genes involved in signal transduction pathways as a result of Smokeless Tobacco exposure to primary human oral epithelial cells**

**Primary Author:** Rohan Rajapakse, PhD

**Contributors:** Annesha Basu, Sanam Shahid, Michael Timko

**Introduction:** There is a global increase in the incidence and mortality rate of head and neck cancer (1). The social habit of tobacco use is implicated as the major factor involved in the etiology of the disease (2,3). Smokeless tobacco (SLT) is mainly used orally as an alternative to cigarette smoke and its use in the U.S has been persistent in the recent past (4). SLT is not only an addictive agent, but it also has levels of nicotine and other ingredients comparable to conventional cigarettes (5). More than 30 carcinogens exist in SLT, including volatile and tobacco-specific nitosamines, nitrosamino acids, polycyclic aromatic hydrocarbons, aldehydes and metals (6). Epidemiological and meta-analysis suggested an increase of health risk for cancer and cardiovascular diseases with the use of SLT products (7,6). Surprisingly, little is known about the mechanistic basis leading to the disease occurrence. That is partly due to both for not having a well define model system and dynamic of chemical constitutes. A better understanding of the response mechanism may foster to uncover relevant biomarkers in developing potentially reduced exposure products (PREPs).

**Objective:** This study is conducted to determine the time course of gene expression associated with specific signaling pathways in human oral epithelial cells after exposure to smokeless tobacco. A differentiated layer of epithelial cell is created as a way to mimic reasonably similar physiological atmosphere. A dose and time dependent response is observed for cell viability and cell proliferation assays indicating that this model system is responsive to the treatment. Expressions of 84 genes representing 18 different signal transduction pathways are quantitated. This is accomplished by using real-time polymerase chain reaction arrays at 1h, 3h, 6h and 24h time points following exposure to smokeless tobacco. Changers in gene expression are observed on many cellular processes including cell cycle regulation, cell adhesion, inflammation, apoptosis, DNA breaks-down including Akt pathway activation.

**Methods:** Progenitor cells isolated from human oral gingival tissue were purchased (ZenBio, NC) and maintained as primary human oral epithelial cells (HOEP) on serum-free defined media (CNT-24, ZenBio, NC) following manufacture's instructions. Cells at day 7 differentiations were taken for experiments. For gene expression analysis, cells were treated with 10mg/ml of smokeless tobacco (SLT) for indicated time points whereas control samples were mock treated. Smokeless tobacco (moist snuff) extract was prepared by using research grade reference 1S3 moist snuff (a kind gift from Dr. David Danehower, North Carolina state University) as described in the literature (18). Cells were grown on coverslips in 6 well plates (Corning, NY) when reached appropriate time points washed two times with PBS, fixed with 80% ice-cold Methanol for Involucrin (Abcam, MA), permeabilized with 0.5% Triton for 10 min at room temperature. After three times wash with PBS, the cells were blocked for 1h with PBS containing 2 % BSA plus 5% calf serum and then incubated at 4 CO overnight with primary antibody. The Neutral Red Cytotoxicity Assay (NR assay) was taken to assess the viability of cells after exposure to SLT. The protocol for NR assay was based on guidelines set by National Institute of Health (Guidance document on using in

vitro data to estimate in vivo starting doses for acute toxicity, 2001.). Cell proliferation was determined by 5-bromodeoxyuridine (BrdU) incorporation following manufactures instructions. At each time points after exposure to SLT, cells were washed twice with PBS and lysed with adding 1 ml of TRIzol (Invitrogen, CA) followed by isolation of RNA following manufacturer's instructions (RNeasy Qiagen). Data were expressed as mean  $\pm$  standard deviation (SD). Statistical analysis with student's-t test was performed and the level of significance set at 0.05 (p).

**Results:** Oral mucosal epithelial cells are the first line of cells comes into contact with smokeless tobacco product upon its placement in the oral cavity. This serves as a physical barrier that protects underlying cells and tissue from potential adverse effects of the products (26). The differentiated cultures of primary oral epithelial cells were created as way to mimic normal physiology of the oral epithelial tissue. Two and 3 fold difference in the expression of Keratin1 and 10 was observed comparative to undifferentiated cells at day 7 and 11, respectively. Interestingly, Involucrin expression was 3 times higher at day 7 where as 11 times higher at day 11 in differentiated cells compare to controls suggesting treatment with calcium leads cells to differentiate. The effect of smokeless tobacco for cell viability was closely associated with both incubation time and the dose. The dose of 10mg/ml of smokeless tobacco was chosen as a dose for the following experiments based on cell viability data. Three different time points were selected for preceding experiments as follows; 1h (acute exposure), 3h and 6h (intermediate exposure) and 24h (long term exposure). Anti-proliferative effects of smokeless tobacco came into effect with longer incubation indicating cell viability independent effect. There are 8 key genes that play a vital role in the inflammation were significantly regulated with the treatment (Fig; 4) that include IL-8, IL-1A, LTA, MMP10, NOS2, PTGS2 (COX-2), SELPLG and TNF-alpha.

**Conclusion:** In summary, in this study, a set of biologically relevant genes was examined by PCR array to generate comprehensive information for potential biomarkers. Our data indicate that the active exposure of differentiated oral epithelial cells to smokeless tobacco leads to express gene profiles for specific signal transduction pathways in a time and dose dependent manner. Signaling pathways involving, cell cycle regulation, apoptosis, cell-cell adhesion and inflammation were modulated with the treatment. Data presented here are more consistent with reports demonstrating that smokeless tobacco can induce Akt pathway and modify cellular function. Although these observation are promising, studies are under way to see the extent of phosphorylation of those gene that are regulated in this experiment as a way to further understand the effect of smokeless tobacco on oral epithelial cells at protein level.

## **Measles immune status in an inner city pediatric oncology patient cohort during the measles outbreak of 2015**

**Primary Author:** Nupur Mittal, MD

**Contributors:** Paul Kent , MD (RUMC) Antonio Logan ,(RUMC)

**Introduction:** Survivors of pediatric cancer are at risk of long- term consequences of therapy one of which is loss of pre-existing protective antibodies predisposing them to illnesses such as Measles. Measles in recipients of immunosuppressive chemotherapy can have mortality rates up to 50%. Up to 35% of children < 7 Years lose humoral immunity to measles as a result of chemotherapy induced alterations in immune system. Despite the strategies WHO for improving measles vaccine coverage, the disease still continues to circulate leading to outbreaks in developed countries. In 2015, the US experienced a measles outbreak. 189 cases (40% < 18 years) were reported across 24 states including Illinois. Measles is a highly infectious from 48 hours prior to first symptoms. Our small pediatric oncology practice shares office and floor space with other pediatric practices, placing our patients at risk for infection by measles. Prior to this study, it was not our standard practice to check measles titer prior to initiation of chemotherapy

**Objective:** To assess measles susceptible pediatric oncology survivors in our practice

**Methods:** Because of the new risk to our patients we chose to check measles protective humoral immune status in our patients from January-June 2015, the period of measles outbreak in USA. Patients under 21 receiving chemotherapy between January 2015 and June 2015 in our department were included in prospective review. We defined immunity according to our lab standards.

**Results:** A total of 31 (15 female) patients were included. Three patients (approx 10%) had non protective measles antibody levels. One of these three patients was previously unimmunized, 2 were < 3 years at diagnosis and had leukemia, one was diagnosed with hepatoblastoma. All came every weekly to the clinic for chemotherapy and thus waited in the shared waiting area. None of the patients developed measles.

**Conclusion:** Measles outbreaks in the US pose a grave threat to immunocompromised children. This danger is increased in the nosocomial setting with shared clinical space. 100% vaccination for all children, stringent isolation strategies in pediatric clinic waiting areas and standard practice of checking measles immune status in all pediatric patients prior to chemotherapy initiation may help prevent this devastating disease in this sensitive population.

## EPIGENETIC INACTIVATION OF MIR-9 IN EVI1 HIGH PEDIATRIC AML : A ROLE FOR HYPOMETHYLATING AGENTS IN PEDIATRIC AML

**Primary Author:** Nupur Mittal, MD

**Contributors:** Liping Li (UIC) Zhijian Qian (UIC)

**Introduction:** EVI-1 hyper expression seen in 25% of pediatric AML patients is associated with an inferior prognosis. The role of EVI1-induced aberrant methylation in AML is elusive. Oncogenic role of miR-9 have been reported in solid tumors, however is undetermined in AML. We illustrated a unique epigenetic role of miR-9 in murine myelopoiesis previously. Clinical trials in adult AML patients have evaluated hypomethylating agents however, why only certain AML patients respond to these drugs is unknown. Pediatric experience with hypomethylating drugs is limited.

**Objective:** Our objective is to determine the role of miR-9 in EVI1high pediatric AML patients and to establish if hypomethylating agents can be used as a therapeutic strategy in these patients

**Methods:** AML cell lines (AML-1, Kasumi-3, U 937) and 38 primary AML pediatric samples obtained from Children's Oncology Group were checked for EVI-1 and miR-9 expression by q-RT PCR. Methylation of the CpG enriched miR 9 promoter was evaluated by direct sequencing of bisulfite-converted DNA. Human EVI1high/EVI1low AML cell lines and patient cells were treated with 5-AZA, analyzed for miR-9 expression, growth, apoptosis and colony formation. miR-9 was re-expressed in EVI1high/EVI1low cell lines and primary bone marrow cells using lentiviral vector and growth, apoptosis and colony formation were assessed. Xenograft models were generated by injecting AML1 cells infected with miR-9-Lego or Lego empty control vector into sublethally-irradiated NSG-hSCF/hGM-CSF/hIL3 mice. When the mice became moribund, bone marrow, spleen and peripheral blood were analyzed for engraftment by flow cytometry.

**Results:** EVI1 hyperexpression in cell lines and AML patient samples correlates with downregulation of miR-9. There was significantly increased methylation of miR-9 promoter in EVI1high cell lines (AML-1, Kasumi-3) and EVI1 high patient bone marrow cells compared to EVI1low cell line (U 937) and EVI1 low patient cells. miR-9 expression was significantly reactivated by 5-AZA in EVI1high in contrast to EVI1low cell lines. Activation of miR-9 using 5-AZA treatment and re-expression of miR-9 by lentivirus results in significant growth inhibition, increased apoptosis and decreased colony formation in EVI1high cell lines / BM samples but does not affect survival of EVI1low cell lines, BM samples and control CD 34 cells. AML1 xenograft mice with ectopic expression of miR-9 had prolonged survival and delayed disease latency compared to those with control vector.

**Conclusion:** Our studies establish the critical role of EVI1 induced hypermethylation of miR-9 promoter in leukemogenesis in EVI1high pediatric AML and suggest that hypomethylation is a potential therapeutic strategy for EVI1high pediatric AML patients.

## Neoplastic lung disease in the DICER1 syndrome

**Primary Author:** Nicholas Khan (RMC)

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**Introduction:** Pleuropulmonary blastoma (PPB), the most common pediatric primary lung malignancy, progresses through stages of malignant transformation, from type I (cystic) PPB to type III (solid) PPB. An unknown percentage of type I PPBs involute after ~7 years to form type Ir(egressed) PPB, which have little to no malignant potential. Pathogenic germline variation in DICER1, an endoribonuclease integral to microRNA biogenesis, is associated with familial PPB, and a variety of other neoplasms, including cystic nephroma (CN) and Sertoli-Leydig cell tumors (SLCT).

**Objective:** To quantify the frequency of type Ir PPB in a DICER1 cohort.

**Methods:** Probands were recruited for history of PPB, CN, or SLCT. Probands and their family members underwent genetic testing for DICER1, and returned medical history questionnaires. A subset of the cohort received a comprehensive evaluation at the Clinical Center of the National Institutes of Health, where participants with a pathogenic DICER1 variant were screened by chest CT. A radiologist systematically recorded details for each lesion detected. PPB frequency was evaluated in probands and family members with and without pathogenic germline DICER1 variation. Log-rank tests were used to assess differences.

**Results:** Non-proband family members with pathogenic DICER1 variation (n=100) were at higher risk for PPB (P=0.001), lung cysts (P<0.001), pleural effusion (P=0.014), lobectomy (P=0.016), and any lung surgery (P=0.001) compared with controls (n=183); probands (n=47) were at even higher risk compared with family members with DICER1 variants (P<0.001). Chest CT revealed type Ir PPB (lung cysts) in 43% (30/69) of non-proband family members with DICER1 variants. Among those age < 18 years, 12 lung lesions were detected in eight participants (8/22; 36%), three of whom had bilateral lung cysts.

**Conclusion:** We establish, for the first time, the frequency of type Ir PPB in a cohort of DICER1-carriers unselected for lung disease. These data may help model the risk of malignant PPB transformation.

**Significance:** The study of the DICER1 syndrome is complicated by the rarity of the disorder and ascertainment bias; if participants are recruited on the basis of PPB diagnosis, they necessarily have a history of lung disease. To reduce this bias, we compared probands to family members with and without pathogenic DICER1 variation. Our study of non-proband DICER1-carriers (and thus not ascertained for any lung disease) showed that a significant minority (43%) harbored type Ir PPB (asymptomatic lung cysts). , Since malignant (type II and III) PPB is very rare (several dozen cases each year in the US), our findings suggest that the vast majority of type I PPB involute to type Ir PPB. These findings have implications for the development of programs to screen for PPB in DICER1-carriers. The genetic and physiologic mechanisms of type I PPB involution merit additional investigation.

## **Functional blocking monoclonal antibody against IL-12p40 monomer stimulates death in prostate cancer cells via IFN-gamma.**

**Primary Author:** Madhuchhanda Kundu, PhD

**Contributors:** Avik Roy, PhD (RUMC); Kalipada Pahan, PhD (RUMC)

**Introduction:** Interleukin-12 (IL-12) is the most common cytokine that plays a crucial role in the pathogenesis of many cell-mediated inflammatory disorders including multiple sclerosis (MS), psoriasis, and Crohn's diseases. However, its role in the pathogenesis of cancer is not properly understood. IL-12 family of cytokines has four different members including p40, p402, p70, and IL-23. Among these cytokines, p40 and p402 have been known non-functional for a long time because of the unavailability of specific functional antibodies.

**Objective:** In our lab we have developed specific monoclonal antibody against p40 that can neutralize its cytokine function. Since cancer is also linked to the chronic cell-mediated inflammation, we are interested to test the effect of this antibody on cancer cell death.

**Methods:** We have determined the levels of p40 and p402 in different cancer cells by ELISA. Surprisingly, we observed that all forms of cancer cells are associated with the elevated level of p40 suggesting its possible role in the cancer pathogenesis.

**Results:** Our present study first-time confirms the existence of p40 monomer (p40) and homodimer (p402) subunits of IL-12 in cancer cells and also explains the molecular mechanism by which these subunits participate in the generation of cancer pathology, at this study, in prostate cancer pathology. Our data clearly demonstrate that different cancer cells are associated with the increased expression of p40 over p402 and the antibody-mediated selective ablation of p40, but not p402, stimulates the death in prostate cancer cells via induction of IFN-gamma production both in cultured transgenic adenocarcinoma of the mouse prostate (TRAMP) cells and also in vivo in tumor tissue. While investigating the mechanism, we observed that p40 was involved in the arrest of IL12 receptor in the membrane abolishing its ability to induce the downstream signaling pathway. Moreover, our results revealed that the ablation of p40 allowed IL12 to bind with IL12 receptor and stimulated the production of IFN-gamma to generate cytotoxicity in TRAMP cells.

**Conclusion:** In our present study, we have endeavored to delineate the role of this cytokine in cancer pathology and also propose a novel therapeutic approach for regression of prostate cancer.

**Significance:** This cytokine has been shown to be beneficial in cancer treatment and there is an ongoing interest in this cytokine, until now there is no study that monitors the endogenous levels of different members of IL12 family of cytokine in tumor cells as there is no concrete tool available so far to measure different IL12 cytokines.



## THE MOONSHOT INITIATIVE AND ITS IMPACT FOR PEDIATRIC ONCOLOGY

**Primary Author:** Anil George, MD

**Contributors:** Paul Kent, MD (RUMC); Lizette Leanos, BA (RUMC); and Nupur Mittal, MD (RUMC)

**Introduction:** During the 2016 State of the Union Address, United States President Barack Obama announced the establishment of a 'Cancer Moonshot' to advance cancer research. As part of this initiative, there is an increased focus on improving the efficacy of clinical research. One such measure of improving clinical research is the application of the Pragmatic-Explanatory Continuum Indicator Summary (PRECIS-2) tool to distinguish explanatory versus pragmatic clinical trials across 9 different domains. In pediatric oncology, the Children's Oncology Group (COG) exists as the world's largest, collaborative children's cancer research entity that encompasses many of these domains. We analyzed all 152 phase III clinical trials in the COG database by utilizing the PRECIS-2 tool to determine the number of COG trials that were consistent with pragmatic clinical trials.

**Objective:** To determine the number of COG phase III clinical trials that met the PRECIS-2 criteria for pragmatic clinical research.

**Methods:** Utilizing the COG database, we identified 152 phase III clinical trials. The protocols for each of the trials were reviewed according to the following domains: eligibility, recruitment, setting, organization, flexibility in delivery, flexibility in adherence, follow-up, primary outcome, and primary analysis. Each of the criterion was scored on a yes-or-no scale to determine if a trial met the criterion identified in the domain.

**Results:** Out of 152 phase III clinical trials identified on the COG website, we found that 149 clinical trials (98%) met all 9 of the criteria as outlined by PRECIS-2 for pragmatic clinical trials. We found that the 3 clinical trials which did not meet all the PRECIS-2 criteria did not meet the primary outcome criterion in being directly relevant to trial participants.

**Conclusion:** Nearly all of the COG phase III clinical trials meet the criteria for pragmatic clinical research. The clinical trials that did not meet the standard of pragmatic research had primary outcomes that were reflective of supportive care and not considered part of standard care. In the United States, 90% of children with cancer are seen at COG institutions. Current treatment paradigms are derived from therapy identified in prior trials that serves as the standard arm of subsequent phase-III trials. The COG has merged evidence-based care that is accessible to all patients with well-designed clinical research to deliver optimum therapy and serve as a model for pragmatic clinical trials.

## **PATHOLOGIC COMPLETE RESPONSE (PCR) FOLLOWING A SINGLE CYCLE OF NEOADJUVANT CHEMOTHERAPY FOR HER2+ BREAST CANCER**

**Primary Author:** Isolina Rossi, MS3

**Contributors:** Katherine Kabaker, MD (RUMC), Katherine Kopkash, MD (RUMC), Paolo Gattuso, MD (RUMC)

**Introduction:** Pathologic complete response (pCR) describes absence of residual cancer on pathologic evaluation following systemic neoadjuvant therapy. As neoadjuvant therapies have become more effective in decreasing cancer burden, pCR has become an attainable endpoint for breast cancer treatment. Studies suggest pCR in estrogen (ER) negative, progesterone (PR) negative, and HER2+ breast cancers after neoadjuvant TCH+P (docetaxel (T), carboplatin (C), trastuzumab (H), pertuzumab (P)) is between 57-66%.

**Objective:** We discuss case presentation, diagnosis, and treatment of single cycle TCH+P resulting in pCR of an invasive ductal carcinoma grade II along with risks/benefits associated with fewer cycles of neoadjuvant therapy.

**Methods:** A case of pCR after a single cycle of neoadjuvant chemotherapy was reviewed. Clinical, surgical, and pathologic details were collected by chart review. Background, national guidelines, and relevant papers were collected using PubMed.

**Results:** A 64 y/o female complained of enlarging left breast mass. ROS was unremarkable and physical exam revealed a 1.5cm non-fixed mass in the inferior breast without skin changes, nipple discharge, or palpable lymphadenopathy. Subsequent imaging noted a 1.4x1.2x1.2 cm lesion on ultrasound and 5.0x5.0 cm mass on mammogram. Ultrasound-guided core biopsy yielded grade II infiltrating ductal carcinoma (IDCA) with ER-PR-HER2+immunostaining. Metastatic workup was negative. The multidisciplinary treatment team decided on neoadjuvant therapy with docetaxel, carboplatin, trastuzumab, and pertuzumab (TCH+P). Cycle #1 was complicated with hospitalizations for nausea, vomiting, diarrhea, dehydration and diabetic ketoacidosis. She refused further treatment, opting for surgical intervention with adjuvant chemotherapy to follow. Physical exam revealed no palpable mass at this time. Surgical pathology revealed no residual sign of carcinoma with a pathologic stage of ypT0N0(sn).

**Conclusion:** pCR of HER2+ IDCA following single cycle neoadjuvant chemotherapy suggests that susceptible cancers may be treated with fewer cycles. Fewer cycles decreases toxicity, adverse events, and financial stress to cancer patients.

**Significance:** There exists a strong association between pCR and long-term outcomes of aggressive breast cancer subtypes (such as triple negative, hormone-receptor-positive, HER2-negative, and HER2-positive w/ hormone-receptor-negative). The neoadjuvant TCH+P regimen of docetaxel (T), carboplatin (C), trastuzumab (H), and pertuzumab (P) has been shown to have a pCR rate between 53-69% in HER2+, hormone receptor negative cancers according to the TRYPHAENA study. Despite high success rates for remission, TCH+P has significant toxic burden on the patient. We present the first reported case of pCR

following a single cycle of neoadjuvant therapy, which suggests that fewer cycles may be sufficient to obtain tumor response.

## **High Burden of Obstructive Sleep Apnea in Subgroups of Chronic Rhinosinusitis: Importance of Phenotyping Chronic Rhinosinusitis Patients for Stratifying Risk Factors for This Major Comorbidity**

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**Introduction:** Chronic rhinosinusitis (CRS) is an inflammatory condition involving the mucosa of the nasal and paranasal sinuses, characterized as CRS with nasal polyps (CRSwNP) and CRS without nasal polyps (CRSSNP). Obstructive sleep apnea (OSA) is a chronic sleep related breathing disorder. It is widely known that patients with chronic rhinosinusitis suffer from sleep disruption, and there is a complex association between CRS and OSA.

**Objective:** The link between CRS and OSA is not well studied. This study aims to identify the risk factors for developing OSA in the CRS population and who should be screened for OSA.

**Methods:** Cohort study of 1004 patients with confirmed CRS. Patient charts were reviewed for those with sleep study confirmed OSA. Patient charts were further reviewed for demographic information (age, ethnicity, race, sex, BMI) and medical history including: duration of CRS, presence of nasal polyps, number of endoscopic sinus surgeries, asthma, asthma hospitalizations, asthma ED visits, AERD, allergic rhinitis, eczema, food allergy, GERD, GERD treatment, anosmia and Lund-Mackay score (LMS).

**Results:** 970 patients were included. Logistic or linear regression analyses were performed to correct for BMI. Blacks were at higher risk for OSA (20.7% vs. 10.5% in Latinos and 8% in whites). Higher age was associated with higher risk for OSA. Male gender was a risk factor for OSA (14.2% in Male vs 9.4% Female). OSA was more common in CRSSNP patients. In CRSSNP cases, OSA was associated with GERD and duration of CRS. 25% of male CRSSNP patients above 40 had OSA; this prevalence increased to 40% in male black CRSSNP patients above 40 years old.

**Conclusion:** Patients with CRS should be screened for OSA. Especially male, black, CRSSNP cases who are older than 40 years old and with BMI over 30.

## Role of Pak1 in modulating production of reactive oxygen species

**Primary Author:** Megan Covington, BA

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**Introduction:** Atrial fibrillation (AF) is associated with increased tissue levels of angiotensin II (AngII) as well as reactive oxygen species (ROS). Previously, our laboratory demonstrated decreased p21-activated kinase 1 (Pak1) in tissue from AF patients and showed that loss of Pak1 increases NADPH oxidase 2 (NOX2) dependent ROS production (NOX2/ROS) and atrial arrhythmia.

**Objective:** Our objective was to determine the mechanism by which Pak1 regulates NOX2/ROS in order to explore Pak1 as a therapeutic target to attenuate NOX2/ROS and arrhythmic activity in AF. We aimed to distinguish if Pak1 attenuates NOX2 through its kinase activity or protein-protein interaction.

**Methods:** Atrial myocytes were isolated from mice and rabbits, and ROS levels were quantified using DCF dye. Rate of fluorescence change was recorded under basal conditions and during AngII stimulation of NOX2/ROS. Pak1 inhibitors (1,4-NHQ, 1,4-NQ, 2-Mc-1,4-NHQ, and Pak18) attenuated its kinase activity or its binding to PAK-interacting exchange factor (beta-PIX), a guanine nucleotide exchange factor (GEF).

**Results:** Experiments showed that attenuation of Pak1 kinase activity increased basal and exaggerated AngII induced ROS production. The increase in ROS for inhibitors 1,4-NHQ, 1,4-NQ, and 2-Mc-1,4-NHQ correlated with their binding affinity to the Pak1 autophosphorylation site. Pharmacological stimulation of Pak1 phosphorylation using FTY720 reduced ROS. Pak18 inhibition of Pak1 caused no change in ROS under basal conditions or during AngII administration.

**Conclusion:** The regulation of ROS production through stimulation and inhibition of Pak1 supports that Pak1 regulates NOX2 through its kinase activity. However, Pak1 dependent protein-protein interaction can play a role in competition between Pak1 and Rac1 for their common beta-PIX binding site and in the attenuation of Rac1 activation, membrane translocation, and NOX2 activation.

**Significance:** Our experiments show that enhancing Pak1 kinase activity in AF can potentially reduce NOX2/ROS and decrease arrhythmic episodes. Furthermore, our data identifies beta-PIX as a relevant GEF for Rac1 dependent NOX2 activation. Therefore, competitive inhibition of the Pak1/Rac1 binding site on beta-PIX could be another pharmacological target to suppress NOX2 activation.

## **Endovascular Revascularization of Branch Vessels During EVAR: A Single Institution's Experience with Parallel Grafts, Fenestrated Grafts, and In-situ Fenestration**

**Primary Author:** Nhi Vo, MS

**Contributors:** Bulent Arslan, MD (RUMC)

**Introduction:** Effective endovascular aortic aneurysm repair (EVAR) requires at least 15 mm of proximal neck length. Extension of the main body stent to ensure an adequate seal at the risk of branch vessel occlusion may be necessary for patients with challenging anatomy and unsuitable for other forms of treatment.

**Objective:** To describe short-term experiences with the use of parallel grafts (pEVAR), fenestrated grafts (FEVAR), and in-situ fenestration (isFEVAR) to treat para-visceral aortic aneurysms.

**Methods:** Elective EVAR cases with risk of para-visceral arterial occlusion were retrospectively reviewed from 2011-2016 and stratified by revascularization technique: pEVAR (n=5), FEVAR (n=5), isFEVAR (n=3). FEVAR cases were performed using the custom-manufactured ZFEN graft (Cook, Inc, Bloomington, Indiana). Patient demographics, comorbidities, fluoroscopy time (FT), technical success rate, 30-day mortality, vessel patency, complications and/or reinterventions were analyzed.

**Results:** Thirteen patients (61.5% female, mean age 73.7) were reviewed; 46% had prior intervention. All had tobacco history; 61.5% were former smokers. Mean max aneurysm diameter (cm+/-SD) were 6.3+/-1.0, 5.8+/-0.8 and 5.4+/-0.7 in pEVAR, isFEVAR and FEVAR cases, respectively. All groups achieved 100% technical success. Mean FT (minutes+/-SD) were 67+/-15.5, 196+/-43.7 and 139+/-80.9 in pEVAR, isFEVAR, and FEVAR cases, respectively. At completion, one (20%) Type I endoleak with near complete resolution occurred in pEVAR cases. Two (40%) endoleaks (Type I, II) occurred in FEVAR cases. No pEVAR or FEVAR-related endoleaks required additional intervention. Two endoleaks (Type I, IV) occurred in isFEVAR cases; embolization was required in one case. At 30-days, one mortality occurred in the FEVAR group due to declining renal function. All remaining patients had 100% patency of revascularized branch vessels. At latest follow-up (weeks) [40+/-26.7 (pEVAR), 39+/-30.4 (isFEVAR), 14+/-6.0 (FEVAR)] all revascularized vessels continued to remain patent.

**Conclusion:** In-situ fenestration, parallel and fenestrated grafts are all feasible techniques for revascularization of complex para-visceral aortic aneurysms with 100% acceptable patency at 30-days.

**Significance:** In-situ fenestration of the main body stent graft in EVAR has only been limitedly described in the literature for descending aortic aneurysms. It benefits as a bailout technique in accidental coverage of branch vessels during EVAR, or when parallel stent grafts cannot be achieved due to anatomy, or in emergent repair where custom fenestrated grafts cannot be made in time. A comparison with other known techniques for revascularization of para-visceral aneurysms is warranted.

## **Correlation between clinical symptoms and flow-volume loop abnormalities in patients suspected to have vocal cord dysfunction**

**Primary Author:** Suzanne LaBelle, BS

**Contributors:** Neha Sharma, BS (UIC); Mollie Brinkman, BS, RRT, RPFT (Rush), Girish Sharma, MD, FCCP, FAAP (Rush)

**Introduction:** Vocal Cord Dysfunction (VCD) is an under-recognized condition characterized by paradoxical movement of vocal cords during inspiration, or tonic contraction, resulting in airflow obstruction causing wheezing, chest tightness, and shortness of breath. Symptoms can be either spontaneous (SVCD) or exercise induced (EIVCD). VCD is often misdiagnosed as asthma, resulting in overuse of medications, frequent preventable hospitalizations and intubations. When correctly diagnosed, VCD is treatable by speech therapy and/or inhaled anticholinergic agents. VCD is traditionally diagnosed by laryngoscopy, a somewhat invasive and distressing procedure, considered gold standard. Since VCD symptoms are unpredictable, laryngoscopy may not always be practical. We hypothesized that inspiratory loop abnormalities (ILAs) on spirometry may be used to clinically diagnose VCD.

**Objective:** To determine the correlation between ILAs and VCD diagnosis.

**Methods:** The study was approved by the Institutional Review Board. The charts of patients undergoing exercise challenge test during the last 5 years were reviewed. Information was compiled on flow-volume loop results, patient age, gender, symptoms, presence of asthma, comorbidities, treatment or therapy, and outcome. Data analysis was then performed to determine the positive predictive value (PPV) and negative predictive value (NPV) of inspiratory loop abnormalities (ILAs) in the flow-volume loop.

**Results:** We reviewed 147 charts. Of 82 patients diagnosed with VCD, 80 had inspiratory loop abnormalities (ILAs) on exercise challenge, and 2 did not. Of 65 patients without VCD diagnosis, 30 had ILAs, and 35 did not. ILAs have a PPV of 72.70% and an NPV of 95.6%.

**Conclusion:** This study shows preliminary support for the use of ILAs as a component of VCD diagnosis. We suspect the PPV is underestimated because not all the patients underwent laryngoscopy, leading to inability to confirm VCD diagnosis in some cases. Based on other demographics collected, we plan to determine a more reliable screening tool utilizing patient symptoms and comorbidities in conjunction with ILAs.

**Significance:** Laryngoscopy, the current gold standard for the diagnosis of VCD, is a somewhat invasive procedure that can cause distress to an already vulnerable pediatric population. Since the VCD symptoms are mostly episodic or related to exercise, visualization of the vocal cords by laryngoscopy during the symptoms may not be practical for each patient. In order to avoid misdiagnosis of VCD and distress from laryngoscopy, we will continue to seek clinical features most related with flow volume loop abnormalities to develop a scoring system, and ultimately provide a reliable, noninvasive, and cost-effective diagnostic tool for VCD. We plan to use the VCD diagnostic scoring in a future prospective study and correlate with endoscopic findings.

## **A Diagnosis More Than Skin Deep: A Case of Late-Stage Pulmonary Langerhans' Cell Histiocytosis with Skin Lesions**

**Primary Author:** Joshua Verson, BS

**Contributors:** Alexander Egusquiza, David C Nguyen

**Introduction:** Langerhans' cell histiocytosis (LCH) is a group of rare diseases with a wide variety of presentations across age groups. We describe a case of pulmonary LCH, which was eventually diagnosed at a late stage despite having additional skin findings for several years.

**Objective:** A 32 year-old male presented with acute worsening of chronic shortness of breath in which he could not walk more than a block. He had smoked cigarettes for 10 years with no occupational exposures. His vitals were within normal limits. His exam was notable for diminished right lung sounds and expiratory wheezes bilaterally.

**Methods:** A chest x-ray showed marked emphysema and bilateral upper lobe reticular opacities suggestive of scarring. Computerized tomography of the chest showed loculated right pneumothorax and hyperinflated lungs with destructive changes secondary to numerous irregular, thick walled cysts and scattered irregular pulmonary nodules. The patient started inhaled corticosteroids, inhaled anticholinergics, and inhaled short-acting beta agonists. He was sent home with oxygen and strongly encouraged to abstain from smoking.

**Results:** LCH is characterized by end-organ infiltration of proliferating monoclonal Langerhans' cells, a histiocyte involved in antigen presentation. The highest incidence of LCH is between ages 5-10 years; the adult incidence is estimated to be less than half as frequent than the pediatric, about one patient in a million. LCH most commonly involves the skin, bones, and lungs. Pulmonary LCH (PLCH) is interesting in that it has a peak incidence in ages 20-40 years and occurs almost exclusively in smokers (>90% of cases).

**Conclusion:** Smoking cessation is the cornerstone of management of PLCH. It has been hypothesized that tobacco smoke can incite the production of cytokines by alveolar macrophages, leading to increased recruitment of histiocytes to the lung parenchyma. In isolated pulmonary pathology, lung transplant with smoking cessation is often curative.

**Significance:** Pulmonary Langerhans Cell Histiocytosis is an extremely rare disease, affecting less than one in one million patients a year. It is vital to not miss the indications of the disease in a patient presenting with similar symptoms to our patient in clinic or the ER. It is also essential to explain to the patient with PLCH the dangers of smoking and how symptoms can even be reversed upon the cessation of cigarette smoking.



## Value of Next Day Angiography and Predictive Factors of Further Intervention in Patients Undergoing Catheter Directed Thrombolysis for Massive and Sub-massive Pulmonary Embolism

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**Introduction:** Catheter-directed thrombolysis (CDT) is indicated in hemodynamically unstable patients with acute massive and submassive pulmonary embolisms (PEs), especially those in which death is likely to occur before systemic thrombolysis can become effective. Factors determining CDT continuation, discontinuation, or need for additional interventions remain unclear.

**Objective:** To primarily assess the utility of next-day pulmonary angiography for CDT in patients with acute massive and submassive PE undergoing continuous pulmonary arterial pressure monitoring, and secondarily, determine factors predictive of further interventions.

**Methods:** Patients undergoing CDT from 2006-2016 for massive (n=14) and submassive (n=18) PE in the section of Interventional Radiology were reviewed. Patient demographics, co-morbidities, pre-procedural labs, non-invasive hemodynamic studies, and technical variables were recorded. Of patients receiving next-day angiography, those requiring further intervention, defined as continued CDT and/or mechanical thrombectomy (n=10), were identified and contrasted with those not needing further intervention (n=17) to assess for predictive factors and discern the role of next-day angiography.

**Results:** Twenty-seven (84.4%) of 32 total patients (56.3% male, 43.7% Caucasian, mean age 66.2) underwent next-day pulmonary angiograph- of which 10 (37%) were identified as needing additional interventions: catheter repositioning/exchange (n=3), mechanical thrombectomy (n=5), both catheter and mechanical exchange (n=2). Factors predicting additional intervention included obesity (9 vs 1, p=0.02) and younger age (48.4 vs 62.5, p=0.02). Between patients necessitating further intervention and those that did not, initial (41.4 vs 35.9, p=0.29), next-day (31.2 vs 26.8, p=0.34), and interval change (5.0 vs 8.6, p=0.65) in pulmonary artery pressures (mmHg) were not statistically significant or predictive. Pre-procedural RV/LV size also did not differ significantly (p=0.96). 30-day mortality were comparable (2 vs 1, p=0.56) between patient subsets.

**Conclusion:** Pulmonary artery pressures and pre-procedural RV/LV size were similar and not predictive of additional interventions. Next-day pulmonary angiography for CDT of acute massive and submassive PEs, however, effectively identified 37% of patients needing prolonged CDT and/or adjunct interventions.

**Significance:** Next-day pulmonary angiography for catheter-directed thrombolysis has clinical utility in helping determine future management of acute massive and submassive pulmonary embolisms.

## Clinical Pathway for Increasing Congestive Heart Failure Follow Up

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**Introduction:** The Centers for Medicare and Medicaid Services reimburse healthcare institutions based on readmissions. Twenty percent of Medicare beneficiaries discharged from the hospital are readmitted within 30 days, costing \$17 billion annually with heart failure the most common diagnosis. Follow up with a heart failure practitioner within one week following hospitalization is associated with decreased 30-day readmissions.

**Objective:** Develop a clinical pathway to standardize heart failure treatment and follow-up.

**Methods:** A multidisciplinary team created a clinical pathway for heart failure in July 2016 for testing, medications, indications for heart failure consultation, and one-week heart failure and three-week primary care follow-up. Physicians were given a presentation on the pathway in August of 2016. Patients in the emergency department with heart failure were admitted using the pathway. If the patient was over age 70, newly diagnosed with heart failure, had worsening renal function, a history of heart disease, prior inotrope requirements, or 2 heart failure admissions in the last 60 days, heart failure was consulted. At discharge, patients were given follow-up with a heart failure practitioner within one week and primary care physician within three weeks. Data on consultation and follow-up were gathered and compared.

**Results:** Initially, 19% of patients admitted with heart failure received consultation with 19.5% and 50% following-up with heart failure and primary care respectively. Following pathway creation, consultation was 50% and heart failure follow-up was 21%. After the August presentation, heart failure follow-up increased to 67% and primary care to 58%. September follow-up rates continued rising.

**Conclusion:** Implementation of the heart failure clinical pathway led to higher rates of heart failure consultation, one-week heart failure and three-week primary care follow up. Future efforts will focus on 30-day readmissions. Higher outpatient follow-up is associated with decreased readmissions, so improvement is expected.

## **Liver Dysfunction Predicts Poor Outcomes in Adult Extracorporeal Membrane Oxygenation Support**

**Primary Author:** Nikola Dobrilovic, MD

**Introduction:** Extracorporeal membrane oxygenation (ECMO) support can provide critically ill patients an opportunity to survive otherwise lethal illness. With roughly half of patients surviving ECMO, it remains unclear how and when to apply this labor-intensive, costly resource. Clear predictors of outcomes have yet to be defined.

**Objective:** We examine the role of liver dysfunction in adult ECMO patients as a potential prognostic marker.

**Methods:** This study reports a five-year, retrospective, single institution experience examining all adult patients for whom ECMO support was utilized. Trends in liver function were examined (albumin, PT-INR, total bilirubin, AST, and ALT).

**Results:** A database of 105 ECMO patients was reviewed, and all adult patients (n=66) were included. Mean age was 53 (range 19-82) years, 35 male, 31 female. Fifty-three percent (35/66) of adult patients met at least one criterion for liver dysfunction. Mean duration of ECMO support was 8 days. Overall hospital mortality was 68% (45/66).

**Conclusion:** Increases in total bilirubin, ALT, and AST levels all correlated with early mortality despite good cardio-pulmonary support. Profound liver dysfunction in patients supported with ECMO is a poor prognostic sign associated with exceedingly high mortality. It is expected that liver function studies will play a significant role in patient selection criteria regarding 1) initiation of ECMO, 2) as a criterion for termination of ECMO, and 3) possibly as a trigger for use of liver support devices.

## Electrical and calcium transient alternans in cell pairs and intact atrium

**Primary Author:** Jaime DeSantiago, M.D., Ph.D.

**Contributors:** Kathrin Banach (Rush University Medical Center, Molecular Biophysics & Physiology)  
Lothar A. Blatter (Rush University Medical Center, Molecular Biophysics & Physiology)

**Introduction:** Cardiac arrhythmias, including atrial fibrillation (AF), require an arrhythmogenic focus (ectopic activity) and tissue inhomogeneity (conduction heterogeneity). Electrical and calcium alternans in atrial tissue represents a risk factor for AF.

**Objective:** Determine characteristics of Ca transient (CaT) alternans in coupled pairs of atrial myocytes and the relationship between cellular atrial alternans and occurrence of AF episodes in the perfused intact heart.

**Methods:** Confocal cytoplasmic calcium measurements in atrial cell pairs. Atrial bipolar electrograms and multielectrode mapping of the epicardial surface.

**Results:** Atrial cell pairs isolated from rabbit hearts were field stimulated at increasing rates until CaT alternans occurred. CaT alternans usually initiated in one cell first. Alternans in the second cell rarely occurred simultaneously (3/11 pairs), but rather started at higher frequencies (5/11 pairs), or did not occur at all (3/11pairs). Stimulation with angiotensin (Ang II) lowered the pacing threshold for CaT alternans and enhanced the degree of alternans, presumably through activation of IP3 receptor-induced Ca release. Under control conditions cell pairs spontaneously switched between concordant and discordant CaT alternans. Concordant and discordant CaT alternans between cell pairs led to intercellular heterogeneity in the CaT amplitude resulting in beat-to-beat intercellular Ca gradients. Ang II enhanced these intercellular Ca gradients. In Langendorff perfused rabbit hearts pacing-induced electrical alternans were recorded with atrial bipolar electrograms and multielectrode mapping of the epicardial surface. The data revealed a high temporal correlation between atrial alternans and episodes of AF: atrial electrical alternans (atrial T wave alternans) triggered AF episodes, and AF induced by burst pacing was followed by atrial T wave alternans. Ang II perfusion enhanced tissue-wide atrial T wave variability, suggesting enhanced electrical tissue heterogeneity and possibly discordant alternans at tissue level.

**Conclusion:** The data demonstrate a causative relationship between cardiac alternans and susceptibility to AF. Therapeutic interventions targeting the inositol-phosphate signaling cascade may reduce the AF risk.

## A Clinical Pathway to Assess Asymptomatic Renal Transplant Candidates Using Myocardial

**Primary Author:** Ibtihaj Fughhi, MD, Msc

**Introduction:** A 2012 AHA/ACC scientific statement proposed 8 clinical risk factors (RF) to assess the need for noninvasive coronary artery disease (CAD) surveillance in asymptomatic renal transplant (RT) candidates. The value of these RF in identifying candidates for noninvasive CAD surveillance and the role of such testing in the clinical context is unknown.

**Objective:** In this investigation, we sought to validate the risk factors set forth by the AHA/ACCF scientific statement, identify a threshold sum of risk factors to prompt noninvasive evaluation for coronary artery disease (CAD), and evaluate the diagnostic and prognostic utility of MPI with single-photon emission computed-tomography (SPECT) when applied in the context of risk defined by the AHA/ACCF statement.

**Methods:** A prospective cohort study of consecutive RT recipients was conducted. The sum of RF identified by AHA/ACC (age > 60, hypertension, diabetes, cardiovascular disease, dyslipidemia, smoking, dialysis > 1 y, left ventricular hypertrophy) was calculated. SPECTMPI scans were analyzed by a 'blinded' reader. Patients were followed for post RT MACE (cardiac death or MI).

**Results:** We followed 581 RT recipients for a mean of  $3.7 \pm 2.3$  y postRT; of those 403 had MPI and 90 had coronary angiogram preRT. The sum of RF (range, 0- 8) was associated with modest discriminatory capacity for obstructive CAD ( $\geq 70\%$ ) as well as postop (30 day) and long term MACE;  $\geq 3$  RF was an optimal threshold to identifying patients at risk for all endpoints . MPI provided incremental predictive value to RF for obstructive CAD ( $\Delta\chi^2 = 5.4$ ;  $P = .02$ ) and long term MACE ( $\Delta\chi^2 = 4.4$ ;  $P = .04$ ) but not postop MACE ( $P = .56$ ). MPI was best predictive of long term MACE in intermediate risk (3-4 RF), but not low and high risk patients . There was an interaction between MPI finding and time lapse between MPI and RT (interaction HR .61;  $P = .03$ ) in regard to long term MACE.

**Conclusion:** This study validates RF proposed by AHA/ACC and defined the role of MPI in the evaluation of RT candidates. Asymptomatic RT candidates with  $\geq 3$  risk factors are at risk and should be considered for noninvasive CAD surveillance. In agreement with the Bayes theorem , intermediate risk patients (3-4 RF) benefit the most from pre RT MPI to define long term MACE risk. Low risk patients (0-2RF) do not seem to benefit from MPI. RT may not be ideal for high risk patients ( $\geq 5$  RF) due to high MACE risk, irrespective of MPI. There was a time dependent attenuation of the predictive value of MPI in this population.

## **Duration of Extracorporeal Membrane Oxygenation Support Does Not Correlate with Survival**

**Primary Author:** Nikola Dobrilovic, MD

**Contributors:** Michel Ilbawi MD, Robert March MD, Burhan Mohamedali MD, Lauren Michalak MS, Omar Lateef, Robert Balk MD, Maja Delibasic MD, Roger Dimitrov PhD, Jai Raman MD PhD

**Introduction:** Complete pulmonary/cardiopulmonary ECMO support can obscure underlying physiology making it difficult to differentiate between recovery and futility. 'Duration of ECMO support' is often used by family and hospital staff to influence withdrawal of care, though, without data.

**Objective:** We examine the role that duration of ECMO support plays in predicting survival.

**Methods:** This study reports a retrospective, single institution experience examining all patients for whom ECMO support was utilized. All consecutive patients over an eight-year period (May, 2008 to May, 2016) were included in the study. Duration of ECMO support was examined as a predictor of survival using binary logistic regression.

**Results:** A total of 146 patients received ECMO support during the eight-year study period (95 adult, 51 pediatric). The number of patients annually receiving ECMO support increased progressively throughout the study. Mean duration of ECMO support was 11 (1-119) days. Overall survival was 56% (82/146). In a binary logistic regression using duration on ECMO (days) to predict the dependent variable survival, duration was not a predictor in the model ( $r=0.053$ , not significant). Subgroup examination (cardiac ECMO, respiratory ECMO, pediatric) also failed to show any meaningful relationships. During the latter years of the study, a trend of patient survival has been observed in select cases after long (30 day) ECMO runs.

**Conclusion:** Duration of ECMO was not a significant predictor of patient survival. However, we have observed a recent trend of successful ECMO outcomes even after a very long duration of ECMO support.

## The Return on Investment of International Patients to American Hospitals

**Primary Author:** Ishani Patel, BS

**Contributors:** Tricia Johnson, PhD (Rush Health Systems Management), Andrew Garman, PsyD (Rush Health Systems Management and National Center for Healthcare Leadership), Samuel Hohmann, PhD, MS-HSM (Vizient), Paola Cieslak (Rush University Medical Center Strategic OutreOutreach), Jarrett Fowler, MPPA (US Cooperative for International Patient Programs), and Shabnam Daneshgar (US Cooperative for International Patient Programs).

**Introduction:** Hospitals have invested substantial resources into establishing international programs. However, a comparative analysis between hospital programs and a collective return is unknown. While studies have been conducted on the motives behind international travel, none have been performed on the return on investment of establishing these programs. This cross-sectional, retrospective study will evaluate the association between hospital investment in international programs and their return on investment- increased patient revenue. We hypothesize that larger and established international programs yield higher patient revenues. International programs will also be analyzed by program size and by program maturity, which may contribute to increased gross international patient revenues. This study will evaluate whether any economies of scale exist, understand the organizational trade-offs, and provide objective information for making the business case to hospital leadership

**Objective:** The purpose of this study is to quantify the economic benefits and costs of an international patient program and evaluate the ROI of international patients for US hospitals. We hypothesize that international patients yield a positive ROI for the hospital (2) hospitals with larger programs will have higher ROI than smaller programs, and (3) hospitals with an established international program will generate increased ROI than newer programs. The results from this study will allow hospitals to develop strong international programs and allocate their resources to make the appropriate investments in generating increased gross international patient revenue. Hospitals will also be able to make a business case for increased international program investment to hospital executives and identify the impact of international patient revenue to the hospital or health system.

**Methods:** This study will examine the costs that hospital incur to develop international programs and the resulting benefits. The association tests will be performed on a sample of 55 hospitals that were members of the US Cooperative for International Patient Programs (USCIPP) in a series of descriptive and bivariate statistical analyses with cost and benefit variables.

**Results:** This study is currently in the data analysis process. Results and conclusions are expected to be completed prior to the forum.

**Conclusion:** This study is currently in the data analysis process. Results and conclusions are expected to be completed prior to the forum.

**Significance:** The management implications of this study are great. By being informed of the investments, revenue and ROI that international programs generate, large or established programs will be able to provide relevant and valid information to newer and smaller programs to enhance their

current structure or aid hospitals in developing a strong international program. For hospitals to be successful, it is essential to invest in the infrastructure and additional services for these patients from the time of inquiry to post-discharge care coordination. By an increase in investment developing and enhancing international programs, a hospital will be able to increase their revenue. This study might help in the development of a business case for international program and examine for any economies of scale as a result of increased investment in international programs which may generate increased international patient volumes.



## **Liver Dysfunction Predicts Poor Outcomes in Adult Extracorporeal Membrane Oxygenation Support**

**Primary Author:** Nikola Dobrilovic, MD

**Contributors:** Lauren Michalak, Omar Lateef, Burhan Mohamedali, Douglas Smego, Robert March, Mazahir Alimohamed, Maja Delibasic, Dragana Radovanovic, Jai Raman

**Introduction:** Extracorporeal membrane oxygenation (ECMO) support can provide critically ill patients an opportunity to survive otherwise lethal illness. With roughly half of patients surviving ECMO, it remains unclear how and when to apply this labor-intensive, costly resource. Clear predictors of outcomes have yet to be defined.

**Objective:** We examine the role of liver dysfunction in adult ECMO patients as a potential prognostic marker.

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**Conclusion:** Increases in total bilirubin, ALT, and AST levels all correlated with early mortality despite good cardio-pulmonary support. Profound liver dysfunction in patients supported with ECMO is a poor prognostic sign associated with exceedingly high mortality. It is expected that liver function studies will play a significant role in patient selection criteria regarding 1) initiation of ECMO, 2) as a criterion for termination of ECMO, and 3) possibly as a trigger for use of liver support devices.

## Obtaining Accurate Blood Pressure Measurements in the Cardiac Intensive Care Unit

**Primary Author:** Emily Lange, RN, BSN, CCRN

**Contributors:**

**Introduction:** According to the American Heart Association (AHA), blood pressure (BP) measurements are one of the most important measurements in medicine, yet they are often inaccurately measured. In 2005, the AHA created guidelines on accurate BP measurement techniques. The problem is that nurses do not always follow the AHA guidelines leading to inaccurate BP measurements and decreased patient safety.

**Objective:** The purpose of this project was to improve patient safety by determining how frequently and why BP measurements did not follow all of the AHA guidelines, identify barriers preventing staff from taking accurate BPs, and create interventions to improve BP accuracy.

**Methods:** Staff members participated in this project with Institutional Review Board approval. Educational sessions were implemented to increase knowledge. Poster reminders were placed on patient monitors and in bedside clinical reference binders. Multiple sizes of BP cuffs were stocked in patient rooms. Manual BP monitors were fixed. Initial and final audits, pre-tests and post-tests, and initial and final surveys were completed.

**Results:** The initial audit and final audit included 46 patients. 43 nurses took the initial survey. 39 nurses took the final survey. 71 nurses took the pre-test. 72 nurses took the post-test. The initial audit showed that staff followed an average of 5.20 out of the 10 guidelines. The final audit showed an increase to 8.54. Posttest scores improved with 6 of 9 questions showing statistical significance.

**Conclusion:** The average number of AHA guidelines used by staff members increased by 60.9%. The final survey showed that most staff agreed or strongly agreed with statements that they utilize the interventions and guidelines. There was a significant increase in the number of staff who agreed that they have all of the supplies to take accurate BPs. This project was implemented on one unit, so the interventions and results may not be relevant to other settings.

**Significance:** If inaccurate BP measurements are taken and recorded, patients can potentially receive inappropriate medications and treatments. Nurses do not always follow all of the AHA guidelines, so it is imperative that they are reminded of the proper techniques and given tools to remember and implement the guidelines.

## Initiative to Address the Psychological Needs of IBD Patients

**Primary Author:** Melissa Halverson, DNP, RN

**Contributors:** Lynne T. Braun, PhD, Professor, Rush College of Nursing Ali Keshavarzian, MD, Chair of Gastroenterology Sharon Jedel, PsyD, Gastroenterology Dept. Lou Fogg, PhD Statistician, Rush College of Nursing Mohamed Bayoumi, MD JoEllen Wilbur, PhD, Rush College of Nursing

**Introduction:** Inflammatory bowel disease (IBD), including Crohn's and ulcerative colitis, severely impact a patient's quality of life. Anxiety and depression are common among IBD patients. Guidelines recommend routine screening for psychological symptoms. A Midwest Gastroenterology Clinic uses two items from the Short Form Inflammatory Bowel Disease Questionnaire (SIBDQ) to screen for depression/anxiety (< 3 on 7-point scale = high anxiety/depression). A retrospective chart review of 244 visits that had a score <3 showed only 41 (17%) of visits had provider documentation of psychological needs and of these only 19 (8%) of the visits resulted in referral to a psychologist. This suggested a deficiency in addressing psychological symptoms in IBD patients.

**Objective:** The purpose of this project was to a) implement and evaluate an initiative to address the psychological symptoms of IBD patients; b) determine if the SIBDQ adequately screened for psychological symptoms.

**Methods:** The initiative included: 1) an educational session by a nurse and psychologist to 8 providers on the prevalence of psychological symptoms and importance of screening/referral; 2) a protocol designed to assist the provider when symptoms are identified, and 3) a best practice alert pop-up integrated into the electronic medical record. The Patient Health Questionnaire (PHQ-9) was used to determine if the SIBDQ adequately screened for symptoms.

**Results:** A 13 item knowledge test was administered pre/post the educational session. Five of 13 items showed improvement post educational session. Charts for all visits (703 over 8 months) were reviewed for documentation of SIBDQ, documentation of psychological need, and referral to a psychologist. Results showed 415 SIBDQ completed and of 162 visits with a score < 3, 126 had documentation (78%). Referrals to a psychologist increased slightly, with 23 of 162 patients (14%) being referred. The PHQ-9 was highly correlated with the SIBDQ depression ( $r=.787$ ,  $p < .001$ ) and anxiety ( $r=.618$ ,  $p < .001$ ).

**Conclusion:** This study evaluated an initiative that raised provider awareness of the prevalence of psychological issues in IBD patients and improved the screening and referral process. Education of providers, implementation of a protocol, and alert were simple interventions that could be utilized in any GI practice

## Effectiveness of an interdisciplinary Asthma Education Program for a Pediatric Clinic

**Primary Author:** Erin Sventy, BS

**Contributors:** Ellen Becker, PhD, RRT-NPS, RPFT, AE-C, FAARC (Rush); Regina A. McClenton, RN, CCCTM (Rush); Klodiana Myftari, Pharm D (Midwestern/Rush)

**Introduction:** Asthma remains disproportionately burdensome among children in lower-income population and minorities living in inner cities. The staff providing care to these patients need strong asthma education skills.

**Objective:** The goal of this project was to enhance asthma and inhaler knowledge and confidence.

**Methods:** A convenience sample of nurses, medical assistants, care managers, and social workers completed a one-hour Asthma Education Workshop. Staff completed surveys pre- and post-workshop on Day 1 and also at a 1 month or 2 month interval. A 5-point Likert-scale question addressed the comfort explaining the asthma action plan (AAP). Knowledge of the AAP was measured through responses to eight questions. A MDI + spacer checklist was used to evaluate inhaler technique. The frequency of repetitions it took to perfect MDI + spacer technique was recorded. Wilcoxon Signed Rank tests were used to assess the AAP knowledge gained and comfort explaining the AAP on Day 1 of the workshop and retention 1 or 2 months later.

**Results:** The 22 participants showed significantly improved AAP knowledge scores on Day 1 pre- and post-test,  $Z = -2.93$ ,  $P = .003$ ; and remained stable between the Day 1 post-test and the 1 or 2 month assessment score,  $Z = -1.51$ ,  $P = .131$ . The comfort with explaining AAP also significantly improved immediately after the workshop,  $Z = -3.25$ ,  $P = .001$ . However, no one was able to perform MDI + spacer technique perfectly on the second assessment one or two months later.

**Conclusion:** A one-hour session achieved the asthma education goals and participants retained the information at the 1 or 2 month assessment. However, further work will be required to improve MDI + spacer technique.

**Significance:** Although asthma knowledge and skills of clinic staff can be improved through the use of a one-hour workshop, inhaler technique training is needed more frequently.

## Respiratory muscle strength as a measure of nutritional status in hospitalized patients

**Primary Author:** Hillary Zellner, BS

**Contributors:** Olivia Moss MS, RD, LND (RUMC); Stephanie Hicks-McGarry BS, RRT (RUMC); Ellen Moran MS, RRT, RPFT, RCP (RUMC); Ellen Becker PhD, RRT-NPS, AE-C, FAARC (RUMC); Sarah Peterson PhD, RD, LDN, CNSC (RUMC); Sharon Foley PhD, RD, LDN (RUMC)

**Introduction:** Hospitalized patients often use lean muscle mass to meet energy needs contributing to malnutrition. Evaluating the extent of lean muscle loss is an essential component of a nutritional assessment but methods commonly used have limitations. Depletion of muscle mass can result in loss of respiratory muscle strength (RMS) and function further contributing to malnutrition. Measures of RMS may assist in the assessment of nutritional status.

**Objective:** The objective of this study is to determine the difference in maximal inspiratory pressure (MIP), maximal expiratory pressure (MEP), and sniff nasal inspiratory pressure (SNIP) in hospitalized patients of varying nutritional statuses.

**Methods:** A convenience sample of adult hospitalized patients free of respiratory and neurodegenerative disorders were nutritionally assessed by a dietitian. Respiratory measures of MIP, MEP, and SNIP were obtained by a respiratory therapist and compared between those assessed as malnourished and normally nourished using Subjective Global Assessment. A sample of 128 patients was needed to detect a medium effect size at 80% power and  $\alpha=0.05$ . A t-test was used to determine differences in RMS measures between the groups. This study was approved by the Rush Institutional Review Board (IRB, #14060202).

**Results:** One-hundred twenty patients completed testing to date, 59 well nourished (49%) and 61 (51%) malnourished, with mean age  $51.5 \pm 16.7$  vs.  $58.0 \pm 16.6$  years, respectively ( $p=0.01$ ). There were significantly lower absolute MIP and SNIP measures in the malnourished compared to well-nourished group ( $p<0.05$ ). When percent predicted values were applied, only SNIP measures were significantly lower ( $62.1 \pm 30.1\%$  malnourished vs.  $78.9 \pm 26.8\%$  well-nourished,  $t(118)=3.23$ ,  $p=0.002$ ).

**Conclusion:** Measures of RMS hold promise as a proxy measure of musculature in a nutrition assessment and appear feasible to obtain at bedside.

**Significance:** Significant differences in RMS demonstrated between well nourished and malnourished patients provide evidence that using these measures hold potential as an alternative, objective and bedside measure of musculature in a nutrition assessment, specifically SNIP.

## Two cases of Median Facial Dysgenesis at the Rush Craniofacial Center

**Primary Author:** Alison Cesarz, MD Candidate

**Contributors:** Alvaro Figueroa, DDS, MS (Rush) Christina Tragos, MD (Rush)

**Introduction:** The following is a case report on two patients with median facial dysgenesis (MFD). MFD occurs in ~2% of cleft lip and palate patients and is characterized by midline facial deficiencies with or without gross brain abnormality. The surgical challenge in MFD is inadequate facial support, and therefore normal cleft protocol does not apply. MFD patients undergo extensive treatment into early adulthood and no treatment protocol exists.

**Objective:** Report on the treatment and outcomes of two pediatric patients with MFD and discuss the Rush Craniofacial Center's multidisciplinary, patient-centered approach and its application to future MFD patients.

**Methods:** Reviewed selected patient histories, treatments, and photos after obtaining patient consent. Expedited IRB approval is in process.

**Results:** Both patients presented with facial malformations at less than one year of age and were evaluated annually by a team of specialists from general pediatrics, genetics, pediatric otolaryngology, plastic surgery, speech therapy, and orthodontics. Patient 1 is 13 months old and represents short-term treatment outcomes. She has undergone nasoalveolar molding (NAM), unilateral cleft lip repair with soft palate closure, and primary rhinoplasty. She is pending hard palate reconstruction and craniofacial growth follow-up. Patient 2 is 13 years old and represents long-term treatment outcomes. She has undergone NAM, bilateral cleft lip and soft palate reconstruction and primary rhinoplasty, bilateral cleft palate reconstruction, orthodontic treatment, surgical midface advancement with external distraction osteogenesis, and pharyngeal flap. She is pending bilateral alveolar bone grafts and final cleft rhinoplasty.

**Conclusion:** Treatment involved evaluation by a multidisciplinary team followed by several surgeries and extensive orthodontic rehabilitation. The aesthetic and functional outcome of patient 2 demonstrates the reconstructive success that can be achieved in MFD despite inadequate facial skeletal and cartilaginous support. Further areas of research may include synthesis and replacement of missing cartilage and bone to maximize support.

## Prevalence of Sarcopenia among General Medical Patients

**Primary Author:** Amanda Van Jacobs, BS

**Contributors:** Ben Bienia MD (Rush), Sharon Foley PhD RD (Rush), Sarah Peterson, PhD RD (Rush)

**Introduction:** Limited data is available to describe the prevalence of sarcopenia, the involuntary loss of muscle mass and strength that occurs with aging, among patients admitted to the general medical floor (GMF). Ideally, the use of a subjective tool to measure nutrition status should be deemed reliable to effectively identify sarcopenic patients.

**Objective:** The aim of this study was to describe the prevalence of sarcopenia and agreement between nutritional status in patients admitted to the GMF.

**Methods:** A retrospective sample of patients admitted to GMF who had subjective global assessment (SGA), abdominal computed tomography (CT) scan, and handgrip strength (HGS) completed within 7 days of admission was utilized. Height, weight and body mass index (BMI) were recorded. Nutritional status was categorized as normal nourished versus moderate/severely malnourished by SGA. Cross-sectional muscle area (cm<sup>2</sup>) and skeletal muscle index (SMI, cm<sup>2</sup>/height (m<sup>2</sup>)) was determined from CT. The average of three HGS measurements (kg) was utilized. Sarcopenia was defined as the combination of low SMI (BMI <25kg/m<sup>2</sup>: <43 cm<sup>2</sup>/m<sup>2</sup>, men/women BMI >25kg/m<sup>2</sup>: SMI <53cm<sup>2</sup>/m<sup>2</sup> and <41cm<sup>2</sup>/m<sup>2</sup>) and HGS (men/women: <30 kg/<20 kg). A Pearson's Chi Squared was utilized to determine the association between sarcopenia and nutrition status measured by SGA.

**Results:** A total of 141 patients were included. Overall the prevalence of sarcopenia was 30% (n=42). An association was observed between sarcopenia and nutrition status (p=0.032); only 55% of sarcopenic patients were classified as moderate/severely malnourished.

**Conclusion:** Approximately a third of patients are sarcopenic and SGA may not accurately identify these at risk individuals. Future research is needed to develop an appropriate nutrition assessment tool to identify sarcopenic patients.

## Rush's Medical Student Hazard Materials Team

**Primary Author:** Nick Dyga, BS

**Contributors:** Josh Verson, BS (Rush); Frederick Serafin RN (Rush); Louis Hondros

**Introduction:** The lack of emergency preparedness training that medical students receive is an unrecognized problem in current medical curriculum. It is imperative that future physicians, regardless of specialty, are equipped to respond to disaster scenarios. Teaching these concepts early on provides the next generation of physicians with the basic skills and knowledge to do exactly that.

**Objective:** Early medical student involvement in disaster education is essential for continued advancement of knowledge and protocols in the emergency preparedness community. Not only will students learn about medical crisis management, but they will also learn to brainstorm creatively, work through equipment failures, respond to a team leader, and work as a team in chaotic situations. Through their training and involvement, the students will see their work as the cornerstone for a real world process that can save lives.

**Methods:** 16 medical students completed 5 hours of awareness and equipment training and formed a student HazMat team. During a citywide bioterrorism drill in June of 2016, 11 of them participated in a simulated decontamination exercise which assessed hospital arrival times, communication skills, proper donning and doffing of HazMat gear, and qualitative decontamination skills of exposed patients.

**Results:** Communication skills, response times, and qualitative decontamination of victims during the simulated drill were the main variables assessed. Observed mistakes fell into one of three categories: equipment access and organization, patient handling and decontamination procedures, and communication.

**Conclusion:** The current medical education system does not include medical students in emergency preparedness training or utilize them as a possible strategic intervention in times of crisis. Our preliminary work has demonstrated that medical students display both eagerness and competence in this arena, and we recommend that large medical centers explore the possibility of having a medical student HazMat team on call alongside the currently trained teams.

**Significance:** Emergency medical teams can never be truly prepared for a disaster, but practicing essential skills and simulating events to be as realistic as possible can positively impact patient outcomes in dangerous situations and medical emergencies. Starting disaster management training at the medical student level is critical, as the next generation of physicians are responsible for shaping our future medical policies.



## **VenaTech LP Filter Retrieval for Filter-Related Thrombosis or Malpositioning.**

**Primary Author:** Osman Ahmed, MD

**Contributors:** Sreekumar Madassery MD, Derek Heussner BA, Patrick Tran BA, Abdulrahman Masrani MD, Bulent Arslan MD, and Ulku Cenk Turba MD

**Introduction:** We describe a new technique in which the permanent type VenaTech LP (B. Braun, Bethlehem, Pennsylvania) inferior vena cava (IVC) filter was retrieved from three patients. The indication for retrieval in two cases was filter-related IVC thrombosis extending to the bilateral iliac veins, which were both successfully treated with catheter catheter-directed thrombolysis prior to removal. The indication for the third case was malpositioning of the filter. All of these filters were initially placed at outside institutions. All procedures represented the initial attempt at retrieval.

**Objective:** The efficient and safe endovascular removal of the VenaTech LP filter in a reproducible manner, requiring only modest fluoroscopy time.

**Methods:** A similar retrieval technique was utilized in each case. All retrievals were performed by 1 of 2 board certified interventional radiologists with over more than 12 years of experience. A single access point was utilized at the right internal jugular vein, and the filter was captured with a snare device. Using the advantage of the thinner outer filter legs of the LP filter, the flexibility of the design was utilized to invert the legs of the filter into an inserted sheath. The fully sheathed filter was then removed from the body.

**Results:** No instances of caval perforation, psuedoaneurysm, or filter fragment migration were observed using this technique. All three procedures were a technical success.

**Conclusion:** Retrieval of the permanent type VenaTech LP filter is technically feasible but should be attempted only in the hands of experienced operators because current experience with the presented technique is limited.

**Significance:** Procedure described in this paper is published in the Journal of Vascular and Interventional Radiology Vol. 27 Issue 11.

**Poster #: 44**

Withdrawn by Author.

## **Understanding optimization processes of electronic health records (EHR) in select leading hospitals: a qualitative study**

**Primary Author:** Chun 'Mark' Moon, MS, BSN, RN

**Contributors:** Rebecca Hills, PhD (University of Washington) and George Demiris, PhD (University of Washington)

**Introduction:** There is little systematic documentation or best practices about optimization of electronic health records (EHR) systems, namely the process that takes place after implementation to maximize the benefits of the system. We do know that in ambulatory settings, optimization following the go-live of the EHR system is critical to successful implementation. But despite its importance, little attention is given to EHR optimization in hospital settings. Too often, implementation of the EHR is considered complete once the system goes live. Sometimes optimization of an EHR is considered, but is an afterthought. Many studies of EHRs, including those on unintended consequences associated with EHR systems, have predominantly focused on EHR implementation and did not take optimization into consideration.

**Objective:** The purpose of this study was to understand the optimization processes undertaken in high performing hospitals following EHR implementation. As US hospitals continue to adopt EHR systems, documenting the experience of EHR optimization efforts taking place at leading healthcare organizations will provide valuable insights on how to leverage EHR systems in the post go-live era.

**Methods:** Informed by grounded theory approach, a qualitative study was undertaken that involved in-depth interviews and a focus group with a total of 15 EHR experts representing 13 healthcare organizations across the United States.

**Results:** The study found optimization processes of the EHR system that included prioritizing exponentially increasing requests, formation of optimization teams or advisory groups, and standardization. The study identified 16 types of optimization which interdependently produced 16 results of optimization and 11 barriers and 20 facilitators to optimization.

**Conclusion:** The study provided a rich description about optimizing EHRs in hospital settings.

**Significance:** The findings highlighted the importance of recognizing optimization and dedicating resources for the sole purpose. The study noted an outcome-focused approach on clinical decision support and found that optimization was more than improving an EHR system.

## Neonates receiving anti-VEGF injections for retinopathy of prematurity: a 5-year retrospective analysis

**Primary Author:** Trevor Washburn, BS

**Contributors:** Rachel Weinstein, BS; Jill Zaveri, MD; Jack Cohen, MD

**Introduction:** Controversy exists regarding the efficacy and safety of agents that inhibit vascular endothelial growth factor (VEGF) when used off-label to treat newborns with retinopathy of prematurity (ROP).

**Objective:** We performed a retrospective analysis to better understand the long-term outcomes of intravitreal anti-VEGF therapy as a first line treatment of ROP in neonatal inpatients at Rush University Medical Center (RUMC) from 2010 to 2015.

**Methods:** Patients with ROP who received anti-VEGF treatment during their inpatient admission between 2010 and 2015 were collected in a database consisting of 30 eyes of 16 patients. A retrospective chart analysis was conducted to identify patients with subsequent pediatric eye examinations at RUMC. Each patient's vision, alignment, refraction, anterior segment and fundus examinations were reviewed. Additional data included the patients' developmental status and history of breast feeding.

**Results:** Of 30 eyes receiving anti-VEGF medications, 9 were seen for pediatric follow-up or consultation at RUMC. All of these follow-up patients were females between 2 and 3 years old. Bevacizumab was administered in 5 eyes at varying doses. Ranibizumab was administered in 4 eyes at the half dose of 0.25 mg per 0.025 mL. Anterior segment findings were unremarkable in all patients with the exception of an anterior polar cataract deemed visually unremarkable. All eyes were able to fix and follow without evidence of amblyopia. Two patients were referred to the pediatric ophthalmologist for pseudostrabismus, but subsequent chart review demonstrated that all patients were orthophoric without evidence of strabismus. While cycloplegic refraction varied from -3.50D to +1.50D, no anisometropia greater than +1.00D was noted between eyes and none of the patients required glasses. All patients with follow-up were diagnosed with developmental delay; however, confounding perinatal and peripartum factors, such as IVH and intrauterine drug exposure, make it difficult to ascertain the cause of delay.

**Conclusion:** The results of our study align with current literature in demonstrating that anti-VEGF therapy can improve outcomes such as vision, strabismus, refraction, and fundoscopic findings in infants with ROP without substantial short-term morbidity. However, more information is needed regarding the long-term systemic and developmental effects of intravitreal anti-VEGF therapy in neonates.

**Significance:** Anti-VEGF intravitreal injections should be continued for the treatment of ROP but requires further research on the potential long-term effects on neonate development.

## Stop the Swelling: Improving Edema Management in Post-Operative Orthopedic Patients

**Primary Author:** Katie Kluga, DNP, RN, OCN, CHPN, CMSRN

**Contributors:** Susan Weber Buchholz, PhD, ANP, FAANP (Rush University); Pamela A. Semanik, PhD, MS, APRN (Rush University)

**Introduction:** Severity of post-operative edema in total knee arthroplasty and total hip arthroplasty is positively correlated with increased length of stay (LOS) in rehabilitation facilities. A chart audit (n=30) in one midsize urban rehabilitation facility revealed that 96% of patients had edema on admission and LOS was 19.2 days. EBP project findings fill the practical gap of post-operative edema management in knee and hip arthroplasty patients.

**Objective:** The purpose of this project was to develop a standardized edema program to improve assessment/management of post-operative edema and reduce LOS in a rehabilitation facility. The objectives were to: (1) standardize staff (nurses and certified nursing assistants) edema knowledge, (2) standardize patient edema knowledge, and (3) improve post-operative edema management.

**Methods:** To standardize staff edema knowledge, a 20-minute online educational video, edema assessment guide, and management checklist were constructed to explain the etiology, risk factors, and methods used to manage edema. A ten item multiple choice knowledge test was administered before and after staff viewed the educational video. To standardize patient edema knowledge, a printed education handout was utilized. Following education, patients were interviewed to assess their knowledge and compliance with edema therapy. Chart audits were completed to determine: 1) documentation of edema assessment/management and 2) LOS.

**Results:** Average staff knowledge scores (n=50) increased pre to post educational video (64% versus 70%). Of patients interviewed post education (n=24) 38% were able to list two characteristics of edema. A chart audit (n=30) demonstrated that 97% had edema upon admission. LOS was 16.3 days, or 3 days fewer than prior to implementation of the standardized edema program.

**Conclusion:** Challenges were encountered in staff finding time to view the educational materials. Implementation of a standardized post-operative edema program for staff and patients resulted in a notable decrease in LOS.

**Significance:** Edema education is recommended for orthopedic patients in rehabilitation facilities.

## Perceptions of Ambulatory Workflow Changes in Primary Care

**Primary Author:** Michael Hanak, MD

**Contributors:** Colleen McDevitt, RN (Rush) and Daniel Dunham, MD (Rush)

**Introduction:** As healthcare moves to a value-based system, the need for team-based models of care becomes increasingly important to adequately address the growing number of clinical quality metrics required of healthcare providers. Finding ways to better engage certified medical assistants (CMAs) in the process allows providers to focus on more complex tasks while improving the efficiency of each office visit. This paper presents the results of a survey that evaluated various components of a CMA workflow in adult primary care practices within an academic medical center.

**Objective:** To better understand workflow changes in primary care that would lead to increased involvement by certified medical assistants and nurses during the clinical intake process.

**Methods:** Our entire medical staff (RNs and CMAs) went through an on-site training program implementing workflow changes. This training took place over the first two weeks of April 2016. Physicians were notified of the workflow modifications electronically and during faculty meetings three months prior. Two months after the implementation of this initiative, PCPs and CMAs were given a questionnaire to assess their impressions of the workflow changes.

**Results:** Of the 72 providers 35 responded to the questionnaire for a 49% response rate. The response rate for the CMA's was 78% (57/73). Both PCPs (94.3%) and medical assistants (96.5%) agreed that the workflow changes were overall being followed consistently.

**Conclusion:** Practices at Rush that developed team-based models do better on almost all quality metrics. The workflow redesign process was successful in that it expanded CMA tasks while also removing some of the burden of documentation that often falls on providers as a requirement of quality reporting. Furthermore, it empowered CMAs to become more engaged in the process of caring for ambulatory patients while ensuring their feedback was acted on by operational leaders and clinical peers at their practice locations.

## **Reduction in Narcotic Analgesic Use on Labor and Delivery Unit: Examining the effects of institutional policy**

**Primary Author:** Diana Kolettis, MD

**Contributors:** Xavier Pombar, DO (RUMC), Patricia Perry, MD (RUMC), Elisheba Butts, MD (RUMC)

**Introduction:** Post operative pain control is an issue not only in regards to patient satisfaction, but also patient safety. Over-prescription and misuse of narcotic pain medications across the United States has been a popular topic of investigation.

**Objective:** Our study evaluates how a protocol of non-narcotic anesthetics used in the immediate post operative period effects the oral narcotic requirements of our post-cesarean patients.

**Methods:** This is a retrospective cohort study at a tertiary care academic center where a new post operative pain management protocol was implemented. Cesarean sections performed prior to and after implementation of this protocol were dichotomized into 'standard protocol' and 'Toradol protocol' groups. Medical records were reviewed for baseline and perioperative characteristics, pain scores, narcotic use post operatively and length of hospital stays.

**Results:** 208 cesarean sections were identified during the study period, 3 of which were excluded for allergies to either Norco or NSAIDs. Therefore, 110 women were in the standard protocol group and 95 were in the Toradol protocol group. On average, the standard group received 5.39 doses of Norco 10 and the Toradol group received 3.44 doses of Norco 10. Assuming equal variance, a t-score of 3.026 was calculated, with a p value of .003 for doses of Norco 10 administered. After a secondary analysis of the data, a significant difference in the amount of Norco 5 required by the standard protocol and the toradol protocol was identified in patients who underwent a primary cesarean section. Those who underwent repeat cesarean section had similar outcomes as the total sample.

**Conclusion:** The administration of scheduled intravenous Toradol for analgesia after both primary and repeat cesarean sections can reduce the amount of oral narcotic medications used by patients in the post operative period.

## **IMPLEMENTATION OF A MODIFIED PEDIATRIC EARLY WARNING SYSTEM (PEWSS) FOR IDENTIFICATION OF CLINICAL DETERIORATION**

**Primary Author:** Molly Moran, MSN, RN, CCRN

**Contributors:** Valerie Kalinowski, MD, RUMC Department of Pediatrics

**Introduction:** The Pediatric Quality and Safety Committee collected post-event feedback and surveyed the medical and nursing staff to determine barriers to activating the Pediatric Rapid Response Team (pRRT). Consistent with national feedback, lack of recognition of severity of illness was cited as the main barrier to calling a pRRT. The Pediatric Early Warning System (PEWS) has been identified in research to be an objective, reliable tool for use by the healthcare team to identify early patient instability.

**Objective:** Identify the purpose of early warning systems in the pediatric population. Discuss the process and challenges of adapting an early warning system on inpatient units. Discuss the process and challenges of applying an early warning system to the Emergency Department and pediatric admissions.

**Methods:** PEWS scores were retrospectively applied to pRRTs from the previous calendar year. Findings suggest PEWS would have triggered a pRRT on average 6.8 hours sooner for patients admitted to the General Pediatric Unit (GPU). In addition, when PEWS scores were applied to patients transferred from the GPU to the Pediatric Intensive Care Unit (PICU)  $\leq 12$  hours after admission, 71% had PEWS scores that would have placed them in a higher level of care at the time of admission.

Education was created for all healthcare providers in the Emergency Department (ED) as well as the GPU and PICU. PEWS was implemented December 2015 as part of the admission process from the ED as well as for all inpatient pediatric units.

**Results:** Our implementation of PEWS found that it can be used to detect early decompensation in infants and children. Our pRRT calls  $\leq 12$  hours after admission has decreased by 82% while transfers to the PICU after a pRRT have increased by 130%. Since implementation of PEWS, there have been no Code Blue Calls on the GPU.

**Conclusion:** PEWS implementation has shown to objectively assess pediatric patients at risk of clinical deterioration. This has great implications for clinical practice as the ability to more quickly assess and escalate care as needed has shown to lead to a decrease in morbidity and mortality.



## **The STAT Acuity Team: An Innovative Solution to Improve Patient and Nurse Outcomes**

**Primary Author:** Holly Losurdo, MSN, RN

**Contributors:** Heather Cook, BSN, RN (RUMC); Shonda Morrow, MS, RN, JD (RUMC)

**Introduction:** The STAT Acuity Team evolved from addressing challenges in patient throughput to consulting, advocating, and supporting clinical needs of nurses by providing specialized care across 14 inpatient units and multiple outpatient, procedural, and public areas.

**Objective:** To assess patient and nurse outcomes post-expansion of the STAT Acuity Team.

**Methods:** A dynamic environment requires the STAT Acuity Nurse to autonomously triage multiple requests during a shift. In an effort to identify patients at risk for decompensation, the STAT Acuity Nurse continually engages in proactive surveillance. Patients are monitored remotely utilizing handheld technology which provides access to the electronic medical record (EMR) and telemetry readings. STAT Acuity consultation is provided to patients identified via surveillance and by bedside nurse or physician request. Consultations may consist of targeted assessment, EMR review, immediate critical care intervention, plan of care revision, staff education, procedural assistance, or expedited transfer to higher level of care.

**Results:** Implementation and expansion of the STAT Acuity team has revealed a decrease in the number of emergency response calls. This calendar year, the STAT Acuity Team has responded to 6,616 nursing consultations and 52 physician consultations. A recent survey (n=237) indicated 94.5% of bedside nurses believed the STAT Acuity Team had a positive impact on patient throughput, having expedited over 275 patient transfers to date in 2016. Bedside nurses reported improved job satisfaction (89.5%), improved patient safety (95%), and that the STAT Acuity Team enhanced their skills and knowledge (86.5%).

**Conclusion:** The inception of the STAT Acuity team has fostered an environment conducive to improved patient and nurse outcomes while providing an opportunity for the registered nurse to practice to the full extent of his/her license. Continued evolution of the role has presented numerous opportunities for interdisciplinary collaboration, education, process improvement, and dissemination of evidence-based practice.

**Significance:** This poster was previously presented at the 13th Annual Edward Hospital Evidence Based Practice Conference.

## Successful Implementation of a 'Model Cell' to Improve Emergency Department Throughput

**Primary Author:** Paul Casey, MD

**Contributors:** Yanina Purim-Shem-Tov, MD, RUMC

**Introduction:** Over the past decade there have been a many applications of lean management to healthcare and specifically to the emergency department (ED).

**Objective:** Evaluate impact of ThedaCare model-cell LEAN process improvements on ED throughput metrics.

**Methods:** We analyzed true north throughput metrics of arrivals, left without being seen (LWBS), arrival to provider, arrival to discharge and patient experience (Press-Ganey surveys). We formed a process improvement team, surveyed staff, and conducted process observations. We organized items into a control-impact analysis, then prioritized based on an effort-impact chart for implementation. On September 1st, 2015 we initiate our new processes and analyzed data pre-process improvement (March 2015-August 2015) and post- (September 2015-July 2016).

**Results:** We found significant improvements in all metrics: LWBS for the time of pre-implementation was 6.2% vs post- implementation 4.8 % (last quarter 3.1%); door to provider, 71 min pre-implementation and 53 min post-implementation (last quarter 36 min); arrival to discharge, 233 min pre-implementation, 219 min post-implementation (last quarter 192 min); overall Press-Ganey University Health Consortium (UHC) rank 13% pre-implementation, to as high as 88% post-implementation.

**Conclusion:** We have demonstrated the successful implementation of a model-cell in the ED can positively impact ED true north metrics and patient experience.

**Significance:** We have demonstrated the successful implementation of a model cell in the ED can positively impact ED true north metrics. We have also created a structure for continuous and sustained process improvement through use of lean process improvement and six sigma methodologies. Such improvement can only happen with the initial and continued buy-in from institutional leadership. We have also learned that such process improvements can only be sustained with an infrastructure to support continued innovations from front line staff. Given the successes in implementing a model cell in the ED the institution has embarked on creating additional model cells throughout and turned focus to strategic capacity management.

## Reducing emotional eating: Development and evaluation of an Internet-based guided self-help intervention

**Primary Author:** Mackenzie Kelly, PhD

**Introduction:** Emotional eating is defined as an increase in caloric intake in response to stress or negative affect. Approximately 40% of the population engages in emotional eating, which has been identified as a factor related to elevated weight status and difficulty achieving and maintaining weight loss in both clinical and nonclinical populations. Despite the prevalence of emotional eating and its association with elevated weight status, an intervention specifically targeting reductions in emotional eating has yet to be developed.

**Objective:** The present study aimed to develop and evaluate an Internet-based guided self-help program targeting a reduction in emotional eating (RedEE Program).

**Methods:** Undergraduate students (N=59) reporting a desire to reduce episodes of emotional eating were randomly assigned to either an intervention or waitlist condition. This study was approved by the institutional review board at the University of Hawaii and all participants provided informed consent. Measures of emotional eating, loss of control over eating, and affect were assessed at baseline and 6-weeks, and participants in the intervention condition were given access to the 6-week RedEE Program following the baseline assessment.

**Results:** A series of one-way ANOVAs revealed that participants who completed at least one of the six intervention modules reported significantly lower levels of emotional eating ( $F(1,44)=6.17, p=.02$ ), desire to eat in response to depressive emotions ( $F(1,44)=9.82, p=.003$ ), loss of control ( $F(1,38)=7.88, p=.01$ ), and negative affect ( $F(1,43)=5.76, p=.02$ ) at the 6-week assessment compared to waitlist participants.

**Conclusion:** Use of the RedEE Program led to significant reductions in emotional eating and related factors among undergraduate students who endorsed a desire to address their emotional eating. The use of a nonclinical sample limits the generalizability of the findings, but future studies will examine the efficacy of the program for individuals in clinical populations where emotional eating has been identified as problematic, such as overweight, obese, and bariatric surgery populations.

**Significance:** This study represents the first known intervention designed to specifically target emotional eating, and the use of an Internet-based self-help format has the potential to increase access to care to individuals who might not seek or receive treatment otherwise.

## **A Nurse-Led Telehealth Program to Decrease Fatigue or Stress in People with Multiple Sclerosis**

**Primary Author:** Kiira Tietjen, DNP

**Contributors:** Susan Breitenstein, PhD, RN

**Introduction:** Fatigue and stress are prominent symptoms for people with multiple sclerosis (MS) and can lead to worsening of physical health outcomes. Health promotion activities have been shown to decrease fatigue and stress, but persons with MS participate in fewer health promotion activities than the general population. No health promotion services were available in a general neurology clinic serving a large rural population in three western states.

**Objective:** The purpose of this study was to: 1) assess the feasibility of implementing MS-REach Out, an evidence-based telehealth health promotion program targeting fatigue and stress, in a community neurology clinic, and 2) to evaluate patient goal attainment and improvement in physical and mental health.

**Methods:** This study used a pre-post single group design. Inclusion criteria were: (1) referral by neurologist and (2) non-responsiveness to previous interventions targeting fatigue or stress. Participants (n=10) were identified by a MS-trained neurologist during scheduled office appointments and referred to the MS certified nurse (MSCN) for participation. MS-REach Out includes an initial face-to-face meeting followed by five scheduled telephone calls over 12-weeks. At the initial meeting, participants chose a goal focused on fatigue or stress management and determined their first health promotion activity toward that goal. During each telephone session, motivational interviewing techniques were used and progress was quantified using a Goal Attainment Scale. A post-survey measured patient self-report of improvement in mood and physical health, and satisfaction with the program. Feasibility was assessed by: program completion and program implementation metrics (time spent with participants, administrative time, resources used).

**Results:** Ninety percent of participants achieved overall progress toward GAS goals. Eighty-eight percent reported improvement in physical and mental health. All participants (8/10) who completed the program viewed the program as helpful and stated they would recommend it to others. The MSCN spent an average of 76 minutes with each participant over 12 weeks.

**Conclusion:** Implementation of MS-REach Out resulted in increased health promotion behaviors and improved physical and mental health. It was well-received by participants and required little time or resources. The intervention has been manualized to fit within the clinic structure and nurse navigator role for program sustainability.

## Factors Associated with Endotracheal Tube Related Pressure Ulcer and Mucosal Injury

**Primary Author:** Edita Meksrailyte, MSc, RRT

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**Introduction:** Medical interventions often require the use of devices that are in contact with various parts of the body, and may exert pressure on specific areas of the body leading to mucosal injury and/or pressure ulcers. Medical device-related pressure ulcers and mucosal injury are iatrogenic complications that prolong hospitalization, increase the risk of morbidity and mortality for patients, especially those who are critically ill, and ultimately contribute to increased healthcare cost.

**Objective:** To assess the relationship between specific risk factors and development of endotracheal tube (ETT)-related pressure ulcer and mucosal injury.

**Methods:** This is a retrospective study involving manual abstraction of pre-specified data from the electronic medical record (EMR) of adult intubated patients in the medical intensive care unit (MICU) at Rush University Medical Center (RUMC). After obtaining Institutional Review Board approval, the medical records of 106 intubated patients who were in the MICU during the first quarter of 2015 were examined to determine the type and strength of the association between specific clinical variables and ETT-related pressure ulcer and mucosal injury.

**Results:** The study revealed that Norepinephrine ( $p = .002$ ) and Vasopressin ( $p = .008$ ) were significantly associated with ETT-related mucosal injury, but Neosynephrine was not ( $p = .585$ ). Additionally, mean Braden scores were lower for patients with ETT-related mucosal injury ( $10.16 \pm 2.17$ ) than for patients whose skin was intact ( $13.08 \pm 3.12$ ), a statistically significant difference of 2.92 (95% CI, 0.71 to 5.2),  $t(49) = 2.651$ ,  $p = .011$ ,  $d = .98$ . Gender and BMI were not significantly associated with development of ETT-related mucosal injury.

**Conclusion:** Patients with low Braden scores and those being treated with specific inotropes may be at increased risk for developing ETT-related mucosal injury, indicating a need for increased vigilance in performing skin assessment in these patients.

## Histopathology in chronic rhinosinusitis varies with sinus culture

**Primary Author:** Ashley Heilingoetter, BA, MPH

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**Introduction:** Structured histopathology reporting facilitates better understanding of the underlying pathophysiology of chronic rhinosinusitis (CRS). The microbiology of CRS has been studied extensively; however, distinct histopathologic changes associated with bacteria and fungi isolated in CRS are largely unknown.

**Objective:** The purpose of this study is to examine the relationship between the microbiology of CRS and histopathological changes seen in tissue samples from patients with CRS who underwent functional endoscopic sinus surgery.

**Methods:** A structured histopathology report was utilized to analyze sinus tissue removed during functional endoscopic sinus surgery (FESS) in a group of patients with CRS refractory to medical therapy. Histopathology variables included were degree of inflammation, eosinophil count per HPF, neutrophilic infiltrate, basement membrane thickening, sub-epithelial edema, hyperplastic/papillary changes, mucosal ulceration, squamous metaplasia, fibrosis, fungal elements, Charcot-Leyden crystals, and eosinophil aggregates. Baseline Lund-Mackay scores (LMS) and SNOT-22 scores were also collected. The association of culture data with the aforementioned variables was assessed. The one-way ANOVA test was used to compare means between more than two independent groups. Nonparametric qualitative variables were cross-classified into contingency tables and compared using chi-square testing. All statistical analyses were performed using SPSS, version 24. A p-value of 0.05 or less was considered significant for all statistical analyses.

**Results:** A total of 59 CRS patients who underwent FESS were included. CRS patients with *P. aeruginosa* had significantly increased neutrophilic infiltrate (71.4% vs. 26.9%,  $p = 0.018$ ), sub-epithelial edema (28.6% vs. 3.8%,  $p = 0.015$ ), and presence of fungal elements (28.6% vs. 5.8%,  $p = 0.042$ ). CRS patients with *S. aureus* had significantly more hyperplastic/papillary changes (20% vs. 2.3%,  $p = 0.018$ ), mucosal ulceration (13.3% vs. 0.0%,  $p = 0.014$ ) and a trend toward increased squamous metaplasia (33.3% vs. 14.2%,  $p = 0.091$ ).

**Conclusion:** Distinct histopathologic changes were noted based on sinus culture data specifically for *S. aureus* and *P. aeruginosa*. These findings may have important implications on the extent of surgical management and prognosis after surgery.

**Significance:** In recent years, the microbiome of CRS has been analyzed extensively, yet the impact of these organisms on a tissue level is still unclear. This study aims to elucidate specific histopathologic changes associated with pathogens commonly found in CRS and how these changes may vary based on the organism. In our group of patients, significant histologic changes were identified in the tissue samples of patients with cultures positive for *S. aureus* and *P. aeruginosa*, which may impact how these patients are managed clinically in the future.

## Increasing the Appropriateness of Cardiac Monitor Use

**Primary Author:** Brent Nathan, MD

**Contributors:** Jordan Dale MD (RUMC IM), Scott Hasler MD (RUMC IM), Manya Gupta MD (RUMC IM)

**Introduction:** Because of the increasing over-use of cardiac monitors in non-critical care settings, the 2013 Choosing Wisely campaign published the recommendation, 'Don't order continuous telemetry monitoring outside of the ICU without using a protocol that governs continuation.' Furthermore, the American Heart Association (AHA) has released a consensus statement regarding the settings in which cardiac monitors are indicated as well as their duration of use.

**Objective:** 1. Review the appropriate-use criteria and recommended duration for cardiac monitors. 2. Discuss the impact of an optimized EMR order-set and education on the appropriate use of cardiac monitors.

**Methods:** we altered our electronic ordering system to separate cardiac monitor orders for intensive-care settings and non-intensive care settings. The intensive-care orders are never discontinued. However, the non-intensive care orders are automatically discontinued after 24 hours unless the order is reviewed and renewal order is placed. The electronic order also includes a reference to AHA recommendations on appropriate diagnoses and durations for cardiac monitoring (however, the order does not require that a specific indication is selected in order to place the order). In addition to the order-optimization, we held an interactive educational conference for house staff and faculty, where the new order protocol as well as the AHA consensus statement were reviewed.

**Results:** We reviewed the average number of cardiac monitor orders placed on general medicine floors per month as well as the average duration of use for a several year period leading up to our intervention. We then looked at the same parameters for several weeks after the intervention. Pre-intervention, cardiac monitors were being ordered on 31.2% of general medicine patients which decreased to 6.3% of general medicine patients post-intervention. Additionally, we saw the average duration of cardiac monitors usage decrease from 62 hours (95% CI 60:34 to 64:08) pre-intervention to 34 hours (95% CI 25:52 to 43:44) without a significant difference in length of stay duration. We also saw the percent of hospitalization spent on telemetry decrease from 60% (95% CI 59.7% to 61.2%) pre-intervention to 41% (95% CI 34% to 48%) post-intervention.

**Conclusion:** Through optimization of our EMR-order set, as well as education, we were able to show a significant reduction in the number of hours our general medical patients spend on the cardiac monitor.

**Significance:** While further research is needed to determine the ultimate impacts of these outcomes, we are hopeful that it will result in less alarm fatigue, less nursing time devoted to cardiac monitors (both in terms of direct bedside care and charting), increased patient mobilization and ability to ambulate, and decreased length of stay. Ideally these outcomes would also lead to noticeable cost savings for our institution.

## Assessment of Patient Engagement in the Health Management of Adults in a Medicaid Population

**Primary Author:** Ingrid Forsberg, DNP APN FNP-BC

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**Introduction:** Primary care redesign is necessary to meet required changes to delivery of care, and to reduce costs due to possible duplication of services and the overuse of emergency rooms (episodic care). As a part of that necessary redesign, care managers became members of the health care team to help patients obtain primary care and engage in their plan of care. The relationship between the patient and care manager is an element of patient engagement which has not been well measured in the newly insured Medicaid population.

**Objective:** To describe relationship as an element of engagement between the patient and their care manager and to discuss patient--care manager relationship characteristics-in a high risk Medicaid population.

**Methods:** After IRB approval and consent of patient, The Scale to Assess Relationship (STAR) survey was administered to 30 patient -care manager pairs. The survey includes items regarding positive collaboration between patients and their care manager, as well as supportive and non-supportive care manager input. Descriptive statistics and correlations were examined based on age, sex and recent emergency room (ER) visits.

**Results:** The results of the STAR survey indicated that both patients and care managers perceived strong collaborative relationship or friendship. When the 30 pairs are viewed together, there was high congruence within patient and care manager dyads. Females had a slightly higher number of ER visits. Patients who reported ER visits had a lower 'Positive Collaboration' score - and interestingly, their care managers thought the opposite. This discrepancy speaks to the patient's perception of the relationship as one of a good rapport but not necessarily supportive.

**Conclusion:** Further evaluation of the relationship and the implementation of strategies for improvement of care manager -patient relationships for women with high ER use in this Medicaid population may be of benefit.

**Significance:** Findings support the development of a protocol on best practices in patient-care manager relationship and engagement, and supports the value a nurse care manager brings to the patient care team. Findings will be used to build an ongoing learning system for care managers to direct interventions and engage patients in their care. Objective data obtained on patient-care manager relationship provided information on patients' perception of care and gave direction to care managers on areas for improvement.



## Distinct histopathologic features of radiation-induced chronic sinusitis

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**Introduction:** Chronic rhinosinusitis (CRS) after radiation therapy to the paranasal sinuses is a common occurrence. The histopathologic features of radiation-induced CRS have yet to be determined and may have important implications on disease management.

**Objective:** The purpose of this study was two-fold, 1) to distinguish specific histopathologic findings among CRS patients who have received radiation therapy, and 2) to investigate whether or not such histopathologic findings suggest the need for specific methods of disease management (i.e. surgery, antibiotics, steroids) in this patient population.

**Methods:** A structured histopathology report was utilized to analyze sinus tissue removed during functional endoscopic sinus surgery (FESS). Variables included tissue present, degree of inflammation, eosinophil count per HPF, neutrophil infiltrate, inflammatory predominance, basement membrane thickening, sub-epithelial edema, hyperplastic/papillary changes, mucosal ulceration, squamous metaplasia, fibrosis, fungal elements, Charcot-Leyden crystals, and eosinophil aggregates. Histopathology variables, Lund-Mackay Score (LMS) and SNOT-22 scores were compared among patients with radiation-induced CRS (CRSr) and a cohort of patients with CRS without nasal polyps (CRSsNP).

**Results:** 15 CRSr and 43 CRSsNP patients who underwent FESS were included. Compared to CRSsNP, CRSr cases had increased squamous metaplasia (40.0% vs. 11.6%,  $p = 0.016$ ) and sub-epithelial edema (33.3% vs. 9.3%,  $p = .027$ ). Additionally, CRSr patients had significantly greater mean LMS ( $13.47 \pm 5.13$  vs.  $4.45 \pm 6.73$ ,  $p < 0.001$ ). CRSr cases exhibited no difference in eosinophil count ( $p=0.283$ ) or neutrophilic inflammation ( $p=0.823$ ) when compared to CRSsNP patients.

**Conclusion:** Radiation-induced CRS exhibits increased squamous metaplasia and sub-epithelial edema when compared to a cohort of patients with CRSsNP. CRSr cases demonstrate no difference in the inflammatory milieu compared to CRSsNP, lending further credence to the unique nature of radiation to the development of CRS in this patient group. These findings may have important implications on extent of surgical intervention and medical management.

**Significance:** Several endotypes of CRS have been reported, including CRS with and without nasal polyps. To date, no study has investigated the possibility of CRS patients after radiation therapy warranting their own endotype due to unique histopathologic features of their disease. The findings from this study may impact treatment decision-making of otorhinolaryngologists taking care of patients with CRS following radiation therapy by promoting more targeted, specific therapeutic regimens aligned with specific disease mechanisms of CRS post-radiation cases.

## Relationship between resting energy expenditure and muscle mass among critically ill patients

**Primary Author:** Faith Doan, BS

**Contributors:** Sarah Peterson PhD, RD (Rush), Kristen Lach MS, RD (Rush), Sharon Foley PhD, RD (Rush), Ben Bienia MD (Rush)

**Introduction:** Indirect calorimetry is the gold standard for determining resting energy expenditure (REE) in the intensive care unit (ICU). However due to difficulties with this technology, predictive equations are used despite the possibility of inaccurate estimation of energy requirements. Muscle mass is a significant predictor of REE and may be a component of this inaccuracy.

**Objective:** The purpose of this study was to examine the relationship between muscle mass, REE, and the difference between REE and estimated energy requirements.

**Methods:** A convenience sample of ICU patients with REE measured via indirect calorimetry from 8/2007-8/2016 and a diagnostic abdominal CT scan were included. Height, weight and body mass index (BMI) were recorded. Estimated energy requirements were calculated. Cross-sectional muscle area (cm<sup>2</sup>) was determined and skeletal muscle index (SMI, cm<sup>2</sup>/height (m<sup>2</sup>)) was used to categorize low muscle mass (BMI <25kg/m<sup>2</sup>: <43 cm<sup>2</sup>/m<sup>2</sup>, men/women BMI >25kg/m<sup>2</sup>: SMI <53cm<sup>2</sup>/m<sup>2</sup> and <41cm<sup>2</sup>/m<sup>2</sup>). Pearson's correlation and Mann Whitney U were used for statistical analysis.

**Results:** Preliminary results from 32 subjects found REE and muscle mass were significantly correlated ( $r=.598$ ;  $p<.001$ ). The median delta between REE and estimated energy requirements was 354 (117,551) calories. There was no difference between REE and estimated energy requirements delta among patients with low versus normal muscle mass. However, obese patients with low muscle mass had a significantly higher delta between REE and estimated energy requirements (530 versus 307 calories,  $p=0.04$ ) compared to those with normal muscle mass.

**Conclusion:** Calorie requirements for ICU patients appear to be influenced by muscle mass. Identifying obese patients with low muscle mass is important to avoid inaccurate calorie dosing.

**Significance:**

## Reducing Falls in Low and High Risk Patients on an Orthopedic Unit Using a Multifactorial Fall Prevention Program

**Primary Author:** Nicholas O'Hearn, MSN, MBA

**Contributors:** Perla Flores, RN, BSN (ROPH); Claudia Pilati, RN, BSN (ROPH); Shelly Mazur, RN, BSN (ROPH); Alma Munson, PCT (ROHP)

**Introduction:** Falls continue to be a considerable challenge across the care continuum; it is currently the most reported adverse event in hospitals. Currently no study supports a specific intervention as hospitals continue to struggle with the safety initiative. In 2008, the Centers for Medicare and Medicaid Services (CMS) began limited or no reimbursement for care in hospitals related to falls. In 2015, the Centers for Disease Control (CDC) stated that expenses related to falls in US hospitals reach \$31 billion. Rush Oak Park Hospital's orthopedic unit experienced a 50% increase in falls in fiscal 2015. Developing a culture of safety and accountability is foundational for success in fall prevention in the acute inpatient setting.

**Objective:** To determine factors that contributed to increased falls rate; to implement evidenced based practice strategies to decrease falls; and perform continuous assessment of falls rate post implementation.

**Methods:** A one-year retrospective, multidisciplinary review of patients who have fallen on the orthopedic unit was analyzed. Reviews showed that these falls were related primarily for the need for toileting or the environment or equipment. Orthopedic patients often utilize a variety of equipment, such as IV pumps, sequential compression devices, epidurals, patient-controlled analgesia machines and ice machines. Based on the findings, a list of factors and subsequent interventions tailored to the alert orthopedic and general medicine population was developed. In addition to the universal fall precaution protocol, the use of a safety checklist developed with multifactorial interventions specific to the alert, orthopedic patient was used. The day and night shift nursing and PCT staff perform a bedside safety assessment checklist at the beginning of each twelve-hour shift. To incorporate all staff members, the checklist is completed by a nurse or patient care technician (PCT) from the current shift with a nurse or PCT from the oncoming shift.

**Results:** 100% reduction in falls on the unit in the nine months from the inception of the project to the end of fiscal 2016.

**Conclusion:** Developing a multifactorial fall prevention program specific to the needs of the orthopedic population is fundamental for preventing falls. This staff-driven fall reduction project reached the goal of having a 100% reduction of falls on the unit. In addition to a reduction in falls the project also heightened staff and patient awareness to the potentially hazardous environment.

## Promoting Patient Engagement in Primary Care: A Quality Improvement Project to Reduce No-shows

**Primary Author:** Stephanie Hoheisel, BSN, RN, CCRN

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**Introduction:** Primary care no-shows negatively impact patient health outcomes, provider productivity, clinic revenue, and access to care for other patients in need.

**Objective:** This project aimed to decrease a primary care provider's no-show rate by repeatedly engaging patients with goal setting and action planning. This strategy aimed to strengthen patients as partners in their care to improve treatment and appointment adherence and other health-related behaviors. No study has evaluated goal setting and action planning on primary care no-show rates.

**Methods:** An evidence-based tool was created for patients to select one health-related goal, briefly explain an action plan, and rate their confidence to achieve the plan. Clinicians guided patients through structured behavioral change discussions. Patients with three or more completed visits with two or more episodes of engagement qualified as 'repeated engagement'. Goals and confidence were documented in the patient's electronic health record (EHR).

**Results:** 285 patients (60%) were engaged during the six-month project. Average age was 66 years with 51% males. Other demographics were: 58% white, 31% black, 11% other; 45% retired, 29% employed, 26% un-employed; 12% new patients. Engaged patients had 14.6% fewer no-shows than non-engaged patients. This rate of change was significant (3.9%;20/510) to (18.5%; 64/282) using chi-square ( $\chi^2=49.49$ ,  $df=1$ ,  $p<.001$ ). The provider's overall no-show rate did not change significantly (10.8%; 108/1002) to (11.7%; 112/955): chi-square ( $\chi^2=0.45$ ,  $df=1$ ,  $p=.501$ ). Seventy percent of repeatedly engaged patients had zero no-shows to consecutive appointments and 33% showed improved confidence to reach goals.

**Conclusion:** Engaging patients with goal setting and action planning may decrease no-show rates in primary care. Repeatedly engaging patients may improve confidence for positive health-related behaviors. A structured tool facilitates discussions and EHR documentation is desirable for re-visiting goals at future encounters. This primary care strategy is feasible and cost-effective without negatively affecting clinician workflow.

**Significance:** As stated, no study to date has evaluated goal setting and action planning on reducing primary care no-show rates. This patient-centered strategy is innovative in that it goes beyond simply reminding patients of upcoming appointments, but rather employs behavioral engagement techniques aimed to make patients more eager to attend future appointments. This project was implemented for both english and spanish speaking populations. There were statistically significant findings. This strategy had not been attempted prior to project implementation.

## **Evidence-Based Technological Caregiver Skill Building Intervention for Dementia Family Caregivers: Pilot Study**

**Primary Author:** Ben Inventor, PhD, CNP

**Contributors:** Carol J. Farran, DNSc (Rush University, CON); Peter Zurawski (Grand MARKeting Solutions); Janie Urbanik (Rush University) Olimpia Paun PhD (Rush University, CON)

**Introduction:** Family caregiving is a growing public health concern and caregivers of persons with Alzheimer's disease or other related dementias (ADRD) need appropriate, timely, and ongoing education and support to successfully meet their caregiving responsibilities. Well-designed interventions can significantly reduce risk concerning caregiver mental and physical health, and improve care recipient outcomes. Few interventions are translated into everyday practice; and most rely on in-person, professionally-led delivery methods, making them inaccessible to many family caregivers.

**Objective:** The purpose of this pilot study was to establish feasibility of translating six Caregiver Skill Building Intervention (CSBI) modules to an individualized web-based format and 1) Examine CSBI modules for their ease in intervention implementation and caregiver evaluation of module content; 2) Appraise preliminary CSBI outcomes; and 3) Determine technological challenges in implementing the web-based CSBI.

**Methods:** The study enrolled 92 family caregivers to complete 6 web-based CSBI modules. Quantitative measures for caregiver clinical outcomes (skill building, burden, depressive symptoms, affect) were used at baseline, 6- and 12-weeks. Both quantitative and qualitative data for program evaluation (content and organization, audio visual quality, intervention relevance, quality of modules) were used at 6- and 12-weeks. Rush University institutional review board approved the study.

**Results:** Caregivers positively evaluated this eLearning process (n=53); significantly increased caregiving skill at 6-weeks ( $p=0.01$ ) and 12-weeks ( $p=0.05$ ); and improved caregiver depressive symptoms ( $p=0.01$ ) and positive affect ( $p=0.05$ ) at 6-weeks. Product strengths include: a) an evidence-based intervention, developed from a prior group-based randomized clinical trial; b) a focus on caregiver management skill, rather than merely teaching facts; c) an interactive approach, enabling caregivers to apply information to realistic scenarios and receive immediate feedback to their responses; and d) convenient and available 24 hours/day 7 days/week from any location with internet access.

**Conclusion:** This web-based intervention provides greater intervention access to family caregivers, than existing in-person caregiver group interventions.

## **Proprotein-Convertase Subtilisin-Kexin Type 9 (PCSK9) and Low Density Lipoprotein Receptor (LDLR) Genotype Distribution and Association with Statins in Filipino American Women**

**Primary Author:** Joanne Michelle Gomez, MD

**Contributors:** Latha Palaniappan, MD, MS (Stanford University School of Medicine)

**Introduction:** Filipino American women (FAW) have high incidence of coronary heart disease (CHD) and high LDL cholesterol (LDL-C). The distribution of rs11206510 proprotein-convertase subtilisin-kexin type 9 (PCSK9) and rs1122608 low density lipoprotein receptor (LDLR) single nucleotide polymorphisms (SNPs), known for genetic influences on LDL-C, is unknown in this population.

**Objective:** To examine the genetic determinants of LDL-C, their association with LDL-C, and effects of statins on LDL-C given the genetic determinants in this high-risk population.

**Methods:** Data were obtained from the FAW Cardiovascular Study (N=338) of women ages 40-65 year-old from four major USA cities between 2011-2013. Allele frequency calculation, LDL-C determination, and lipid analysis were done using Roche Modular methodology. Luminex-oligonucleotide ligation assay procedure was used to determine genotype.

**Results:** The distribution of rs11206510 PCSK9 genotypes was 88% TT, 11% TC and 1% CC, and the rs1122608 LDLR genotype distribution was 83% GG, 17% GT and 0% TT. These SNPs showed no effect on LDL-C. Mean LDL-C levels were significantly lower in participants on statin in the homogenous genotypes but not in heterogeneous genotypes. FAW on statin medications had lower LDL levels regardless of their PCSK9 or LDLR genotypes.

**Conclusion:** Most FAW had a gain of function allele of PCSK9 and LDLR, similar to previously studied ethnic populations. The predominance of gain of function alleles in FAW cohort may account for the high percent of subjects with elevated LDL-C. In a population at high risk for hypercholesterolemia, optimal treatment with statins or PCSK9 inhibitors should be considered where appropriate.

## **Apostle Islands National Lakeshore: Search-and-Rescue and Emergency Medical Services Operations, 2006-2015**

**Primary Author:** Elan Small, BA

**Contributors:** Sarah Burbank, Jeanette Lorme (Rush), Karl Carlson, U.S. Park Ranger (Apostle Islands National Lakeshore), Timothy Erickson, MD, FACEP, FACMT, FAACT (Brigham and Women's Hospital, Harvard Medical School), David Young, MD (Rush)

**Introduction:** Apostle Islands National Lakeshore (APIS) lies at the northern tip of Wisconsin and is home to a network of 21 islands along Lake Superior.

**Objective:** The goal of this report is to investigate Emergency Medical Services (EMS) and Search-and-Rescue (SAR) trends at APIS in an effort to improve visitor safety and resource allocation.

**Methods:** This study is a retrospective analysis reviewing APIS SAR Reports and Annual EMS Summary Reports from January 1st 2006- December 31st 2015 (excluding 2008 for EMS). Information related to incident type, incident year/month/day/time, individual demographics and activities, injury/illness type, cost, and contributing factors were recorded and analyzed in frequency tables. EMS analysis was limited to incident type.

**Results:** From 2006-2015, APIS SAR conducted 133 total missions assisting 261 individuals- 58 injured/ill, 199 not injured/ill, 4 fatalities and 25 documented saves. SAR incidents cost, on average, \$4,544 and most frequently occurred during August, and on Saturdays. The majority of assisted individuals were male (68%), and the most frequently recorded age group was 20-29 (17.6%). The most common activity resulting in injury was hiking (46.7%) and hypothermia/cold exposure accounted for over half of all injuries/illnesses (51.7%). The most frequently reported contributing factor was wind. EMS responded to a total of 85 incidents with the majority of the EMS incidents involved first aid (40.04%).

**Conclusion:** APIS aligns with many trends observed in other wilderness recreation areas, including SAR's most frequently involving males between 20-40, occurring on the weekend, as well as hiking being the most common activity resulting in injury/illness. APIS deviates from other wilderness recreation areas in that it also experiences significant increases in SAR incidents in late winter/early spring due to its well-known ice formations. Interestingly, the average cost per SAR was over twice the previously reported national average, due to the use of vessel and aircraft support during water rescues.

**Significance:** APIS's SAR incident rate of 6.4 per million visitors is substantially lower than most previously examined wilderness recreation areas, warranting further investigation into APIS visitor safety measures to highlight potential models that can be implemented in other parks.

## Prescribing Practices at the Emergency Department in Female Patients with Acute Pain

**Primary Author:** Haley Ford, PhD

**Contributors:** Yanina Purim-Shem-Tov, MD, MS, FACEP (RUMC); Linzy Wagner, BS (RUMC); Frances Aranda, Ph.D., MPH, MS, (RUMC); Teresa Lillis, PhD (RUMC); Stevan Hobfoll, PhD (RUMC); John Burns, PhD (RUMC)

**Introduction:** Pain is a common reason for emergency department (ED) visits in the U.S. Prior research has shown that prescribing practices differ by race/ethnicity, with more Caucasians prescribed opioids than non-Caucasians. Fewer African Americans are prescribed opioids than Latinos. Prescribing practices differ across diagnoses because some types of pain are less responsive to pain medication. Inadequate pain treatment is a public health concern because it is associated with reduced quality of life (e.g., mental health problems).

**Objective:** This research presents data on diagnoses and prescribing practices in the Rush University Medical Center (RUMC) ED in a sample of 183 women, ages 18-40, experiencing acute pain at the time of their ED visits.

**Methods:** Demographics, diagnostic information, and medications prescribed by the ED were collected from participants' medical records. The study was approved by RUMC's Institutional Review Board, and informed consent was obtained from all participants.

**Results:** Fewer African Americans (21.1%) were prescribed medication than were Caucasians (26.9%) and Latinas (27.3%). Over-the-counter (OTC) medications were prescribed to fewer Latinas (21%) than to African Americans (31.4%) and Caucasians (30.8%). The most common diagnostic categories were infectious (33.3%), undetermined (27.2%), and musculoskeletal (20%). Participants with a musculoskeletal diagnosis were given more medication, whether prescription (44.4% of patients) or OTC (50% of patients).

**Conclusion:** The results were largely consistent with prior research on prescribing practices for pain. This research expanded the scope by including OTC medications, which were prescribed to more African Americans and Caucasians, and by examining prescribing practices by diagnosis. Consistent with typical practice, more patients with musculoskeletal pain, which responds better to pain medications than does visceral pain, received medications. The prescribing patterns at RUMC's ED are similar to those in EDs across the country.

**Significance:** These results are important because they highlight the need for further research on whether patients receive adequate treatment for acute pain regardless of their race/ethnicity.



## **A Cost Effective Approach to Surgical Simulation: Use of Inanimate Surgical Simulation Models**

**Primary Author:** Aleksandra Wojtowicz, BS

**Contributors:** Benjamin Veenstra, MD (Rush), Nathan Walsh, CHSOS, CHSE (Rush), Jose Velasco, MD (Rush)

**Introduction:** Surgical skill training is an integral component of surgical education. Halstead base education may no longer be feasible and in use. Mannequins, virtual reality simulators, anatomy and animal laboratories, and training boxes have been used; yet, no consensus exists as to which one is more effective. Furthermore, some are expensive and may not be readily available for individualized training.

**Objective:** Four inanimate, tactile models were built to bridge the gap in surgical education curriculum.

**Methods:** These include: carotid endarterectomy, laparoscopic vena cava repair, laparoscopic inguinal hernia repair and laparoscopic para-esophageal diaphragmatic hernia repair. The carotid endarterectomy model contained a plaque that residents had to dissect, remove, and repair. The laparoscopic vena cava model is an actively bleeding punctured vessel that residents must successfully repair. The inguinal hernia model included landmarks needed for a safe repair via pre-peritoneal access. The diaphragmatic hernia model was created using task trainer with, with hiatal hernia defect diaphragm, crura, hernia sac, esophagus and stomach. All models were revised and validated following feedback by five advanced, laparoscopic surgeons, and resident pre and post surveys. A cost comparison study was conducted using commercially available models.

**Results:** All physicians: 5 attendings and 15 surgical residents agreed that the four surgical simulation models were an accurate replica of the pathology, attesting to their validity in preparing them for the operation. The total cost for the carotid endarterectomy, laparoscopic vena cava repair, laparoscopic inguinal hernia repair and laparoscopic para-esophageal diaphragmatic hernia repair was \$49.76, \$85.95, \$186.90, \$289.53, respectively. Compared to animate cadavers, which range between \$1,060-\$2,000, all four models are a small fraction of the cost, a mere 4.69-14.48%. Similarly, the inanimate models are only 0.20-0.30% of the cost of virtual reality simulators, whose costs are \$94,000-\$100,000.

**Conclusion:** These models can be incorporated into the surgical training curriculum. They are cost effective and reliable.

**Significance:** Inanimate surgical models help bridge the existent gap between cognitive learning and skill psychomotor training in the operating room while adding an opportunity for individualized training.

## **Steroid Intervention: Acute Chest Syndrome**

**Primary Author:** Antonio Logan, BS

**Contributors:** Stephen Dvorak (RMC); Paul Kent, MD (RMC)

**Introduction:** Sickle Cell disease (SCD) is a complex inflammatory vasculopathic disorder with multisystem manifestations. The Acute Chest Syndrome (ACS) is the leading cause of death in SCD. On bronchial lavage fat embolism is the most common cause with only 4.5% of ACS having a bacterial etiology. Red cell transfusions and incentive spirometry are the standard of care, yet patients are usually treated primarily with antibiotics and IV fluids. Corticosteroids have been shown to benefit Some ACS patients.

**Objective:** Because knowledge about the inflammatory/vasculopathy of SCD is limited and ACS has similar features to bacterial-pneumonia, intervention with corticosteroids is rare. We describe successful treatment of ACS with high dose solumedrol.

**Methods:** Complete blood counts were used to monitor the levels of the patient with ACS on mechanical ventilation.

**Results:** A 26 year-old with SCD, well controlled with monthly exchange transfusions/hydroxyurea, presented at the ED with 3-days of dyspnea and lung consolidations. Treated as bacterial pneumonia, the patient deteriorated with persistent, tachypnea, increasing multi-lobe lung consolidations, rising WBC/platelets (50,000/1,472,000), and rising pCO<sub>2</sub>. He developed ARDS requiring intubated. Despite multiple antibiotics, bronchoscopy, IV fluids and exchange transfusions (HbS = 15%), the patient's condition became life-threatening. All blood/bronchoscopy cultures/analysis showed no infection, no hemolysis, nor heart disease. On day 14 solumedrol 1,000mg daily x 3 days was started. Within 72 hours he was extubated, the pCO<sub>2</sub> declined (66 to 39), acidosis resolved, and fevers stopped. Over 7-10 days, the WBC/platelets declined (52,000 to 14,000; 1.5 million to 494,000) despite the HbS increasing to 55%. The patient was discharged on HD 22 and made a full recovery.

**Conclusion:** Systemic steroid therapy is not currently standard of care for ACS, however this option should be considered in severe ACS. We believe better education about the risks/benefits of steroids in ACS and the inflammatory nature of the disease is needed.

## **Dosing Factor in Pediatric and Adult Hemophilia Patients Using Ideal Body Weight Versus Actual Body Weight**

**Primary Author:** Adam Kidwell, BS

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**Introduction:** Hemophilia A and B are X-linked inherited bleeding disorders that cause significant morbidity. Adoption of prophylactic treatment with regular factor replacement infusions has dramatically improved life expectancy and quality of life in patients with hemophilia (Manco-Johnson et al 2007). Dosing of factor replacement therapy is currently based on actual body weight (AW), yet nearly half of the hemophilia patients in a demographic study of the United States population were considered either overweight or obese based on their body mass index (BMI) (Curtis et al 2015).

**Objective:** Given the obesity epidemic in the United States, we have hypothesized that there is a role for dosing factor based on ideal body weight (IBW). Estimation of dosing based on IBW could cut current expenses by almost 50 percent, an annual savings of approximately \$136,000 (Graham et al 2014).

**Methods:** We began a retrospective review of patient recovery studies to determine the effect of factor dosing based on AW versus that based on IBW. Recovery was calculated by comparing pre-infusion factor activity and the 1-hour post infusion activity. Data was analyzed to determine the difference between factor infusion based on AW and theoretical factor based on IBW for dose given and factor activity.

**Results:** Patients who fit the inclusion criteria (n=40) had BMI's ranging between 16.9 and 42.1. Patients were stratified by BMI's below or at 25 (normal, n=23) versus greater than 25 (overweight or obese, n=17). Patients with a BMI below 25 had a high correlation between the Factor Discrepancy and Dose Discrepancy (0.789 (p<0.05)). However, in patients with BMIs above 25 there was no correlation between Dose Discrepancy and Factor Discrepancy (0.240 (p=0.322)).

**Conclusion:** This data suggests that IBW can be an effective way to dose patients who are at a normal BMI of 25 or less but in patients who are overweight or obese (BMI >25) IBW does not provide a reliable method to predict post-infusion factor activities. Further, prospective studies are needed to determine factor-dosing regimens for hemophilia patients who have a BMI over 25.

## MEASURING NURSES BELIEFS AND CONFIDENCE TO IMPLEMENT EVIDENCE-BASED PRACTICES

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**Contributors:** MaryCarol Racelis , MSN, APN, ACNS-BC, Rush University Medical Center; Davena J Beal RN (former Rush employee) and Mary Heitschmidt PhD, RN, APN, CCRN, Rush System for Health

**Introduction:** Evidenced based practice in health care involves using results from controlled, replicated research studies in conjunction with the clinician's knowledge base and the patient's preferences to make the best clinical decisions for each patient. Use of EBP in clinical decision making improves patient outcomes and reduces health care costs. However, nurses across the nation do not consistently use EBP in patient care, and report that health care organizational cultures do not support nurses' use of EBP.

**Objective:** To measure nurses' beliefs about the value of EBP (Evidence-Based Practice) and their confidence to implement into practice at a large mid-west academic medical center.

**Methods:** After IRB review, the Professional Nursing Staff EBP/Research Committee utilized the EBP Beliefs Scale (Melnik, BM, Finout-Overhold, E, & Mays, MZ. (2008) to determine baseline nursing perceptions of EBP. An electronic link was sent to all nurses via email inviting them to participate in the anonymous survey. Email reminders were sent before the survey closed. Descriptive statistics were used to analyze survey and demographic data.

**Results:** A total of 675 nurses completed the initial survey for an overall response rate of 30%. The majority were staff nurses (74%), who had a BSN degree (64 %) with over 20 years of nursing (33%) experience. Nurses believed that EBP results in the best care for patients (93%) but were unclear of how to find and overcome barriers to implement EBP (37%).

**Conclusion:** The results are similar to a national survey that was conducted assessing EBP. Currently, interventions to increase perceptions of EBP are being implemented hospital wide in collaboration with other shared governance committees and the Center for Clinical Research and Scholarship at the Rush College of Nursing. Reassessment of nurses EBP beliefs is planned 16 months after the initial survey.

**Significance:** Providing ways to increase nurses understanding and implementation of EBP will improve the care they provide and patient outcomes.

## **Familiarity of neonatal tracheostomy care in the NICU**

**Primary Author:** Courtney Miller, BS

**Introduction:** Tracheostomy is one of the most common procedures performed on critically ill patients. If the tube is displaced within the first seven days post-operatively, it can be difficult to replace it because of soft tissue obscuring the stoma. The stay suture technique is a method that allows for the safe replacement of the tracheostomy tube in the event of unexpected decannulation. Because a wide range of healthcare professionals are directly involved in the care of patients with a tracheostomy, they need to be familiar with ways to manage complications such as the use of stay sutures in the event of accidental decannulation.

**Objective:** The aim of this study was to evaluate the level of knowledge of healthcare professionals regarding stay sutures on neonatal tracheostomy tubes.

**Methods:** Seventy pediatric intensive care unit health professionals of a teaching hospital in Chicago, IL were sent an online questionnaire, comprising a simple clinical scenario and unambiguous questions regarding management of accidental dislodgment of the tracheostomy in the early post-operative period as well as the ability to properly identify the stay sutures, the purpose of the stay sutures and how to use them.

**Results:** Forty-four of 70 participants fully completed the survey. 43% of respondents could correctly identify stay sutures. 20% could correctly state the purpose of the stay suture. 52% knew when the stay sutures should be used and 43% knew how to properly use them. Analysis of a subgroup showed that 60% of attending physicians, 33% of resident physicians, 29% nurses and 33% respiratory therapists could properly identify the stay sutures.

**Conclusion:** The level of knowledge of the non-ENT health professionals working in the PICU was insufficient regarding the use of stay sutures in the event of accidental dislodgment of the tracheostomy in the early post-operative period.

## Development, Conduction, and Dissemination of Mock Tracers to Evaluate Care of Transgender Patients

**Primary Author:** Carley King, MSN, RN, CNL

**Contributors:** Megan Calabria MSN, RN, CNL (Rush University CON)

**Introduction:** There are many barriers that transgender patients experience when accessing health care. Barriers to adequate health care include issues such as difficulty obtaining health insurance, the scarcity of appropriate social programs for Lesbian, Gay, Bisexual, and Transgender (LGBT) individuals, and lack of knowledgeable health care providers. Providing sensitive care in a safe, inclusive environment for transgender patients can be the first step to eliminating some health disparities found in this population.

**Objective:** A large urban medical center in the Midwest is recognized nationally as a leader in LGBT health care equality. Little is known, however, about the structure and processes of care in the nurse to patient relationship and how these affect care particularly with transgender patients. Better understanding of the structures of care are needed to improve care to this vulnerable population.

**Methods:** This quality assurance project used The Joint Commission style mock tracer to look at the structure and processes of patient care. This included one-on-one interviews with 8 nurses providing care on 4 inpatient units (psychiatry, surgical, emergency department, post anesthesia care). A series of 8 tracer questions, based on the literature, covered: experiences caring for transgender patients, prior training, comfort level, knowledge of transgender specific health issues.

**Results:** The majority of staff interviewed reported they were comfortable caring for transgender patients and believed they provided quality sensitive care. However, staff members were not always aware of how to assess for gender identity/sexual orientation or how to obtain social and sexual histories that can be complex. They often neglected to assess for hormone use and were unaware of the implications of hormone therapy on health status. The mock tracers also revealed an incident of confusion between a patient's legal and preferred name, resulting in duplicate medical records and delayed care.

**Conclusion:** This quality assurance project revealed positive staff attitudes toward caring for transgender patients. However, they could benefit from additional training assessing the needs of transgender patients. Evaluating current system processes and staff attitudes provides the basis for system, educational, and training interventions to increase staff readiness to adequately care for transgender patients. Modifications to the registration process combined with education and training will improve health outcomes and patient satisfaction within the transgender population.

## **Rush University Urology Prostate Biopsy Performance Improvement**

**Primary Author:** Andrea Strong, RN

**Contributors:** Leslie A. Deane, MB.BS, MS, FRCSC, FACS; Shahid Ekbal, MD, FACS; Myriam Guillen; Kimberly Woodson, MPH, RN, BSN, CCRN; Nancy Antoine, MBA, RDMS, RVT; Sheila Dwyer; Megan Lowe, BSN, RN; Benjamin Gerling, BSN, RN (RUMC)

**Introduction:** Greater than 1.3 million prostate biopsies are performed annually in the United States. Many men undergoing this procedure have had a less than satisfactory experience and especially report this when a repeat biopsy may be necessary. Their concerns range from a lack of pre-procedural education to peri-procedural discomfort and the not insignificant risk of infection. We sought to implement a strategy to enhance patient acceptance of this procedure in our outpatient ambulatory clinic.

**Objective:** Commencing in April 2015, the Rush University Urology Prostate Biopsy Performance Improvement Team was established and comprised of a Performance Improvement Coach, a nurse champion and two physician sponsors. The goal was to improve the prostate biopsy procedure by enhancing patient and staff education, ensuring adherence to nationally accepted policy standards, and boost overall patient experience. The areas identified for improvement spanned the entire process, from procedure scheduling to discussing biopsy results. Evidence based practice, American Urological Association (AUA) and Society of Urologic Nurses and Associates (SUNA) recommendations, and local and institutional resources were tailored to guide the improvement efforts.

**Methods:** Process metrics included percentage of patients called the day after the procedure and percentage of patients who completed the biopsy preparation correctly. Pre-implementation data was collected from May 2015 through December 2015 and post-implementation data was collected February 2016 through March 2016.

**Results:** Data analysis showed a 69% increase in the number of patients called the day after procedure and a 38% increase in the percentage of patients who completed biopsy preparation correctly. Outcome metrics included number of patients with post biopsy sepsis and patient satisfaction results. Post implementation data was collected February 2016 through March 2016 and showed a 0 % post biopsy infection rate. In addition, strict adherence to asepsis with all providers donning PPE and maintenance of an equipment visibility barrier between patients and providers was established in 100 % of patients.

**Conclusion:** This performance improvement project provides early and initial data that the implementation of an institution and practice driven, evidence based improvement project enhances patient satisfaction and improves measurable outcomes related to prostate biopsy. We have continued the data acquisition to assess whether there is persistent long term improvement and whether these outcomes are durable. It may serve as a guideline for other practices seeking similar improvements.

## **Validation of the Mediterranean Eating Pattern for Americans II (MEPA II) Screener in a Chicago population**

**Primary Author:** Michelle Li, MS

**Contributors:** Christy C Tangney, PhD; Heather Rasmussen, PhD; Olivia A Moss, MS; Leah A Cerwinski, MS; Candace L Richards, MS; Brad Appelhans, PhD

**Introduction:** Screening tools that measure accordance or adherence to a Mediterranean diet have been validated in Spanish and Greek populations, but not in an American population.

**Objective:** The purpose is to determine the validity of a screener called Mediterranean Eating Pattern for Americans (MEPA II) against the gold-standard, multiple 24-hour diet recalls.

**Methods:** The MEPA II was designed to capture foods consistent with a Mediterranean dietary in the American food culture. Convergence was assessed in U.S. adults participating in the Study of Household Purchasing Patterns, Eating and Recreation (SHoPPER). Multiple nonconsecutive 24-hour recalls were conducted by registered dietitians over two weeks. Then, the MEPA II screener was completed by participants. Nutrient analyses of key foods and nutrients reflecting a Mediterranean pattern were calculated for the averaged recalls and compared to MEPA II screener scores.

**Results:** The sample included 69 Chicago residents. Majority of the sample was Black (61%). Based on the average recalls, men reported 2509 (967) kilocalories, with 14.5 (3.6) % of calories from monounsaturated fats, 11.9 (2.7) % from polyunsaturated fats, and 11.4 (1.8) % from saturated fats. For women, the reported intakes were as follows: 1989 (558) kilocalories, with 13.3 (3.1) % of calories from monounsaturated fats, 8.2 (2.3) % from polyunsaturated fats, and 11.3 (2.9) % from saturated fats. MEPA II screener scores ranged from 2 to 14, with a median of 10. Spearman correlations between MEPA II scores and nutrients derived from recalls were significant for nutrients consistent with a Mediterranean dietary pattern: dietary fiber, beta carotene, vitamin C, and folate. Intakes of foods consistent with this pattern: whole grains, fruit, dark green vegetables, legumes, and added sugars.

**Conclusion:** Additional reliability and validity testing, especially with bio-markers of the key food components on MEPA II, will be needed before this tool can be used with confidence.



## **iPad Use by Medical Students to Educate Patients during the Pediatric Clerkship-A Pilot Study**

**Primary Author:** Michelle March, BS, MPH

**Contributors:** Alisa Brennan, BS; Kyrie Hungerford, BS; Stephanie Schmitt, BA; Amir Jahanshad, BS; Jennifer Szotek, BS; George Ziegler, MD; Elizabeth Van Opstal, MD (Rush University)

**Introduction:** Current research suggests multimedia-based patient education methods are preferred and more effective, but research for the use of iPad-based education within pediatrics is limited. iPads are commonplace in the daily lives of medical students as well as patients/caregivers, yet this technology and these students remain underutilized in the process of patient education.

**Objective:** - Evaluate patients'/caregivers' level of understanding before and after receiving iPad-based teaching - Empower medical students as patient educators via training and feedback sessions

**Methods:** From September 2015 to December 2016, students in the pediatric clerkship watched an informational video on pediatric patient education with iPad technology and received in-person instruction. Medical students self-selected a topic related to individual patient care and conducted an educational intervention with patients/caregivers in an inpatient setting using an iPad or other resources. Pre- and post-surveys were completed by the patients/caregivers. Following this, students shared their teaching with peers in small group sessions.

**Results:** A total of 128 pre- and post-surveys were collected from patients/caregivers. Collectively respondents' comfort level with the topic presented increased from 3.74/5 to 4.73/5, p-value < 0.001. Most frequently selected topics included: Pulmonary/Allergy/Immunology (23%) and Gastroenterology (13%). 81.25% of students utilized the iPad as a learning tool. 93.40% of respondents viewed the iPad as an acceptable teaching tool. Comparison of the iPad (n= 104) to other traditional teaching methods (e.g. drawings, handouts, verbal explanations) (n= 24) resulted in a p-value= 0.84.

**Conclusion:** iPads serve as modern-day, universal learning tools for patients/caregivers in an inpatient pediatric healthcare setting. Through educational interventions, medical students enhance patient care, and increase patient and parent understanding of relevant medical topics.

**Significance:** This study provides a platform to integrate medical students and tablet technology into patient education within the inpatient setting.

## **Effects of age, bolus volume, bolus viscosity, and effortful swallow on penetration and aspiration in healthy, older adults**

**Primary Author:** Melissa Peterson, BS

**Introduction:** During swallowing, penetration occurs when the material being swallowed, or bolus, mistakenly enters the laryngeal vestibule; aspiration occurs when the penetrated bolus enters the trachea. Both penetration and aspiration (PA) increase risk of morbidities including aspiration pneumonia and/or death. Therefore, when speech-language pathologists observe PA in patients, various recommendations are made to help minimize PA occurrence. Aging-related changes in the swallowing neuromuscular system may affect the incidence of PA in non-patient, healthy older adults, but this is unclear. Previous studies in healthy older adults have been limited to only one bolus volume or viscosity, but, in patients PA varies by both volume and viscosity. Furthermore, only one study has investigated the effect of effortful swallowing, a common therapy technique used to minimize PA occurrence in patients. Lastly, anecdotal evidence suggests that clinicians may erroneously conclude PA indicates dysphagia in otherwise healthy adults without disease known to result in dysphagia resulting in inappropriate therapy recommendations and referrals.

**Objective:** To investigate the relationship between age, volume, viscosity, and swallowing effort on PA in healthy, older adults

**Methods:** This study is a secondary analysis of a cross-sectional prospective study in which 31 healthy, older adults divided into three age groups (60s, 70s, 80s) swallowed 32 boluses systematically varying in volume, viscosity and swallowing effort. For this study, videofluoroscopic recordings of these 932 swallows were scored using the Penetration-Aspiration Scale (PAS). Summary statistics and Repeated-Measures ANOVA were used to analyze the relationships between variables.

**Results:** Data collection is on-going. Preliminary results from 12 participants reveal penetration incidence to be greater in older ( $f=31.25\%$ ) than younger participants ( $f=22.54\%$ ), and a significant viscosity x condition interaction ( $p=0.031$ ).

**Conclusion:** Preliminary results suggest PA is common in healthy, older adults, and that incidence varies by age, viscosity, and swallowing effort.

**Significance:** Outcomes may help establish PA norms and guide speech-language pathologists to appropriate treatment recommendations for older patients.

## Occurrence of Valproate-induced Neutropenia in Management of Schizoaffective disorder

**Primary Author:** Cicely Moreno, MD

**Contributors:** Van Horn, Rebecca (RUMC)

**Introduction:** The most commonly reported hematologic adverse effect of valproate (VPA) treatment is thrombocytopenia. While on the other hand, neutropenia secondary to valproate has only been reported in two isolated adult cases and in isolated pediatric cases as mild and transient. The most recent study regarding its effects on neutrophils noted that serum VPA levels had a significant but weak adverse effect on neutrophil counts in large neuropsychiatric patient population. Here we report a significant occurrence of valproate-induced neutropenia within less than a week of its initiation. A 32 year-old African-American male with Schizoaffective disorder was treated with VPA and quetiapine. Pre-treatment ANC was 4.03 cells/mm<sup>3</sup>. Five days after VPA initiation, patient developed neutropenia with absolute neutrophil count (ANC) of 1.34 cells/mm<sup>3</sup>. Upon VPA discontinuation, the ANC quickly normalized to value of 5.06 cells/mm<sup>3</sup>. Interestingly, quetiapine appeared to be noncontributory to patient's neutropenia.

**Objective:** To report a case of VPA-induced neutropenia.

**Methods:** A case reviewed of a 33 year old male with Schizoaffective disorder managed on VPA and quetiapine. A literature search was performed using PubMed using key words: valproic acid, valproate, Depakote, neutropenia, pancytopenia, thrombocytopenia, antiepileptics.

**Results:** VPA, although commonly reported as well tolerated, can cause rare immunological side effects.

**Conclusion:** This case report of VPA-induced neutropenia demonstrates the importance of hematologic monitoring in neuropsychiatric pharmacotherapy.

## **Naloxone access among an urban population of opioid abusers**

**Primary Author:** Jenna Nikolaides, MD

**Contributors:** Steven Aks, MD (Cook County Hospital) Michael Rozum, BA (Rush) Lum Rizvanolli (UIC)

**Introduction:** Take-home naloxone has been proposed as one method of curbing the mortality associated with the opioid overdose epidemic. It is unclear if some opioid users have more access to naloxone than others.

**Objective:** Does naloxone awareness and access differ between people who abuse different types of opioids?

**Methods:** A convenience sample of 101 patients was surveyed in an urban academic emergency department (ED), over a 6 month period (April to October, 2016). A 14 question survey was drafted, validated by a panel of medical toxicologists, piloted, and then edited for clarity. The survey was then administered to ED patients by standardized trained research assistants. Inclusion criteria: opioid abuse within the previous 3 months, age greater than 18 years. Exclusion criteria: acute intoxication and inability to consent, incarceration, involuntary psychiatric admissions, and those taking opioids as prescribed were excluded. Data was analyzed using descriptive statistics. This study was approved under IRB exempt status.

**Results:** The average age of survey responders was 47.3 years old; 72% were male; 57% black, 31% white; 15% Hispanic. For current method of opioid abuse: 38% inject heroin, 72% snort heroin, 8% abuse prescription pills. When asked about naloxone, 55% had heard of it and 22% had access to it at some point. Of the 54/101 responders with a history of injecting heroin, 76% (41/54) had heard of naloxone, and 39% (21/54) had access to it at some point. Of the 47/101 who had never injected heroin, only 32% (15/47) had heard of naloxone, and 2% (1/47) had access to it.

**Conclusion:** Snorting heroin was the most common method of opioid abuse among our urban population. However, heroin injectors had better naloxone awareness and access. Those that had naloxone reported a high rate of use. Limitations include the survey format and its single-center urban setting.

**Significance:** Naloxone distribution appears to be missing certain populations of opioid abusers.

## A Pilot Study of Video Self-Modeling in Fragile X Syndrome

**Primary Author:** Suzanne LaBelle, BS

**Contributors:** Anne Hoffmann, Ph.D., CCC-SLP (RUMC)

**Introduction:** Fragile x Syndrome (FXS) is a genetic disorder marked by developmental delays and impairments in pragmatic language for social purposes. Interventions for pragmatics in FXS have received little to no research. Video self-modeling (VSM) has been used in several studies with individuals with autism spectrum disorder (ASD). This study directly assesses initial efficacy of VSM on pragmatic language skills in adolescents with FXS.

**Objective:** This study aims to assess the efficacy of VSM for pragmatic language skills in individuals with FXS, and determine feasibility of implementing VSM into school settings.

**Methods:** After approval by the IRB and informed consent of participants, this study implemented VSM adapted from Buggey's studies of ASD for intervention for four individuals with FXS. Baseline testing included the Stanford-Binet, Fifth Edition test, and Autism Diagnostic Observation Schedule-Second Edition. Ongoing data collection consisted of 15 minute observation three times a week before, during, and after VSM intervention, in which target behaviors were marked as either occurring during an opportunity or not occurring.

**Results:** Participants 1 and 2 had target skills of appropriately greeting peers. Participant 1 had 26.92% pre-, 39.29% during, and 50% post-video success. Participant 2 had 5.88% pre-video, 0% during-video, and 4% post-video success. Participants 3 and 4 had target skills of initiating and maintaining conversation with non-preferred peers. Participant 3 had 4.76% pre-video, 31.71% during-video, and 61.11% post-video success. Participant 4 had 14.63% pre-video, 40% during-video, and 48.28% post-video success. No statistical analysis was performed due to this being a pilot case study.

**Conclusion:** This study shows preliminary support for the efficacy of VSM in pragmatic language intervention for individuals with FXS, and the ease of incorporating VSM into school settings. Each of the participants, with the exception of 2, made improvements in the use of their targeted behavior. We suspect that anxiety inhibited his use of greetings.

**Significance:** This study highlights the importance of studying successful ASD behavioral interventions in FXS, because though these individuals may portray similar behaviors, the underlying anxiety in FXS can cause unforeseen difficulties. Future studies of VSM efficacy for behavioral interventions in FXS should aim to work with a larger sample size in order to draw conclusive, statistically significant data. Continued studies of interventions for pragmatic skills in individuals with FXS are essential to their success in daily functioning and future goals.

## Root Cause Analysis and Interventions for Reduction of CLABSIs in a Pediatric CICU

**Primary Author:** Kathleen English, MSN, RN, CNL

**Contributors:** Amber Kujath, PhD, RN, ONC (Rush CON)

**Introduction:** Central line-associated blood stream infections (CLABSIs) have been associated with increases in cost, length of stay, and mortality. To address a recent surge in CLABSIs, a quality improvement project was initiated on a pediatric cardiac critical care unit at a large academic medical center. The chart review revealed that the numbers of CLABSIs had doubled from 2015 (n=4) to 2016 (n=8). The goal was zero CLABSIs for this unit.

**Objective:** The purpose of this project was to identify contributing factors to increased CLABSI occurrence, review relevant evidence, and propose recommendations to decrease CLABSIs.

**Methods:** A root cause analysis was conducted using a fishbone diagram. The investigator identified staffing as one of the potential causes of increased CLABSIs on the critical care unit. Monthly staff overutilization data were collected and compared with CLABSI rates. The data analysis suggested a potential association between staffing shortages and increased CLABSI rates. A literature review was also conducted to identify common contributing factors for increases in CLABSIs. Published data supports evidence of increased infection occurrence related to nurse staffing shortages. There is also evidence that perception of adequate staffing improves quality indicators (CLABSIs).

**Results:** The quality improvement project helped identify staff shortages as a potential cause of increased CLABSIs on a pediatric cardiac critical care unit. Further investigation is needed to evaluate the effect of using critical care-designated float nurses to reduce CLABSIs on the pediatric critical care unit.

**Conclusion:** Utilization of a designated critical care trained float pool was discussed as a potential strategy to decrease the rate of unit CLABSIs. This implementation would build upon an existing float pool team within the hospital and focus a particular group to the high acuity unit.

## **The impact of levodopa-induced dyskinesias on speech acoustic measures in Parkinson's disease**

**Primary Author:** Carly Blodgett, B.A.

**Contributors:** Emily Wang, Ph.D./Department of Communication Disorders and Sciences, Rush University Leo Verhagen, M.D., Ph.D./Department of Neurological Sciences, Rush University

**Introduction:** Levodopa is a common and effective medication used to treat Parkinson's disease (PD). However, its long-term use is often complicated by motor disturbances including levodopa-induced dyskinesias (LID) and/or dystonias. LID are difficult to treat and can occur at various points during a medication cycle. Thus, appropriate treatment of LID requires accurate monitoring. LID affecting the head, neck, and trunk complicate the dysarthria profile of individuals with PD, often resulting in a classification of mixed hypokinetic-hyperkinetic dysarthria. However, the literature lacks consensus regarding the exact impact of LID on the speech and voice of individuals with PD.

**Objective:** We hypothesize that certain acoustic speech measures can capture and reflect this impact. The present study aims to evaluate the relationship between LID and acoustic speech measures selected to reflect speech changes in individuals with PD.

**Methods:** Data for this retrospective study have been retrieved from video and audio recordings of 10 surgical candidates with PD during the 'off' medication state and 10 matched clinical patients during the 'on' medication state. The participants are matched by disease progression, dyskinesia severity, and gender. Eight acoustic speech measures are being analyzed for their sensitivity to global changes as well as variations in respiration, phonation, and prosody as a result of interruptions in speech movements. Statistical analyses involve descriptive statistics, correlations with established scales reflecting dysarthria and disease progression, and p-values generated by SPSS. All participants gave informed consent at the time of data collection and this study has been approved by Rush University's Institutional Review Board.

**Results:** The analysis is ongoing and it is expected to be completed in a month. Although there are observable changes in speech movement associated with levodopa-induced dyskinesias the outcome of this pilot study will provide a more definite answer to the relationship between speech and levodopa-induced dyskinesias in Parkinson's disease.

**Conclusion:** The findings of this study will provide the pilot data for future research working toward the use of acoustic speech measures as a means to monitor motor fluctuations in individuals with PD for better clinical management.

## **Barriers to Non-Barrier Methods: An Illustration of Discrepancies Among Illinois Medicaid Patients Seeking Long-Acting Reversible Contraceptive (LARC) Devices**

**Primary Author:** Megan Sax, MD Candidate

**Contributors:** Julia Cormano, MD

**Introduction:** The U.S. Centers for Disease Control and Prevention classifies Long-Acting Reversible Contraception (LARC) devices as the most effective reversible family planning method. These devices have been shown to reduce maternal and neonatal morbidity and mortality, as they allow for adequate inter-pregnancy spacing in addition to preventing unintended pregnancy. Despite mandates set forth in the Affordable Care Act (ACA) and strategies initiated by the Illinois Department of Healthcare and Family Services (HFS) to improve LARC access, there are still many barriers for underinsured individuals to obtain desired LARC devices.

**Objective:** Our objective is to identify common barriers to obtaining LARC device coverage among patients with active insurance under various Illinois Medicaid Managed Care Organizations (MCOs).

**Methods:** All patient recruitment and documentation of efforts to obtain coverage were completed in July, 2016, at Alivio Medical Center in Chicago, IL. Three inquiries of denied coverage were selected for investigation and individual flowcharts were created to document the efforts exerted in an attempt to obtain coverage. Specifically, we examined the ParaGard Copper IUD with Family Health Network, Nexplanon Implantable Rod with IlliniCare Health, and Nexplanon Implantable Rod with Illinois Medicaid.

**Results:** Regardless of multiple efforts made by medical and pharmaceutical teams, ultimately, none of the three patients received coverage for their desired LARC device, and we were unable to identify a consistent reason for denied coverage. We found general Illinois Medicaid to be the most difficult to navigate, both online and by telephone.

**Conclusion:** Identifying and reducing barriers to accessing LARC devices is an essential example of prioritizing public health, endorsing existing healthcare expansion policy, and advocating for patient autonomy. We hope this work may serve towards highlighting the shortcomings of existing policy and regulation. Increased standardization and uniformity across MCO LARC device protocol and third party vendors may facilitate achieving access to LARC devices.



## Long-term Effect of Delayed Auditory Feedback on Hearing Threshold in Patients with Parkinson's disease

**Primary Author:** Eric Hulse, B.S.

**Contributors:** Emily Wang, Ph.D./Communication Disorders and Sciences, Rush University Valeriy Shafiro, Ph.D./Communication Disorders and Sciences, Rush University Leonard Verhagen, M.D., Ph.D./Neurological Sciences, Rush University Medical Center

**Introduction:** The wearable in-the-ear SpeechEasy® device is registered with FDA as an anti-stuttering device. It's a device that can take incoming acoustic signals, modify them in both amplitude domain and the frequency domain, and then redeliver them into a listener's ear with the modifications. It was first investigated as a therapeutic option for hypokinetic dysarthria in Parkinson's disease (PD) by our group in 2008. While the results demonstrated positive treatment effects on hypokinetic dysarthria in PD, the question remains whether long-term use of the device could lead to detrimental effect on hearing in a typically aging population.

**Objective:** Since the SpeechEasy® device has the capacity to provide various levels of increased volume to the wearer, the two main goals of the current study were to determine 1) the various output levels of the SpeechEasy® CF-BTE devices used in the study; and 2) whether the long-term use of this device caused a significant shift in our subjects' hearing thresholds.

**Methods:** To achieve the two main goals, we first determined the output of the SpeechEasy BTE-CF in different settings across varying intensities of a frequency sweep and then investigated the effect of prolonged device use on hearing thresholds. Two devices used in the study (2008) for fitting were tested. The devices were programmed via the SpeechEasy fitting software. Both devices were programmed identically in each setting for measurement reliability purposes. Once programmed, the first device was secured inside a calibrated Verifit AudioScan test box. Outputs of the device were then measured using a frequency sweep ranging from 200 Hz to 6300 Hz. The frequency sweep was presented at four intensities per device: 55 dB SPL, 65 dB SPL, 75 dB SPL, and 90 dB SPL. In practical terms, these intensities represent quiet conversation, normal conversation, loud conversation, and, not so practically, the speaker limit of the test box, respectively. After both devices were measured in the first setting, the devices were reprogrammed and measured in the second, third, and fourth settings separately using the aforementioned criteria. All fifteen subjects who wore the SpeechEasy® device for one year in the Wang et al. 2008 study were included. Seven met inclusion criteria for determining if a potential standard threshold shift occurred during device usage. Real-ear measurements collected during the Wang et al. (2008) study were analyzed to determine if the SpeechEasy device exceeded the most comfortable loudness level (MCL) or uncomfortable loudness level (UCL) of the study subjects.

**Results:** Device measurements using the AudioScan Verifit produced 3,072 data points, or 1,356 data points per device. Correlational statistics revealed a significant correlation ( $> 0.8$ ) between both devices for all device conditions averaged across all six intensity settings. The highest degree of correlation was observed for the 'Intensity-Only' setting (0.995) while the lowest degree of correlation was observed for the 'Intensity + FAF + DAF' condition (0.878). This indicates the two devices function very similarly. Next,

all four conditions were analyzed to determine maximum device output when both devices were programmed to intensity setting 6 and the frequency sweep was presented at 90 dB SPL. The 'Intensity-Only' condition produced the highest output intensity, 115 dB SPL at 630 Hz, while the 'Intensity + FAF' condition produced the lowest output intensity, 87 dB SPL at 3150 Hz. The 'Intensity + DAF' condition produced the second highest output intensity, 101 dB SPL at 800 Hz, and the 'Intensity + FAF + DAF' produced the second lowest output intensity, 94.5 dB SPL at 3150 Hz. Lastly, the 'Intensity-Only' condition was analyzed to determine the dB SPL difference between device intensity 1 (lowest) and device intensity 6 (highest) for all four intensity input levels across all frequencies within the frequency sweep. The differences between the device intensities ranged from 18 dB SPL to 24.5 dB SPL (200 Hz to 5000 Hz) with an average intensity difference of 21.9 dB SPL. In terms of standard threshold shifts caused by the SE device, it appears that this device will not cause hearing loss if programmed correctly. Six out of seven patients evaluated during the study demonstrated no significant shift in hearing thresholds after prolonged device use. Regarding the one patient who demonstrated a standard threshold shift, this shift was most likely due to non-device related reasons. Real-ear measurements revealed individuals in the moderate to severe hearing loss group were under-amplified at 2000 Hz and beyond. The subject demonstrating a standard threshold shift was part of this group, therefore the device could not have been responsible for the shift in hearing.

**Conclusion:** The results indicate that the SpeechEasy® device will not cause hearing loss if programmed correctly. However, because SpeechEasy® device is capable of producing potentially high output levels if programmed incorrectly, a standardized device fitting protocol must be considered.

**Significance:** This is the first investigation of impact of long-term use of a wearable in-the-ear SpeechEasy® device, which is capable of changing both output intensity and frequency, on human hearing threshold. It highlights the importance of standardized fitting protocol when use this device to treat speech disorders clinically.

## Screening School-age Children for Language Impairment in Pediatric Primary Care

**Primary Author:** Kerry Ebert, PhD

**Contributors:** Melissa P. Holmes, MD (RUMC)

**Introduction:** Approximately 7.4% of children are affected by primary language impairment (LI). LI negatively impacts academic and social outcomes of affected children. It is highly under-recognized and may not become apparent until the school years. There are few screening protocols for this age group. Screening tools in the primary care setting must be feasible given staff limitations in time, availability, and training.

**Objective:** The purpose of this project was to develop a screening tool for LI in early school-age children and assess its feasibility and preliminary psychometric properties.

**Methods:** This project was approved by the Rush IRB. Thirty-five 6-8 year olds and their parents were recruited during well-child visits at the Rush Pediatric Primary Care Center. Parents completed a 5-item questionnaire regarding language development. Children completed a 10-item sentence repetition task administered by a student volunteer. Feasibility was assessed using data on screening time, feedback from clinic staff, and scoring accuracy for the student volunteers. Psychometric properties were assessed via internal consistency analyses and via identification accuracy for a small group of children (N= 12) who completed a follow-up language evaluation.

**Results:** Feasibility: Average time to complete the screener was 2 minutes, 10 seconds. Clinical staff reported the screening project was minimally disruptive to clinical operations. Binary scoring agreement between student volunteers and an expert listener averaged 93.8%. Psychometric properties: Cronbach's alpha indicated good internal consistency for both the parent questionnaire ( $\alpha = .88$ ) and the child task ( $\alpha = .78$ ). The parent and child components were moderately and significantly correlated,  $r = .438$ ,  $p = .011$ . Within the limited sample who completed follow-up, the screener demonstrated perfect sensitivity and specificity in identifying children with LI.

**Conclusion:** The screening tool for LI is feasible within the primary care setting. Preliminary psychometric properties are promising.

**Significance:** The project establishes a new tool for quickly identifying LI within the pediatric primary care setting.

## Community Participation in Young Adults with Intellectual and Developmental Disabilities

**Primary Author:** Madeline Minogue, BS

**Contributors:** Kathleen McGahon (Rush), Michelle Martin (Rush), Laura Cuttone (Rush), Molly Bathje, PhD, OTR/L (Rush)

**Introduction:** Adults with intellectual and developmental disabilities (IDD) are more socially isolated than their peers. The World Health Organization recognizes participation as an important component of health. However, there are few studies about community participation in young adults with IDD and those studies mainly focus the barriers to participation or measuring individuals' presence within communities, instead of their sense of inclusion within communities.

**Objective:** This study examined the lived experience of community participation in young adults with IDD

**Methods:** following Creswell's six step approach for qualitative research. Four young adults and their parents provided consent and assent for participation. Semi-structured interviews were recorded and transcribed for analysis. Pairs of student researchers initially analyzed the data, followed by a group analysis (of 4 students) that identified significant statements and categorized them into themes. The final iteration of data analysis was completed with the faculty advisor, where agreement of themes was reached.

**Results:** One hundred sixteen significant statements were identified and categorized into 9 themes which included: Need for Physical Safety; Need for Support, Presence of an Activity; Logistical Challenges; Understanding Context; Family as a Community; Identifying with Previous Communities; Positive Outcomes; and Desired Future Participation.

**Conclusion:** Themes indicated several factors either support or inhibit participation, and that participants had a strong desire to be a part of communities. Based on results, it is recommended that individuals' family contexts be considered an important community participation opportunity and that young adults with IDD are a unique population. Participants also identified as members communities they no longer have access to, indicating that supporting transitional roles or modified participation may help increase active engagement in communities. Limitations included a small sample of similar individuals from one specific post-secondary education program. This study provides preliminary data for a population with insufficient health research and confirms the need for further research.

## **Treatment Seeking Behavior for Church's and their Congregations on Chicago's West Side**

**Primary Author:** Erick W. Skaff, MD Candidate (Rush)

**Contributors:** Elizabeth Lynch, PhD (Rush); Catherine Feit, RN (Rush); Laurin Mack, PhD (Rush); Samantha Marinello, (Rush)

**Introduction:** Healthy Chicago 2.0 made it a goal to increase utilization of mental health treatment among those with the greatest need and Rush's Community Health Needs Assessment specifically noted a substantial lack of mental health resources on Chicago's predominantly African American west side.

**Objective:** Churches and pastors are important institutions for low resource African American communities and their mental health treatment. Barriers to mental health treatment and coping strategies for addressing mental health treatment were examined at 9 churches on Chicago's west side.

**Methods:** Nine pastors and eight congregation members were given a semi-structured 60-minute interview. Qualitative analysis was conducted to identify common themes. The research received IRB approval.

**Results:** When asked about barriers to seeking mental health treatment, respondents noted limited resources (13), lack of recognition of mental illness (12), and stigma (8). When the limited resource theme was looked at further, lack of access to treatment centers (11) was a greater barrier than insurance or financial concerns (5). When asked about how people in your congregation and community cope with mental health issues and where they seek treatment, the most frequent response was negative coping strategies (10). This includes not coping (6), isolating themselves (3), and substance use (5). Informal networks of support were the major source of positive strategies with 9 respondents stating people either received help from church (8) or talked to others (4). This is compared to only 5 people who mentioned community members receiving professional help.

**Conclusion:** The research is limited because of its small size and church specific sample. Any potential future intervention must provide: (1) resources in the form of affordable treatment centers and (2) education in order to recognize mental illness and de-stigmatize it.

## Association Between Insurance Status and Hospital Utilization for Alcohol and Drug Use

**Primary Author:** Kathryn Rooney, BA

**Contributors:** Raj C. Shah, MD (Rush Alzheimer's Disease Center)

**Introduction:** Rush University Medical Center's (RUMC) most recent Community Health Needs Assessment (2016) identified mental health and substance use as 1 of 4 priority health needs in the area. After the Affordable Care Act (ACA), health care delivery systems are changing to improve access to mental health care. The main goal of this project is to understand the socioeconomic factors associated with hospital utilization for SUD in the communities serviced by RUMC.

**Objective:** Primary aim: analyze the association of insurance status with hospital utilization for substance use in persons residing in the communities served by RUMC. Secondary aim: explore the association of insurance status with hospital utilization for pre- and post-ACA.

**Methods:** Primary analysis will utilize a chi-squared test to compare inpatient hospitalizations for alcohol and drug use among individuals who have insurance and who do not have insurance. Secondary analysis will utilize a chi-squared test to examine the association between insurance status and hospital utilization for differences pre- and post- implementation of the ACA. Using a one-way ANOVA, we will also examine differences in hospital utilization for substance use among individuals with the following types of insurance: Medicaid, Medicare, private insurance, and self-pay/no insurance. Data will be extracted from the CAPriCORN Common Data Model database at RUMC, which has received IRB approval.

**Results:** From 2011-2015, there were 2365 encounters attributed to SUD, with 1909 encounters from individuals with insurance and 456 without insurance. We found there was a greater percentage of individuals who sought care for SUD without insurance than expected. Full analysis is not completed.

**Conclusion:** Our study found there was a greater percentage of individuals who sought care for SUD at RUMC without insurance than expected. Although full analysis is not completed, we hope our results will yield insight into the socioeconomic factors associated with hospital utilization for SUD.

**Significance:** SUD is a significant problem in the United States. According to the 2013 National Survey on Drug Use and Health, 24.6 million Americans aged 12 or older, or 9.4 percent, had engaged in illicit drug use within the past month. This percentage has grown from 7.9 percent of the population aged 12 or older in 2002. Furthermore, almost 90% of individuals who meet criteria for substance use disorder do not receive long-term treatment services. Given the overwhelming treatment gap for SUD and the new approaches to health insurance after implementation of the ACA, research is needed to understand the current impact of insurance status on hospital utilization for substance use in Chicago. By analyzing the association between insurance status and hospital utilization for substance use, this study will enable shared decision making regarding the impact of insurance on treatment for substance use.

## Improving Access to Healthcare for Patients at a Homeless Shelter - A Needs Assessment

**Primary Author:** Cory Kosche, BS

**Contributors:** Wainwright, Mary Katherine (Rush); Shanu Gupta, MD (Rush)

**Introduction:** Student-run, volunteer based clinics for the homeless community are an important source of acute care for this population. At our clinic in Chicago's west side, a growing trend of patients presenting for chronic illness management was noted, despite Medicaid expansion.

**Objective:** We wanted to assess challenges to health care access faced by our clients. Here we report the results of our needs assessment data, as well as subjective reports from an interprofessional focus group, and the solutions created to begin addressing the issues.

**Methods:** Patients seen at the clinic over a period of four months were administered a questionnaire assessing their health insurance status, access to a PCP and specific barriers to accessing adequate health care. In the second part of the project, we held a focus group with caseworkers from the shelter, shelter staff, homeless residents, a physician, a health systems management student, and a medical student. We specifically explored barriers to health care access and discussed potential sustainable solutions.

**Results:** In total, we collected data on 104 unique patients. We found that 63.7% of responders have active health insurance and 36.3% are uninsured. Of those who are insured, 52.4% reported being insured under Medicaid, 27% specifically reported being on a County Care plan, 11% reported Medicare coverage, and the remainder were on private plans or unsure. Moreover, of the insured patients, 64.6% denied having a PCP. The most common reported barriers were lack of knowledge of how to get a PCP and lack of desire to see a PCP and/or distrust of providers. In collaboration with staff and residents of the shelter, we created easy-to-understand resources for applying for Medicaid and getting a PCP, a map of local physicians accepting patients, and an incentive program for completing an initial visit with a PCP.

**Conclusion:** Many homeless individuals are being enrolled in Medicaid without explanation of how to access services. These insured individuals continue to rely on free clinics and emergency rooms. Lack of knowledge of how to obtain a PCP is the primary barrier to seeking care. We are restructuring our clinic model to incorporate access discussions, follow-up, and incentives for obtaining a PCP.

**Significance:** With the implementation of the Affordable Care Act, healthcare accessibility should have theoretically increased for the homeless population. The growing trend of patients presenting at our free clinic with complaints related to chronic illness seemed to suggest otherwise. By assessing and addressing the healthcare and access to care needs of this population, we will ideally be able to increase their access to a higher level care and decrease the volume of patients seeking care for chronic illness at the clinic.

## **Risk Stratification, Patient Complexity, and Care Coordination in a Medicaid Population**

**Primary Author:** Kathryn Swartwout, PhD

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**Introduction:** Most care coordination models fail to use efficient ways to target high risk patients using social determinants of health. The Activation and Coordination Team (ACT) Model was designed by an interprofessional team at RUMC to allocate resources efficiently and facilitate care coordination in primary care settings.

**Objective:** This study examines patient placement into one of four ACT Complexity Quadrants that determine care coordination resource allocation based on 11 medical and 15 social indicators. Objectives are to 1) determine whether initial health screening accurately identifies patient risk levels and 2) test validity of Complexity Quadrant placement.

**Methods:** A cross-sectional and retrospective design is used to analyze health assessment and clinical data. The sample includes 198 adults enrolled in Medicaid managed care. Initial screening was conducted to determine risk levels, and medium/ high risk individuals receive comprehensive assessments and are designated for care coordination. In this study, low risk patients were also given comprehensive assessments. An algorithm assigned patients to Quadrants reflecting medical and/or social complexity. Demographic, health, psychosocial, and utilization characteristics were compared across risk levels and Complexity Quadrants, using ANOVA, Chi square, and multiple regression analysis.

**Results:** Despite mean age of 39 years, patients had high prevalence of obesity, chronic pain, and ED usage. Approximately 2/3 of the 134 patients in medium/high risk categories were assigned to the high medical/high social need Complexity Quadrant. Additionally, 50% of those initially screened as low risk were assigned to high medical/ low social or high social/low medical Quadrants. Quadrants differed significantly on health and social indicators, such as days of poor health, but did not differ on difficulty managing symptoms or ED visits.

**Conclusion:** Complexity Quadrants may provide a method for optimizing care coordination interventions.

**Significance:** This study is critical to establishing ACT credibility and successful implementation for this high risk population.



## Salud comunitaria y la escuela: Using Classroom Modules and a Community Garden to Encourage Wellness in Students

**Primary Author:** Mallory Davis, BS, MD Candidate

**Contributors:** Sarah Burbank (RMC)

**Introduction:** Childhood obesity rates have been steadily increasing in the United States over the past three decades. Within Chicago, obesity is especially prevalent among children who live in minority communities, such as the predominantly Hispanic neighborhood of Pilsen. Fruit/vegetable intake and exercise are the two most modifiable risk factors for childhood and adult obesity. This project aims to address health disparities in the Pilsen neighborhood through delivery of 6 nutrition and mindfulness modules, supplemented by hands-on activities such as caring for a community garden, mindfulness classes, and healthy cooking classes, to adolescent students-ages 10-15-attending a Chicago after school program.

**Objective:** a. Assess if education modules that are both didactic and interactive can be utilized to educate adolescents about the importance of fruit and vegetable consumption in prevention of obesity and chronic disease. b. Determine if interactive curricular components in a nutrition curriculum can improve attitudes and knowledge about fruits/vegetables and nutrition

**Methods:** Six didactic modules will be delivered to two schools in Pilsen, and one school (interventional group) will also receive interactive components during each module. The modules are as follows: Module 1 Food Environment: Media, Policy, Advocacy and Nutrition Module 2 Nutrition Basics: Calories and Nutrients; Interactive Component: Paint garden signs Module 3 Interpreting Nutrition Labels and Portion Size; Interactive Component: Plant seedlings Module 4 Balancing Physical Activity and Nutrition; Interactive Component: Mindfulness/Yoga Exercise Module 5 Healthy Substitutions in The Kitchen; Interactive component: Cooking class Module 6 Nutrition and Heart Health; Interactive Component: Blood pressure skill lab Extra session in interventional group: Community Gardening Benefits and Safety; Community gardening day Curriculum resource: Community Voices for Health Kids Take Action Created by American University School of Education Teaching and Health 2013 Pre and post test surveys will be administered to a control and intervention school that will assess various factors-attitudes, knowledge, perception/self-efficacy for making healthy eating choices, exposure, and willingness-that can be attributed to influencing fruit and vegetable consumption.

**Results:** The original pilot study (done academic year 2015-2016) yielded the following results: Comparison of the pre and post attitudes surveys revealed an average increase of 1.29 points by the end of the intervention.

**Conclusion:** The seeming success of the pilot project last year provides validation for repeating the intervention this year (academic year 2016-2017). Because the original purpose of the project was for the Dean's Summer Community Service Project, a research component was not the intent; however, the new project design will incorporate a control group to compare attitude survey scores in students that

receive the interactive components/gardening experience with those who receive only didactic modules.

## Vaccine Awareness in the Community of Canaan, Haiti

**Primary Author:** Yasmin Abedin, BS, MPH

**Contributors:** Veronica M. Esmero, DO (RUMC) Joseph P. Musto, MD (RUMC) Jennifer Towbin, MD (RUMC)

**Introduction:** During the devastating earthquake that struck Haiti in 2010, all health services were interrupted. Since the earthquake, various health organizations have been invested in delivering health care to Haiti, including vaccinations.

**Objective:** Recently, Rush University Medical Center helped build the Jerusalem Clinic in Canaan, Haiti, with the hopes of delivering sustainable health care. There is limited data regarding vaccinations in Canaan. A needs assessment/survey was completed at the Jerusalem Clinic in order to evaluate the knowledge of certain vaccines.

**Methods:** A thirteen-question vaccine survey was created and interpreted in French, and delivered at the Jerusalem Clinic in Canaan, Haiti from 8/1/16-8/5/16. Data was entered into Microsoft Excel Spreadsheet for analysis and interpretation.

**Results:** A total of 174 surveys were collected from 8/1/16-8/5/16. 89.1% of the surveys were done by females and 10.9% were done by males. The average age of participants was 39 years. Of note, 93.7% of the participants had knowledge of the Tetanus vaccine and only 33.9% had knowledge of the of the HPV vaccine. Majority of participants attributed barriers to the travel distance to receive it (22.4%) and cost (17.8%). 71.8% stated that their doctors kept record of vaccines and 94.3% stated that records were kept on paper. Additionally, 92.0% of the participants received at least one vaccine and 97.7% had an openness to receiving vaccines.

**Conclusion:** Participants were least familiar with the HPV vaccine, thus there needs to be awareness. It is important to address barriers that patients face and to ensure that patients have regular physician visits to receive vaccines. In the future, it may be interesting to investigate which vaccines patients received. Additionally, as the Jerusalem Clinic awaits approval from the Haitian Ministry of Health, there is potential for it to become a vaccination center and also adopt an electronic medical records system.

## Empowering Adolescents to Take Control of their Health

**Primary Author:** Terry Gallagher, DNP, APN

**Introduction:** Adolescents aged 13-19 who were residents of the same low-income housing development in Chicago were recruited to participate in a program titled 'Teen Advisory Panel' to help identify the health needs facing their community and to design the curriculum used in a program to improve their decision-making regarding their health.

**Objective:** To present the implementation and evaluation of a pilot program to empower low-income adolescents to take control of their health.

**Methods:** This population was chosen because it was determined that adolescents in this community lacked the protective risk factors identified by the CDC for adolescent health, i.e. positive parenting practices, school connectedness and open communication with parents and were at risk for STIs, teen pregnancy, and substance abuse. The 6 session program was created based on best practices for adolescent engagement, along with results from a community assessment. Outcome measures included: attendance records, creation of decision-making modules, and participation of peer leaders in creating their own presentations for their peers on health.

**Results:** 39 adolescents were recruited and each attended at least one session, with an average session attendance of 17. Six learning modules were created using the input of the adolescents to address health concerns they identified regarding substance abuse and sexual health, amongst others. The modules and curriculum used were decided upon by majority vote of the teens in attendance. These modules and peer led sessions will be used to create a year-round 'Adolescent Empowerment Program (AEP),' with an adolescent advisory board to provide ongoing input.

**Conclusion:** The program's success relied upon establishing a trusting relationship between the nurses who implemented the program and the adolescents. The newly created AEP has been implemented in with teens in the community, with measures of effectiveness being studied to include health services utilization and long-term health outcomes of STI incidence rates and pregnancy rates.

**Significance:** Most programming in the United States focused on adolescent health occurs in and around school communities. Not all adolescents spend 8 hours per day in school, and schools are not always the center of the adolescents' community. Taking health interventions into communities where adolescents live removes barriers of school attendance and also focuses on a smaller, more homogenous group, rather than trying to adapt a program to multicultural groups that may also have language barriers or cultural concerns.

## **The Tour for Diversity in Medicine: Mentoring Diverse Students in their Backyard and Discussing Their Opinions on the Path to Health Professions**

**Primary Author:** Robert Trevino, MS, PhD

**Contributors:** Brandi K. Freeman, MS, MD (University of Colorado), Kameron Matthews, MD, JD (US Department of Veteran Affairs), Alden M. Landry, MD, MPH (Harvard Medical School)

**Introduction:** Studies suggest the 'leaky pipeline' plays an important role in the shrinking pool of diverse applicants for health professional school. Negative experiences in classes/ advising & knowledge gaps about applying are two factors. A study from AAMC elucidated that increased exposure to mentorship would help minority students become more successful applicants to medical school. To strengthen the pipeline for diverse learners, we need to rethink traditional strategies for providing outreach & support as current measures haven't met the growing needs.

**Objective:** The Tour for Diversity in Medicine (T4D) was established in 2012 as a grassroots effort to mediate pipeline leakiness. The mission is to educate, inspire, & cultivate future health professionals of diverse racial and ethnic background by forming local connections in order to fulfill a national need. To foster the educational pipeline, T4D uses the experiences of current minority health professionals & graduate students as well as a unique curriculum targeting students on their own campuses.

**Methods:** T4D sites are selected by the following criteria: public, serve predominantly minority populations, serve students in rural areas, serve lower socioeconomic background communities, or focus on unique populations (ie community college or high school). T4D & the partner school/ pre-health advisors facilitate logistics as tours occur on individual campuses. Students are recruited through academic advising offices & social media. The needs of the learners dictate programming; webinars & blogs allow continued exposure to T4D.

**Results:** T4D has visited 40 campuses in 28 states over 9 tours. Undergraduate institutions visited by T4D possess more students receiving Pell grants vs national average, lower incoming SAT/ ACT scores vs national average, & low four/ six year graduation rates for minorities. In total, over 3,000 students have participated in T4D tours; over 80% identify as coming from backgrounds underrepresented in medicine. Currently 39 mentors participate, including graduate students (6), medical residents (15), & early career health professionals (18, representing medicine, dentistry, podiatry, research, & health career advising); all self-identify as underrepresented. In focus groups, T4D participants articulated perceived challenges to entering health professions, including financial, personal, academic, & motivational [Freeman, et al. Academic Medicine, 2016]. Learners often searched for academic support & mentorship yet struggled to find health professionals willing to support their goals. Other focus groups addressed students' perceived solutions to previously published challenges. A majority of students also completed surveys about their experiences in college; results are in process. Lastly, daily evaluations were completed that strengthen the workshops for the next site.

**Conclusion:** T4D has reached thousands of students by visiting their home universities. T4D mixes academic advising, storytelling, hands-on experiences, & tiered mentorship. Mentors empower students

to continue their journeys to health professions through embracing the common experiences with students by sharing stories about successes & hardships in their path. Programming fills knowledge & mentorship gaps for individuals at different levels. Other lessons from the road include the importance of parental engagement, understanding stressors students face outside of academic pressures, & the need for academia to identify ways to collaborate with novel programs to support the success of diverse students.

**Significance:** T4D utilizes a tiered mentoring model to address the leaky pipeline. Mentorship functions as a chain where experiences of those advancing are shared with those rising to highlight challenges and offer solutions. Programming is designed to fill the knowledge and mentorship gaps for the needs of individuals at different levels. T4D aims to increase the number of health professionals remaining in the pipeline, especially in target populations at-risk for falling out. As an outlook to the future, increasing the diversity of the health care professional population can positively impact the access and quality of care for underserved medical populations.

## **Worksite access to primary care services: Health-seeking behaviors and health outcomes among low-income foodservice workers.**

**Primary Author:** Angela Moss, PhD, MSN, APN-BC, RN

**Contributors:** Lou Fogg, PhD (RU CON); Arlene Miller, PhD, RN, FAAN, (RU CON)

**Introduction:** Low-income workers with chronic/complex medical conditions require regular health check-ups, but due to work schedules and lack of financial resources, many cannot regularly access healthcare. Although access to healthcare improves health and quality of life, little is known about health-seeking behaviors and health outcomes in low-income adults with worksite access to healthcare.

**Objective:** The purpose of this study is to determine the impact of worksite access to primary care services on: health-seeking behaviors (healthcare utilization and satisfaction), health outcomes (health-related quality of life), and work outcomes (intent to continue working) among low-income foodservice workers.

**Methods:** A cross-sectional comparative design was used. The setting included two facilities of an international foodservice company: one with and one without a health center onsite. Inclusion criterion included: (1) employment at one of the two facilities; (2) holding a non-management position (line workers, drivers, maintenance, chefs); and (3) fluent in English, Spanish or Chinese Mandarin. Measures included: CAHPS patient satisfaction (15-items); healthcare utilization (5-items); The Duke Health Profile (17-items), PROMIS Social Activity (8-items), Reilly Work Productivity (6-items), and Finnish Workplace Ability Index (7-items). 500 questionnaires were distributed over ten days in the employee cafeterias.

**Results:** 218 (57% male, 43% female) surveys were completed. Mean age was 42.7, mean income was 30-\$40K. The majority (93%) were ethnic/racial minorities, 59.8% were immigrants. Drivers, maintenance and chef workers with worksite access utilized primary care providers more and urgent care less ( $p=0.028$ ), and reported higher quality of life than those without worksite access ( $p=0.008$ ), controlling for ethnicity. Line workers reported lower income and lower healthcare utilization across both sites.

**Conclusion:** Worksite access to healthcare may have a positive impact on utilization of more costly urgent care services. Worksite access may be only part of the equation for improving health outcomes in low-income minority workers.

**Poster #: 95**

Withdrawn by Author.



## Utility of Modern Arthroscopic Simulator Training Models: An Updated Systematic Review

**Primary Author:** Kevin Wang, BS

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**Introduction:** Previous literature suggests that arthroscopic simulation training improves simulator performance without a clear benefit on clinical performance. In the past decade, there has been a substantial increase in the number of arthroscopic simulator models.

**Objective:** The purpose of this study was to determine the utility of modern arthroscopic simulators in transferring skills learned on the model to the operating room.

**Methods:** A systematic review of all English-language studies relevant to validated arthroscopy simulation models using PRISMA guidelines from 1999 to 2016 was performed. Three independent reviewers analyzed all studies deemed appropriate for inclusion. A meta-analysis was conducted using a random-effects model to evaluate the effects of simulator training on simulator performance as measured by task completion time and clinical performance as measured by ASSET score on live or cadaveric arthroscopy.

**Results:** Of an initial 230 studies, 46 were included. A total of 1295 participants at various levels of training were evaluated. Twenty-four studies (52%) incorporated a simulator training program. Final performance was evaluated on simulators in 36 studies (78%), sawbone models in 9 (20%), cadavers in 7 (15%), and live intraoperative performance in 4 (9%). Twenty-one studies (46%) evaluated simulator performance with experience level, with 20 of these 21 (95%) demonstrating a positive correlation. Twenty-four studies (52.2%) compared performance before and after simulator training, with 23 (96%) of these demonstrating improvements after training. Meta-analysis of 4 studies (115 subjects) demonstrated an effect size (Cohen's d) of 1.62 (CI: 1.08-2.16) of simulator training on simulator completion time, and analysis of 3 studies (84 subjects) demonstrated an effect size of 0.364 (CI: -0.116-0.843) of training on ASSET score.

**Conclusion:** This review and meta-analysis suggest that training on arthroscopic simulators improves simulator performance without clear, direct translatability to clinical performance. Further work is needed to determine what kinds of simulation models provide translatability to clinical skills.

**Significance:** With the limitation on resident hours, there has been an increased interest in simulation models. One of the hopes of simulation models is that training on these models will provide translatable skills that are immediately applicable in the clinical environment. Our systematic review and meta-analysis shows that in the literature available to date, the skills gained from arthroscopic simulator training do not translate to immediate clinical gains.

## Design and implementation of a wellness curriculum for internal medicine residents

**Primary Author:** Sarah Rimar, MD

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**Introduction:** The burnout rate among medical residents has reached an all-time high. This poses dire consequences to patient care, safety, and the health care system as a whole. The American College of Graduate Medical Education has become increasingly aware of this problem, but research on the efficacy of existing interventions is limited. The internal medicine program at Rush University Medical Center has lost multiple residents to suicide within the last decade. These events have ignited a mission within the residency program to incorporate wellness into the curriculum. July 2016 marked the beginning of an intern wellness pilot program.

**Objective:** The objective of this program was to develop a community where interns feel engaged and empowered while exploring tools designed to build resiliency skills.

**Methods:** Eleven interns self-selected to participate in the yearlong curriculum composed of monthly small group sessions. Once the group began, no additional interns were allowed to join. To ensure a safe environment, the group members were asked to keep information shared by any group member in confidence at all times. Each session was one-hour in length and occurred during lunch on days when noon conference was cancelled, which guaranteed that attendees did not miss any educational material. Senior residents were asked to hold the intern pagers during these sessions to allow for uninterrupted participation. A chief resident and an internal medicine attending, both trained by the Center for Mind Body Medicine, led each session.

**Results:** At the end of each session, participants were given a brief anonymous survey. All data from these surveys have been compiled and averaged to date. The first question asked whether the session helped them gain new insights into residency experiences thus far; 89 percent responded yes. The second question asked whether the session helped them recognize and address personal or psychological issues affecting professional performance; 95 percent responded yes. Lastly, they were asked to rate each session as outstanding, good, fair, or poor. 75 percent found the sessions to be outstanding, and the rest rated as good.

**Conclusion:** Although a small sample size, our results suggest that our interns have benefit from small-group wellness-focused initiatives. Despite the overall positive evaluations thus far, the implementation of the intern wellness program has met challenges. First, scheduling issues and patient emergencies prohibited interns from attending some sessions. Even when interns were present, they were often carrying pagers and dealing with work-related matters during the sessions. Interns were reluctant to ask their seniors to cover their pagers, in part due to concern that some seniors did not understand the purpose of the wellness sessions. These are a few of the many barriers to designing a wellness curriculum at the graduate medical education level. Review of the literature suggests that these interventions may meet fewer challenges at a medical school level.

## A student led quality improvement curriculum and experience in the Pediatric Clerkship

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**Introduction:** The Association of American Medical Colleges (AAMC) has stated that high-quality education and high-quality patient care is delivered when medical students are incorporated into the culture of safety. The third year core clerkships are one of the first opportunities for students to participate in Quality Improvement (QI).

**Objective:** 1) Introduce pediatric third year medical students to quality improvement curriculum and training 2) Provide students the opportunity to design and implement a longitudinal QI project on inpatient pediatric unit

**Methods:** At the start of the third year in the early summer of 2016, medical students volunteered to receive online and in-person QI training based on the Plan-Do-Study-Act template. This curriculum was adapted from the Internal Medicine Clerkship. These students, (QI 'Champions') chose to focus on improving pediatric patients' understanding of the roles of different members on the inpatient health care team. These students then led and engaged their peers to participate in the PDSA cycles during the clerkship.

**Results:** We were able to develop a student-lead QI curriculum; each sextet of students has continued in the PDSA Cycle. In the first sextets, students identified the lack of understanding of health care provider roles. Subsequent groups then planned an intervention of educational slides to explain roles and developed a pre and post survey. Students are currently in the process of collecting surveys, with results expected in the next month.

**Conclusion:** With the help of faculty leaders and QI champions, student-led QI projects allow third-year medical students to gain clinically relevant exposure to patient safety and become familiarized with the PDSA process.

**Significance:** Integrating quality improvement education into clerkship curriculum is a valuable way to expose third-year medical students to the QI process while contributing to overall patient safety. The minimal time commitment required by faculty and students, and online curriculum, allow for its widespread implementation.

## A 50 Year Meta-analysis of Anatomy Laboratory Pedagogies

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**Introduction:** The debate regarding anatomy laboratory teaching approaches is ongoing and controversial. To date, the literature has yielded only speculative conclusions due to general methodological weaknesses and a lack of summative empirical evidence. As such, the question remains, 'What impact, if any, does dissection have on learning anatomy within formal, informal, and hidden curricula?'

**Objective:** This study compared the effectiveness of instructional laboratory approaches used in anatomy education to objectively and more conclusively synthesize the existing literature.

**Methods:** Studies published between January 1965 and December 2015 were searched through five databases. Titles and abstracts of the retrieved records were screened using eligibility criteria to determine their appropriateness for study inclusion. Only numerical data were extracted for analysis. A summary effect size was estimated to determine the effects of laboratory pedagogies on learner performance and perceptions data were compiled to provide additional context.

**Results:** Of the 3,035 records screened, 327 underwent full-text review. Twenty-seven studies, comprising a total of 7,731 participants, were included in the analysis. The meta-analysis detected no effect (standardized mean difference = -0.03; 95% CI=-0.16-0.10; p=0.62) on learner performance. Across studies, student performance on knowledge examinations was equivalent regardless of being exposed to either dissection or another laboratory instructional strategy. This was true of every comparison investigated (i.e., dissection vs. prosection, dissection vs. digital media, dissection vs. models/modeling, and dissection vs. hybrid).

**Conclusion:** In the context of knowledge gains alone, dissection is no better and no worse than alternative instructional modalities. It remains unclear what role dissection plays in the long-term retention of anatomical knowledge and whether ancillary skills essential to clinical practice can emerge as a consequence of anatomy teaching, in general, or whether they are best imparted through active dissection.

## **Sim one, do one, teach one - senior resident-led pediatric intern procedural skill training**

**Primary Author:** Svetlana Melamed, MD

**Contributors:** Louis Fogg, PhD (Department of Research, College of Nursing) Beverley Robin, MD (Department of Pediatrics, Rush Medical College)

**Introduction:** The Accreditation Council for Graduate Medical Education requires graduating pediatric resident competence in common pediatric procedures,<sup>1</sup> but graduating residents lack these skills.<sup>2</sup> Senior residents teach procedural skills to junior trainees. Simulation-based procedural training (SBPT) allows repetitive practice and has been shown to improve resident procedural skills.<sup>3,4,5</sup>

**Objective:** To assess whether senior pediatric resident-led SBPT for pediatric interns improves 1) intern procedural skill, confidence and knowledge and 2) senior resident procedural and teaching confidence.

**Methods:** A needs assessment of pediatric residents and faculty at Rush University Children's Hospital found gaps in pediatric residents' procedural skills. A SBPT curriculum (lumbar puncture [LP], intravenous [IV], cardiac defibrillation [CD]) was developed and delivered to senior residents. Interns then received four, 2-hour, senior resident-led SBPT sessions over 2 months. Interns' procedural skill performance was video-recorded and assessed by trained, blinded raters. Interns' pre- and post- training skills, confidence and knowledge were compared. Seniors residents' procedural knowledge and confidence performing and teaching the procedures was measured pre- and post-training.

**Results:** Twenty-five senior residents underwent SBPT. Confidence performing LP and CD improved significantly ( $p=0.001$ ;  $p=0.002$  respectively). Confidence teaching procedures improved significantly ( $p=0.03$ ;  $p=0.012$ ; 0.00 for IV, LP and CD respectively). Nine interns completed SBPT. Interns' IV placement, confidence performing LP, and procedural knowledge improved significantly ( $p=0.008$ ;  $p=0.027$ ;  $p=0.001$  respectively). Interns significantly outperformed 2nd year residents (non-SBPT) in IV and CD skills ( $p=0.008$ ;  $p=0.017$  respectively) and procedural knowledge ( $p=0.03$ ), even though 2nd year residents had performed significantly more pediatric IVs and LPs on actual patients ( $p=0.023$ ;  $p=0.00$  respectively).

**Conclusion:** Senior pediatric resident-led SBPT significantly improved pediatric interns' procedural skills, procedural knowledge and confidence, and enhanced senior residents' confidence performing and teaching pediatric procedures. SBPT interns outperformed 2nd year residents despite 2nd year residents having more experience on actual pediatric patients.

**Significance:** This study addresses an important gap in the procedural skills training for pediatric residents. It demonstrates the efficacy of a procedural skills curriculum for pediatric interns that uses few, readily available resources and can easily be replicated.

## Gut barrier structure and HIV infection

**Primary Author:** Marc Hersh, BS

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**Introduction:** A rapidly evolving literature suggests that disruption of the normal microbial environment of several organ systems influences HIV transmission, disease progression and the potential for a vaccine or cure. HIV-infected individuals with incomplete CD4 T-cell recovery upon combination antiretroviral therapy (cART) (aka non-responders (CD4<350cells/ $\mu$ l)) display high levels of immune activation and microbial translocation. However, whether a link exists between gut damage and poor immunological reconstitution remains unknown.

**Objective:** The goal of our proposed study was to improve understanding of the mechanisms of persistently elevated microbial translocation, immune activation and inflammation in cART-treated HIV infected patients who respond well to treatment compared to non-responding patients.

**Methods:** We conducted a cross-sectional study of the gastrointestinal tract in 26 cART-treated HIV infected individuals: 13 immunological non-responders (CD4. <350 cells/ $\mu$ l), 13 full responders (CD4. >500 cells/ $\mu$ l) along with 10 healthy non-HIV infected controls. We assessed gut structure by quantifying junctional complex proteins (Occludin) in right colon by means of immunohistochemistry and further assessed gut function by analyzing microbial translocation and inflammatory parameters (LBP, sCD163, IL-6, sCD14) in patient serum samples by ELISA.

**Results:** We found no significant differences between levels of inflammatory markers between HIV responders, non-responders, and healthy controls. When HIV patients were grouped together, regardless of CD4 status, there was a statistically significant difference between markers of Lipopolysaccharide Binding Protein (LBP) in healthy controls when compared to HIV patients. There was also a non-statistically significant difference, but trending inverse association between levels of Occludin and sCD14.

**Conclusion:** We did not find any statistically significant data supporting that HIV immune non-responders and responders were different based on tight junction staining and inflammatory markers. A future goal of this study is to evaluate presence of endotoxin core antibodies, which bind to and neutralize Lipopolysaccharide (LPS). LPS is increased in HIV patients and is a marker of microbial translocation. Increased presence of LPS could compensate for other immune mediators making it an important future target of our research.

**Significance:** Despite effective viral suppression with combined antiretroviral therapy, individuals with HIV continue to have excess non-AIDS morbidity and mortality, which appears to be driven in part by microbial translocation and the resultant immune activation. By understanding the characteristics of immune non-responders, further studies could develop novel therapies to decrease morbidity and mortality of cART-treated HIV infected patients.

## Social Jet Lag and Risk Factor for Aggressive Disease in IBD

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**Introduction:** Social jet lag (SJL), a measure of chronic circadian disruption, is an habitual discrepancy between an individual's endogenous circadian rhythm and actual sleep times. SJL typically occurs on weekends due to social obligations, and can cause chronic sleep loss and circadian disruption. Recent research has shown that social jetlag is associated with elevated levels of C-reactive protein (CRP), an indicator of inflammation. Inconsistent sleep patterns, which can disrupt the activity of the circadian clock and induce pro-inflammatory responses, are common in persons with Crohn's disease (CD) and ulcerative colitis (UC), two distinct phenotypes of inflammatory bowel disease (IBD).

**Objective:** The purpose of this study was to investigate the association between SJL and indicators of IBD severity (age of diagnosis, history of bowel surgery, use of steroids, use of biologic medications, and perirectal Crohn's disease).

**Methods:** A cross-sectional study design was used. Eighty-three subjects with biopsy-proven CD and 40 UC subjects were recruited from a gastroenterology clinic serving over 300 patients. Subjects completed the 10 item Munich Chronotype Questionnaire (MCTQ), a measure of SJL, which covered week-day and week-end bedtime, length of time to fall asleep, time of awakening, and use of alarm clock. SJL was defined as a difference of > 2 hours between the midpoint for sleep on week-days and week-ends. Indicators of IBD were obtained from chart reviews and scored as present or absent. Chi square analysis was performed to determine differences in indicators of disease severity between persons with and without SJL.

**Results:** Data on SJL were available for 78 of the 123 subjects. Of these 78 subjects, 21% had SJL. While subjects with SJL were significantly younger at age of diagnosis, no significant differences were found for any other indicators of IBD severity.

**Conclusion:** SJL was related to early age of IBD diagnosis, which is a known risk factor for a more aggressive disease course. Since SJL is a modifiable factor, additional studies are warranted to test interventions that attempt to synchronize sleep patterns with the circadian clock in persons with IBD.

## Swallowing function and Masako maneuver in Parkinson's disease

**Primary Author:** Chelsea Visk, BS

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**Introduction:** Parkinson's disease (PD) is a neurodegenerative disease which affects swallowing function. The incidence and prevalence of dysphagia in PD are high, and aspiration pneumonia is one of the leading causes of death in PD. Also, dysphagia in patients with PD negatively impacts the quality of life leading to isolation and depression. Currently, there is little research supporting dysphagia treatment specific to the PD population; therefore, there is a need for controlled research studies to inform evidence based practices.

**Objective:** In the proposed study, it is hypothesized that high frequency, high intensity dysphagia treatment involving the Masako tongue-hold maneuver will improve swallowing for patients with idiopathic Parkinson's disease and oropharyngeal dysphagia. Improved swallow function will be demonstrated by increased duration of tongue base and posterior pharyngeal wall contact, decreased pharyngeal transit time, and reduced post-swallow pharyngeal residue.

**Methods:** The study will include 3-5 subjects between the ages of 50 and 85 who are diagnosed with idiopathic Parkinson's disease and complain of swallow difficulty. Prior to treatment, the patient will undergo a series of objective and subjective measures of swallow function and quality of life. The proposed treatment phase involves 4 weeks of treatment which includes two sessions per week. The patient will be instructed to complete 120 tongue hold or Masako maneuvers per day. Following the four weeks of treatment, the clinical and videofluoroscopic swallowing evaluations will be repeated following the same protocol used and outcome measures obtained during the pre-treatment evaluation. Outcome measures will be analyzed using descriptive analysis. The means and standard deviations for subjects will be calculated for pre- and post-treatment to determine the effect of the treatment utilizing the Masako maneuver on swallowing. This study has been approved by the Institutional Review Board (IRB) at Rush University.

**Results:** Results to be determined. Preliminary results include improved swallow function as confirmed by objective and subjective measures.

**Conclusion:** Conclusions not yet defined.

**Significance:** Parkinson's patients don't live very long.



## An Anatomic Anomaly of the Aortic Arch

**Primary Author:** James M. Williams, PhD

**Contributors:** Gagan Grewal(RMC), Mohammad R Jaffery(RMC), Joseph F Kramkowski(RMC), and Mollie Lesser(RMC)

**Introduction:** In typical anatomy, the branches of the aortic arch from proximal to distal are the brachiocephalic trunk, left common carotid artery, and left subclavian artery. Previous studies have shown anomalies of aortic anatomy as a marker of thoracic aortic disease (Moorehead P.A. et al, 2016). However, the prevalence of aortic anomalies has been shown to vary from 0.2 - 35.6% (Paraskevas G. et al 2008 & Ahn S.S. et al, 2014). The large variability is likely due to unclear classification criteria for anomalies of aortic anatomy.

**Objective:** We describe an anomaly of aortic anatomy unexpectedly found during the dissection of a 79-year-old female cadaver

**Methods:** The dissection of a formalin-fixed cadaver was performed in the Rush Medical College (RMC) Anatomy Lab as part of the RMC first-year medical student anatomy program. The cadaver was African-American and died from coronary heart disease. The aortic anomaly was found during dissection of the superior mediastinum after the anterior thoracic wall was resected.

**Results:** An abnormal aortic branching pattern was found in 1 out of 34 cadavers in the RMC Anatomy Lab. Only the brachiocephalic trunk and left subclavian artery originated directly from the aortic arch. The left common carotid artery was found to originate from the brachiocephalic trunk. The bifurcation of the common trunk into the brachiocephalic trunk and left common carotid artery occurred approximately 1-2 cm from the aortic arch.

**Conclusion:** We present a unique configuration of the aortic arch where the left common carotid artery branches from the brachiocephalic trunk. Understanding the types of aortic branching abnormalities is crucial for surgeons performing procedures involving the great vessels of the heart.

**Significance:** The configuration of the aortic arch anomaly we have described can be used as a reference for surgeons and further classification of anomalies.

## Measuring Post-Bariatric Surgery Adherence

**Primary Author:** Megan Hood, PhD

**Contributors:** Mackenzie Kelly PhD (Rush), Emily Feig MS (Rush), Victoria Webb MS (Rush), Lauren Bradley PhD (Rush), Joyce Corsica PhD (Rush)

**Introduction:** In order to maximize long-term weight loss after bariatric surgery, patients are instructed to follow specific diet, exercise, and vitamin use behaviors, in addition to attending regular follow up appointments. Adherence to these post-surgery behaviors has been associated with more positive post-surgery outcomes, though measurement of adherence varies significantly across studies, limiting the ability to generalize results.

**Objective:** To 1) conduct a comprehensive literature review of measures of assessing post-bariatric surgery behavioral adherence and 2) to develop a self-report measure for use in assessing adherence in this population.

**Methods:** First, a comprehensive literature review was conducted to order to thoroughly assess measures of adherence that have been used in this population previously. Second, a multi-step process was conducted to design and develop a self-report measure of behavioral adherence after bariatric surgery. This process included 1) an evaluation of clinical standards for post-surgery behavioral recommendations and review of recommendation materials in a subset of bariatric surgery programs to identify item content, 2) multiple iterations of measure formatting and development based on expert feedback, and 3) piloting of the proposed measure.

**Results:** The comprehensive review indicated significant variation in assessment of adherence to post-surgery behavioral recommendations. Following the multi-step measure development phase, a two-part adherence measure was created. Part 1 was designed to assess 1) knowledge of behavioral recommendations and 2) adherence behaviors. Part 2 assess barriers to adherence. Both measure components indicated initial acceptability with the pilot sample.

**Conclusion:** Accurately assessing post-surgery behavioral adherence is necessary to improve understanding and intervention in patients following bariatric surgery. The development of a self-report measure to address this need will fill an important gap and may improve patient outcomes and quality of life.

**Significance:** Better understanding adherence, and the factors that impact adherence, is vital to the provision of appropriate health care, as non-adherence is highly prevalent and leads to major gaps between clinical efficacy and effectiveness in practice. In bariatric surgery, behavioral adherence after surgery in areas such as diet, exercise, vitamin use, and appointment attendance, is considered a key factor in patient long-term success. Despite the importance of this issue, measurement of adherence is inconsistent, suggesting the need for a well-validated measure to aid in provider assessment and in improving patient-provider communication about this important issue.

## **Innovative Behavioral Interventions for Weight Regain after Bariatric Surgery**

**Primary Author:** Lauren Bradley, PhD

**Contributors:** Evan M. Forman (Drexel University), Stephanie G. Kerrigan (Drexel University), Stephanie P. Goldstein (Drexel University), Meghan L. Butryn (Drexel University), J. Graham Thomas (Brown University), James D. Herbert (Drexel University), David B. Sarwer (Temple University)

**Introduction:** Bariatric surgery is the most effective treatment for obesity, however weight regain is common and compromises the significant health benefits initially obtained. Weight regain is largely attributed to behavioral factors, particularly suboptimal adherence to the restrictive postoperative diet. Factors that make it challenging to adhere to dietary recommendations include the return of hunger, food cravings, and interest in food following the initial postoperative weight loss phase. Acceptance-based behavioral interventions appear to be particularly well-suited to this population, as they teach patients willingness to have these difficult internal experiences, while at the same time engaging in valued behavior (e.g., living a healthy life).

**Objective:** To develop and evaluate an acceptance-based behavioral intervention targeting weight regain after bariatric surgery in both a group-based and remotely-delivered format.

**Methods:** We developed a 10-week program that provided acceptance-based skills to facilitate engagement in weight-control behaviors for post-bariatric surgery patients who demonstrated weight regain. Such skills included distress tolerance, willingness to engage in behaviors despite discomfort or decrease pleasure, clarity of personal values, and linking values to in-the-moment decision-making. We conducted two open trials, evaluating the program both in an in-person group format ( $n = 8$ ) and remotely via online modules and phone coach calls ( $n = 11$ ).

**Results:** Results indicated that this approach was acceptable to patients, with high mean rating of program satisfaction for both the in-person (4.3/5.0) and remote-based (4.7/5.0) versions of the program. Most importantly, this treatment was shown to be effective for stopping and reversing weight regain using both the group format ( $3.6 \pm 3.0\%$  weight loss) and the online delivery ( $5.1 \pm 5.5\%$ ) from pre- to post-treatment. In addition, significant changes in both eating-related and acceptance-based variables were observed.

**Conclusion:** Overall, these pilot data provide initial support for the feasibility, acceptability, and preliminary effectiveness of acceptance-based interventions for individuals who have undergone bariatric surgery.

## Improvement of Malnutrition Documentation after Implementation of a Best Practice Alert

**Primary Author:** Sarah Peterson, PhD, RD

**Contributors:** Diane Sowa MBA, RD (Rush), Leslie Klemp MS, RN, NE-BC (Rush), Brian Stein MD (Rush)

**Introduction:** Initial examination of malnutrition documentation of hospitalized patients at our tertiary medical center in 2013 demonstrated only 9% of adult patients identified as malnourished by a registered dietitian (RD) received a code at discharge related to malnutrition. As a result, a best practice alert (BPA) was created to alert providers via the electronic medical record (EMR) whenever a patient was identified as malnourished.

**Objective:** The purpose of this quality improvement project was to describe improvements in documentation after the creation of a malnutrition BPA.

**Methods:** Upon documentation of the degree of malnutrition in the RD flowsheet, a BPA fired for any provider (MD, NP, PA, etc.) opening the EMR; the BPA continued to fire until malnutrition was added to the problem list or dismissed (due to disagreement with the RD assessment, provider not on primary team). Providers were prompted to select the appropriate degree of malnutrition, add it to the problem list, and document malnutrition at least once in the medical record. The total number of BPA fires from the creation of this alert (April 2016) through June 2016 were collected.

**Results:** A total of 693 patients (8% of all admissions) were identified as malnourished; of these, 588 patients (85%) received an ICD-10 code specifically relating to malnutrition. Only 15% patients received codes that did not match the RD assessment of malnutrition. Both reimbursement and average DRW weight appear to have increased approximately 30% among patients coded for malnutrition compared to those without malnutrition

**Conclusion:** The creation of a malnutrition specific BPA successfully improved documentation of malnutrition among providers. However, evidence of discordance among RD classification of malnutrition and assignment of ICD-10 codes after discharge identifies a need for further education among providers and documentation specialists.

## Infant Feeding Practices in the First Six Months of Life and Subsequent Growth Performance

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**Introduction:** Infant growth is measured with CDC or WHO standards, as a static or change (longitudinal) outcome. There is a need to define optimal growth in relation to feeding practices (FP), especially in diverse samples.

**Objective:** To determine the association between infant FP (breastfeeding, formula or both) and indicators of growth (i.e. weight-for-length z-scores/percentiles) in infants aged 6 months or less using the modified Infant Feeding Practices Study II questionnaire (mIFPSq II).

**Methods:** The validated mIFPSq II was administered to caretakers of infants who gave informed consent (ORA # 13042901). We examined demographic correlates of infant FP in relation to WHO growth indicators using SPSS, version 22 (IBM, Chicago, IL).

**Results:** Caretaker's race-ethnicity was 26% non-Hispanic white, 25% Hispanic, and 34% non-Hispanic black. Nearly 50% had a college degree or higher with 23% with high school education or less. Of the 194 dyads, 51% were enrolled in WIC. More than half of the infants <4 months of age (n=98) consumed breast milk or mixed feedings, while 57% of older infants (≥6 months (n=46)) were formula fed ( $\chi^2$ ,  $p=0.003$ ). For infants with growth data through 6 months of age (n=130), nearly 17% were overweight/obese; one infant was underweight. FP were associated with 1) infant sex; a higher proportion of male infants were breastfed (70.7%) compared to female infants (29.3%,  $p=0.024$ ); 2) caretaker race ( $p=0.007$ ); 3) caretaker education ( $p=0.003$ ), and WIC enrollment ( $p<0.001$ ). Nearly 70% of infants demonstrated rapid weight gain by 6 months (≥0.67 change in weight-for-length z-scores), though no difference among FP was observed.

**Conclusion:** While weight status and weight gain were not different across FP, age and sex of infants, WIC, caretaker race and education were associated with FP.

**Significance:** While there were no observed relationships between weight status/gain and feeding practice, more growth data are needed to adequately characterize correlates of infant growth performance in this diverse sample. Accrual of caretaker/infant dyads are ongoing.

## **Association Between Temporal Distribution of Carbohydrate and Calorie Intake and Hemoglobin A1c (A1c) in Persons with Type 2 Diabetes Mellitus**

**Primary Author:** Jane Petr, BS

**Contributors:** Karen Chapman Novakofski PhD, RD, University of Illinois at Urbana-Champaign; Heather Rasmussen PhD, RD, Rush University; Kathryn Keim, PhD, RD, Rush University

**Introduction:** The American Diabetes Association has no recommendation for distributing carbohydrate and calories throughout the day to optimize glycemic control in people with type 2 diabetes (T2DM). Past research suggests that timing of calorie and carbohydrate consumption may influence postprandial blood glucose and deserve attention.

**Objective:** To examine the temporal distribution of carbohydrate and calories over 24 hours in individuals with T2DM and determine association with hemoglobin A1C (A1C).

**Methods:** Three or four 24-hour dietary recalls were collected from subjects with T2DM. Temporal macronutrient distribution was operationalized by dividing 24 hours into four 6-hour time periods. T1 was breakfast, T2 was lunch, T3 was dinner and T4 was night eating. Association between percent of calories and carbohydrate in each time period and A1C was determined using Spearman's Rho correlations with significance at  $p < 0.05$ .

**Results:** Ninety-eight subjects (72% female) with median A1C of 6.9% (IQR 6.2, 7.8), and age 56 years old (IQR 48, 63) were included in analysis. Median percent of daily calories in T1, T2, T3, and T4 were 18.2%, 33.1%, 36.9%, and 0%, respectively. Median percent of daily carbohydrate in T1, T2, T3, and T4 were 20.9%, 26.2%, 42.9%, and 0%, respectively. There was no significant association between any time periods and A1C.

**Conclusion:** Hemoglobin A1C was not associated with temporal distribution of calories or carbohydrate in this fairly well-controlled sample of individuals with T2DM. This suggests that for people with A1C below 7.0%, distributing more daily calories or carbohydrates at certain time periods may not influence glycemic control.

## Napping in the Forbidden Zone

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**Introduction:** In the hours right before habitual bedtime people have difficulty falling asleep and/or staying asleep. This is called the forbidden zone for sleep or the wake maintenance zone.

**Objective:** To examine whether sex (men, women) or ancestry (African-Americans, European-Americans) influence the ability to sleep during the forbidden zone.

**Methods:** In IRB-approved studies with informed consent, participants (average age = 29 years, range 18 to 44) lived on a 5-hour ultradian light-dark cycle in a time-free environment; 2-hour naps in the dark alternated with 3-hour wake episodes for 3 days. Sleep was measured using wrist monitors (actigraphy) during 15 naps for 23 African-Americans (11 women, 12 men) and 26 European-Americans (13 women, 13 men). Circadian phase assessments before and after the 3 days of napping were used to determine the dim-light melatonin onsets (DLMOs), which mark the time of the circadian clock. Sleep time per nap was analyzed according to when the nap started relative to each individual's average DLMO.

**Results:** Naps that started in the 6-hour interval before habitual bedtime (4 hours before until 2 hours after the DLMO) had less sleep than naps that started during the 8 hours corresponding to habitual sleep time (2 to 10 hours after the DLMO) (mean  $\pm$  SD =  $1.4 \pm 0.3$  vs  $1.7 \pm 0.2$  hours/nap, t-test,  $p < 0.001$ ). There was no difference between men and women or between African-Americans and European-Americans in the 6-hour forbidden zone. Women slept more than men during naps that started in the 8-hour interval corresponding to habitual sleep time ( $1.8 \pm 0.1$  vs  $1.6 \pm 0.2$  hours/nap, t-test,  $p < 0.05$ ).

**Conclusion:** There was a 6-hour forbidden zone before habitual bedtime, which made it just as difficult to sleep for women, men, African-Americans and European-Americans. Women slept more than men during the 8 hours corresponding to habitual sleep time.

**Significance:** Significance: There was a forbidden zone for sleep right before habitual bedtime, despite the fact that participants did not know what time it was or the length of the naps or wake episodes and had nothing to do while lying in bed during the 2-hour dark episodes. This shows that it is difficult to go to sleep earlier than usual, and helps explain why some people, especially night owls and adolescents, have difficulty falling asleep as early as demanded by our early-bird dominated society. Funded by NIH grant R01 NR007677 to CIE.

## The Relation between Physical Activity and Cognitive Change in Older Latinos

**Primary Author:** Shannon Halloway, PhD, RN

**Contributors:** JoEllen Wilbur, PhD, APN, FAAN (Rush); Michael E. Schoeny, PhD (Rush); Lisa L. Barnes, PhD (Rush)

**Introduction:** Cognitive impairment in older Latinos is a concerning issue due to the rapid growth of this population and their increased risk for dementia due to chronic disease. Evidence, primarily from studies of non-Latino Whites, suggests that physical activity (PA) may reduce cognitive decline. Few longitudinal studies have included older Latinos, objective measures of PA, or neurocognitive tests that assess domains of cognition.

**Objective:** The purpose of this longitudinal study was to explore the relation between changes in PA and cognitive decline in older Latinos over an average of five years.

**Methods:** This study used a longitudinal design to examine PA and cognition in a cohort of older, urban Latinos. Inclusion criteria for the baseline sample were age  $\geq 50$  years, Latino ethnicity, no ambulation disability, no evidence of dementia, and Chicago address. The follow-up assessment was approved by the University IRB. Of the 174 baseline participants, 59 (33.9%) participated at follow-up after signing informed consent and HIPAA forms. PA was measured by questionnaire and accelerometer worn for seven days. A neurocognitive test battery assessed episodic memory, perceptual speed, and semantic memory. Change in cognitive function was dichotomized to represent maintenance versus decline. In binary logistic regressions, change in cognitive function was regressed on change in PA.

**Results:** Those who had less decline from baseline to follow-up in self-reported light PA maintained episodic memory, OR=1.16 (95% CI 1.03-1.32), while those who had less decline in accelerometer moderate-vigorous bouts maintained semantic memory, OR=16.08 (95% CI 1.53-168.89), controlling for baseline age, chronic health problems, depressive symptoms, and acculturation.

**Conclusion:** These findings suggest that maintenance of PA with aging may prevent cognitive decline. Limitations included a high attrition rate and inability to establish temporal precedence between PA and cognition. This work can inform future intervention development that aims to maintain PA in order to prevent cognitive decline

**Significance:** We examined the effects of change in lifestyle PA, as measured by self-report and accelerometers, on change in cognitive function (episodic memory, perceptual speed, and semantic memory) in older, community-dwelling Latinos. Unlike previous PA and cognition studies with older Latinos that relied on self-report measures of PA and brief screening measures of cognitive function, we utilized an objective measure of PA and a battery of neurocognitive tests to examine specific cognitive domains. We found significant effects of PA on episodic memory and semantic memory. Specifically, our results indicated that those who had less decline in self-reported light PA maintained episodic memory, while those who had less decline in accelerometer moderate-vigorous bouts maintained semantic memory. Despite our limitations, our findings suggest the potential importance of maintaining PA to prevent declines in cognitive function in older Latinos.



## **Modified Ketogenic Diet: Impact on Seizure Activity, Anthropometrics, and Gastrointestinal Symptoms in Adults with Epilepsy**

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**Introduction:** The low-carbohydrate, high-fat ketogenic diet (KD) effectively reduces seizure frequency in children with epilepsy; however, research is limited in adults.

**Objective:** Therefore, the objective of this study was to determine the impact of a modified KD (mKD) on seizure activity, anthropometrics, and gastrointestinal symptoms in adults with epilepsy.

**Methods:** Enrolled patients from the RUMC Clinic for Dietary Treatment of Epilepsy followed a mKD of 15-50 g net carbohydrate (CHO)/d for three months. The following were obtained at baseline and three-months: two 24-hour dietary recalls (ASA-24), seizure frequency, anthropometrics, and gastrointestinal symptoms (Gastrointestinal Symptom Rating Scale, ranging 1 [no discomfort] to 7 [very severe discomfort]), and compared using Wilcoxon sign-rank.

**Results:** Participants (n=13) were primarily white (62.9%), female (60.0%), aged 39 (27, 46) (median [IQR]), and had a baseline BMI of 32.4 (27.0, 38.6) kg/m<sup>2</sup>. Ten subjects (76.9%) were compliant based on 75 g net CHO/d. Net CHO intake decreased from 166.8 (66.8, 212.8) to 43.8 (17.8, 73.8) g (p=0.03), and total fat increased by 17.1 g (p=0.011). Seizure frequency (n=9) was reduced on the mKD (3 [1, 13] vs 2 [0, 3.5] seizures/d at baseline and 3-months, respectively; p=0.043). Weight and BMI (n=8) decreased by 6.5 lbs (p=0.021) and 3.1 kg/m<sup>2</sup> (p=0.017), respectively; waist circumference (n=6) decreased by 4.0 inches (p=0.043). Overall baseline gastrointestinal scores (n=5) were low, with a median of 1.2 (1.1, 3.2), and did not change with the diet.

**Conclusion:** In conclusion, participants prescribed a mKD were adherent to the diet and experienced meaningful reductions in seizure frequency and anthropometrics. Thus, a mKD diet may be beneficial in reducing seizure activity and adiposity in adults with epilepsy.

## **Donor Milk feeding not associated with different Neurodevelopmental Outcomes in Very Low Birth Weight infants**

**Primary Author:** Grace Tobin, BA

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**Introduction:** The use of mother's own milk (MOM) reduces neonatal morbidities and improves neurodevelopmental (ND) outcome in very low birth weight (VLBW; birth weight<1500 grams) infants. When MOM is unavailable, donor human milk (DM) can replace preterm formula (PF). This intervention reduces necrotizing enterocolitis (NEC); however, the ND impact is unclear.

**Objective:** Evaluate the relationship between dose of DM in the first 28 days of life (DOL) and ND outcomes at 20 months corrected age (CA, age corrected for prematurity) in a cohort of VLBW infants born after the introduction of DM protocol in the RUMC NICU.

**Methods:** A cohort of 189 VLBW infants born post-DM protocol (2013-2014, diet of MOM or DM) was compared to a historical cohort of 177 VLBW pre-DM (2011-2012, diet of MOM or PF) infants. Daily type and amount of enteral intake (MOM, DM, and PF) through 28 DOL and ND outcomes (assessed via Bayley-III) at 20 months CA were compared. To adjust for other risk factors, multiple regression analyses were performed.

**Results:** No significant differences in BW, gestational age, or percent MOM at 28 DOL were found between groups, but there was increased prevalence of multiples ( $p=.004$ ) and older maternal age ( $p<.001$ ) in the post-DM cohort. Post-DM infants had lower incidence of NEC ( $p=.038$ ), and received less surfactant ( $p<.001$ ) and postnatal steroids ( $p=.005$ ). At 20 months CA no significant differences were found in mean Bayley-III scores between pre-DM and post-DM infants.

**Conclusion:** There were no differences in ND outcome between infants born pre-DM and post-DM despite a reduction in NEC during the latter era. Furthermore, percent of MOM through DOL 28 was not predictive of ND outcome. There was a similar percent of MOM at DOL 28 in the two eras, suggesting that DM was used primarily as a bridge to MOM in the first 14 DOL.

**Significance:** VLBW infants often require complex care and have protracted NICU hospitalizations. When MOM is unavailable, using DM instead of PF reduces incidence of NEC and does not appear to be associated with worse ND outcomes at 20 months CA.

## Impact of Donor Milk on Long Term Growth of Very Low Birth Weight (VLBW) Infants

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**Introduction:** When mother's own milk (MOM) is unavailable, donor milk (DM) has been used to avoid formula (F) but has been associated with decreased in-hospital growth rates compared to F and MOM. Few studies have analyzed long-term growth in DM-fed VLBW infants.

**Objective:** To compare growth outcomes (weight [WT], head circumference [HC], length [L]) of VLBW infants, with and without DM, at birth, neonatal intensive care unit (NICU) discharge, and NICU follow-up clinic visits at 4, 8, and 20 months corrected age (CA) using different in-hospital feeding protocols.

**Methods:** Daily enteral intake (proportions of MOM, DM,F) were collected for 28 days of life (DOL) for a cohort of 349 infants. Infant's WT, L, and HC were converted to z scores using sex-specific Olsen and WHO growth charts. Separate multilevel linear growth models assessing changes in WT, L, and HC in short-term (birth to NICU discharge) and long-term (follow-up clinic visits) were used.

**Results:** Growth z scores decreased during NICU stay and increased after discharge. A higher total HM proportion (MOM+DM), but not DM, was associated with greater in-NICU decreases in z scores for all growth parameters, but there were no effects of either total HM or DM on long-term growth.

**Conclusion:** Infants with higher proportions of total HM in the first 28 DOL had slower growth in the NICU, without additional effect with DM. After discharge, overall growth pattern reversed from decreasing to increasing z scores without variation by proportion of total HM or DM. Controlling for total HM, there were no differences in growth trajectories as a function of DM.

**Significance:** Few studies have addressed long-term growth in DM-fed infants and this study showed there were no differences in growth trajectories as a function of DM. Additional studies are needed to elucidate long-term implications of DM-fed VLBW infants.

## Changes in FGM Concentrations and Behavior in Response to Construction in African Wild Dogs

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**Introduction:** African Wild dogs remain at the top of the list of endangered carnivores for 3 main reasons; persecution by humans, habitat fragmentation, and competition with other carnivores (Rafacz and Santymire, 2014). Environmental enrichment can be achieved by the distribution of specific stimuli, ultimately increasing the welfare of AWDs and thus enabling the survival of their species. Increased welfare may come in the form of reduced stress and normal activity patterns. Corticosterone and cortisol are useful indicators of stress and can be measured non-invasively by analyzing fecal glucocorticoid metabolites.

**Objective:** The purpose of the study was to determine whether or not construction activity affects the concentration of FGMs and overall activity levels in AWDs.

**Methods:** 40-45 fecal samples (post-construction) were analyzed using an ELISA specific for corticosterone on 2 AWDs from the Lincoln Park Zoo. This data was compared to previous data done on pre-construction and during construction samples. Statistical analyses will be done using a Repeated Measures ANOVA and a post-hoc test will be done if the null hypothesis is rejected.

**Results:** Preliminary data suggests that in comparison to the baseline values, the FGM concentrations increased ( $U=698$ ,  $p<0.001$ ) during construction (Mean  $\pm$  SEM;  $225.50 \pm 22.00$  ng/g wet feces) relative to pre-construction ( $143.53 \pm 9.22$  ng/g wet feces). The results also showed an increase in overall activity in all AWDs.

**Conclusion:** The data suggests that AWDs may be sensitive to environmental disturbances such as construction activity. Perhaps, limiting construction activity can help increase the welfare of this species by producing a less stressful environment. Or if construction must occur, then providing a hiding place may also prevent drastic increases in FGM concentrations. Taking all of these considerations into account is necessary in order to enable the survival of this species.

## Effects of targeted social cognition training on behavioral and neural measures of emotion recognition in healthy adults

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**Introduction:** Research has shown an increased interest in targeted cognitive training (TCT) as a technique to deter and possibly stop cognitive deterioration in psychiatric disorders, such as schizophrenia. Although TCT has shown promising improvements in certain cognitive deficits, TCT research has largely ignored social cognition training.

**Objective:** The current study investigates whether targeted social cognition training may be a viable method of improving social cognition in patient populations.

**Methods:** To this end, the social cognition of healthy adults from the community was assessed before and after a two-week period, where participants were randomized to complete either 10 hours of SocialVille, a computerized social cognition training program from PositScience Corporation, or 10 hours of common computer games. SocialVille consists of a variety of social cognition exercises, such as face emotion recognition, gaze tracking, and recognizing social incongruences. Behavioral and neural assessments conducted before and after the intervention included a Face Morph task, which required participant to identify the emotions on faces that had been manipulated to vary in degree of emotional expressivity by blending emotional and neutral expressions, and the Penn Emotion Recognition Task, during which participants were asked to identify the emotion of faces while in a MRI.

**Results:** Results indicate that those who completed social cognition training improved significantly more on these tasks than those who completed placebo computer games in behavioral and neural indices of facial emotion recognition. Specifically, intervention condition predicted more accurate recognition of angry, fearful, and neutral faces for those in the social cognition condition. Neuroimaging results indicate that the neural system supporting emotion recognition showed greater changes for the active training group compared to the placebo group.

**Conclusion:** These findings indicate that social cognition can be improved in healthy adults with varying ability at baseline and that neural systems associated with social cognition show a learning-induced neuroplastic response.

**Significance:** Thus, programs, like SocialVille, may be useful tools for targeted treatment in psychiatric populations where social cognition deficits are prominent, specifically schizophrenia and autism spectrum disorder.

## The Relationship Between Respiratory Sinus Arrhythmia, Affective Decision-making, and Psychopathic Traits in Aggressive Youth

**Primary Author:** Haley Ford, PhD

**Introduction:** Psychopathy is a personality disorder with affective (e.g., callousness), interpersonal (e.g. manipulative), and behavioral (e.g., impulsivity) deficits. Psychopathic youth begin engaging in criminal activity at younger ages than their non-psychopathic counterparts. Finally, physiological differences (e.g., lower resting heart rate) have been found in psychopathic youth, and the deficits across domains affect their decision-making.

**Objective:** The current study examined the relationship between psychopathic traits, respiratory sinus arrhythmia (RSA), and performance on the Iowa Gambling Task (IGT).

**Methods:** 86 participants comprised the final sample in this study approved by the University of Alabama Institutional Review Board. Informed consent and youth assent were obtained from participants. Parents reported on observed behaviors indicative of psychopathic traits, as measured by the Antisocial Process Screening Device (APSD) (i.e., impulsivity/conduct problems, callous-unemotional traits, and narcissism). Children also completed the computerized version of the Iowa Gambling Task, and, during the task, electrodes measured interbeat interval, from which RSA was derived.

**Results:** The narcissism subscale was significantly correlated with baseline RSA,  $r=.23$   $p=.03$ . CU traits, impulsivity, and the total APSD score were not significantly correlated with baseline RSA. Neither the total APSD score nor any of the APSD subscales were significantly correlated with RSA-Reactivity (RSA-R) in any of the blocks. The mean score in each block of the IGT indicated that not only did the participants in this study not perform well, they also did not demonstrate that learning of the task occurred.

**Conclusion:** No significant main effects were found for baseline RSA or psychopathic traits on IGT performance. One possibility is that these youth already have depressed levels of RSA due to being aggressive, which may explain the non-significant results for psychopathy and baseline RSA found in this study. Adaptive narcissism may also explain the observed pattern of performance on the IGT.

**Significance:** This study sought to fill some gaps in the literature. For example, no studies have specifically examined RSA in youth with psychopathic traits. Additionally, the relationship between psychopathic traits in youth, RSA, and performance on the IGT has not been researched. This relationship is important to examine because both psychopathic traits and the psychophysiological differences associated with psychopathy affect decision making as well as responsivity to treatment. Thus, these two variables, as well as their interaction, may be potential moderators to include in future treatment studies. Additionally, the presence of these variables may generate clear implications for intervention. For example, assessing RSA in addition to psychopathic traits and other risk factors may improve the effectiveness of an intervention program because it would be comprehensive in nature while also allowing it to be individually tailored to a given child's specific biopsychosocial makeup.

## Predictors of Arm Recovery for Chronic Stroke Survivors

**Primary Author:** Amanda Vatinno, OTS

**Contributors:** Bethany Woodyatt, OTS (Rush); Megan Keller, OTS (Rush); Emily Lander, OTS (Rush); Louis Fogg, PhD (Rush); and Mary Ellen Stoykov, PhD, OTR/L (Rush)

**Introduction:** Individuals with hemiparesis use their affected and unaffected upper extremities significantly less than healthy adults, thus limiting the ability to complete functional tasks. Through the identification of predictors for upper extremity motor recovery following stroke, the most efficient course of treatment can be determined for individuals with hemiparesis.

**Objective:** To examine the predictors of motor recovery from upper extremity hemiparesis including movement repetitions per session, cortical inhibition, and months post-stroke.

**Methods:** Data from two groups were gathered during a randomized, controlled trial (NCT 02277028). The sample included 17 participants over the age of 55 who had sustained a unilateral stroke at least six months prior to enrollment. Participants were selected based on severity of arm impairment (indicated by scores on Fugl-Meyer Test of Upper Extremity Function [FMUE] of 23 to 38) and the ability to tolerate priming (Modified Ashworth Scale score of 3 or less for wrist). Participants were randomly assigned to either a healthcare education group or a bilateral priming group, also known as active-passive bilateral training (APBT). After receiving the education or priming, all participants completed the same task specific training (TST) protocol. Potential predictors of upper extremity motor recovery included baseline FMUE score, baseline Chedoke Arm and Hand Activity Inventory (CAHAI) score, median TST movement repetitions over 15 sessions, months post-stroke, and baseline transcallosal inhibition. A multiple regression was used to examine predictors of motor recovery in all subjects.

**Results:** Motor recovery (increases in FMUE scores) from baseline to six weeks follow-up was found to be significantly related to median TST repetitions across sessions ( $r=.80$ ,  $p<.001$ ) and marginally related to assignment to APBT ( $F=4.12$ ,  $df=(1,16)$ ,  $p=.058$ ).

**Conclusion:** Median TST repetitions predicted 65% of the variance in FMUE. The effect was robust regardless of months post-stroke at time of treatment.

## The Mediating Role of Negative Posttrauma Cognitions on the Relationship Between Potentially Morally Injurious Experiences and PTSD Severity

**Primary Author:** Denise Zou, BS

**Contributors:** Kathryn Sulkowski, BS; Niranjana S. Karnik, MD, PhD; Mark H. Pollack, MD; Alyson K. Zalta, PhD; and Philip Held, PhD

**Introduction:** Potentially morally injurious events have the capability to violate military service members' deeply held moral beliefs or values (Drescher et al., 2011; Litz et al., 2009). Specifically, it has been hypothesized that moral injury can negatively affect service members' cognitions about themselves and world (Frankfurt & Frazier, 2016). Although the link between negative posttrauma cognitions, such as self-blame, negative beliefs about self, and negative beliefs about the world and PTSD severity has been well-established (Blain, Galovski, Meriac, & Elwood, 2013), no study has yet examined whether negative posttrauma cognitions mediate the relationship between potentially moral injurious experiences and PTSD severity.

**Objective:** The objective is to examine whether negative posttrauma cognitions mediate the relationship between potentially moral injurious experiences and PTSD severity.

**Methods:** Data were collected as part of the standard clinical evaluation of 74 treatment-seeking veterans at a non-VA, trauma-focused intensive outpatient program. Measures assessing moral injury, (Moral Injury Events Scale), negative posttraumatic cognitions (Posttraumatic Cognitions Inventory), and PTSD severity (PTSD Checklist for DSM-5) were used to examine the different variables of the mediation model.

**Results:** We tested negative posttrauma cognitions (self-blame, negative beliefs about self, negative beliefs about the world) as mediators of the relationship between potentially morally injurious experiences and PTSD severity ( $F(4, 69) = 9.234, p < .001, R^2 = .349$ ). Results indicated that negative beliefs about the world fully mediated the relationship between potentially morally injurious experiences and PTSD severity ( $\beta = .079, SE = .054, 95\% CI[-.238, -.009]$ ). Self-blame ( $\beta = .083, SE = .063, 95\% CI[-.254, .006]$ ) and negative beliefs about self ( $\beta = -.007, SE = .051, 95\% CI[-.101, .108]$ ) did not significantly mediate the aforementioned relationship.

**Conclusion:** Findings suggest that veterans who endorse a greater number of potentially morally injurious experiences report more negative beliefs about the world, which, in turn, predict increased PTSD severity. Full mediation suggests that moral injury and PTSD are indirectly related and likely distinct constructs.

**Significance:** This study extends prior research on moral injury and PTSD severity, demonstrating that negative beliefs about the world, which may develop following potentially morally injurious experiences can explain the relationship between moral injury and PTSD. Study findings have important implications for the clinical care of veterans and research on moral injury.



## **The Concept of Caring in the Recruitment of African Americans with Chronic Health Disease: An Integrative Review**

**Primary Author:** Charlene Gamboa, MPH, PhD Student

**Contributors:** Wrenetha Julion, PhD, MPH, RN, FAAN, Women, Children & Family Nursing, Rush University, College of Nursing

**Introduction:** African Americans (AA) experience a disproportionate burden of disease, death, and disability compared with non-minorities. An answer to bridge the AA health disparities gap is to facilitate enrollment of AA into health-related research studies. However, AA are recruited into health-related research at rates that are much lower than non-minority populations, and the greatest percentage of underrepresentation is among older AA adults. Therefore, the purpose of this integrative review is to describe how the concept of caring has been used in recruiting older AA into health-related research.

**Objective:** Describe the relevance of Swanson's Theory of Caring to recruitment. Analyze recruiter's impact on older African Americans adults' enrollment into health-related research. Synthesize how caring recruitment strategies can be employed with older AA with chronic health disease.

**Methods:** Swanson's Middle Range Theory of Caring serves as the framework for examining caring in the recruitment of older AA with chronic health disease. Peer reviewed publications between 1993 and 2015, were reviewed based upon the following inclusion criteria: English-language studies, with explicit description of the process for recruiting AA into health-related research. The research question was: How does adoption of a caring framework during the recruitment process influence recruitment, enrollment and outcomes?

**Results:** Three hundred forty-nine articles were reviewed to identify indicators of caring (i.e., knowing, being with, doing for, enabling, maintaining belief). The preponderance of literature focused on recruitment strategies, lessons learned, and barriers to recruitment. Many publications failed to clearly explicate the recruitment process, and evidence of 'caring' recruitment was infrequently evident to varying degrees.

**Conclusion:** Recruitment of older AA into health-related research remains a perplexing problem. Researchers who utilize caring behaviors during the recruitment process can facilitate AA adults' participation in research aimed at reducing health disparities.

**Significance:**

## The Effect of Hyperglycemia on Human Dendritic Cells and the Subsequent T cells They Encounter

**Primary Author:** Nadine Lerret, PhD

**Contributors:** Amanda Marzo, PhD (Rush); Douglas Kuperman, PhD (Rush)

**Introduction:** Inflammation and hyperglycemia are thought to play leading roles in the progression from pre-diabetes into Type 2 Diabetes; however the exact immune mechanisms underlying the rapidly progressing pathogenesis of this disease are unclear. One recent study showed hyperglycemia induces a proinflammatory cytokine profile in human dendritic cells (DCs), leading to their maturation. What effect this has on the T cells that the dendritic cells subsequently encounter in hyperglycemic conditions is unknown.

**Objective:** Whether hyperglycemia alters T cell priming by dendritic cells and results in increased T cell proliferation and an effector phenotype.

**Methods:** Immature human DCs were cultured with different concentrations of glucose (5.5mmol/L, 15mmol/L or 30 mmol/L) for 24 hours. Autologous T lymphocytes (T cells) were then added to the DC cultures in fresh media without the addition of glucose and allowed to proliferate for 5-7 days. Flow cytometry was used to investigate the immunophenotype of the DCs after culture in glucose and the degree of proliferation that T cells undergo after being stimulated with dendritic cells subject to increasing concentrations of glucose.

**Results:** The incubation of DCs with high amounts of glucose resulted in an increase in the expression of DC markers of activation, CD83, and HLA-DR.

**Conclusion:** An elevated glucose concentration leads to the maturation of DCs. These results lay the foundation and support the hypothesis that hyperglycemia alters T cell priming by dendritic cells.

**Significance:** These results provide insights into the intricate inflammatory environment that occurs in the pathogenesis of diabetes in order to lay the foundation for future studies aimed at elucidating therapeutic strategies that inhibit diabetes and-associated inflammation but preserve immunity and immuno-surveillance.

## **Impact of the 'Whiteboard Initiative' at Rush University Medical Center on the Patient Experience**

**Primary Author:** Michael Drunasky, BA

**Contributors:** Francis Fullam, MA (Rush); Jeff Canar, PhD (Rush); Irwin Press, PhD (Rush)

**Introduction:** Better utilizing inpatient whiteboards has been seen as a good way to improve patient-provider communication. In 2016, The Whiteboard Initiative was a pilot launched in the 13W general medicine unit of the tower at RUMC that placed an emphasis on utilizing whiteboards to improve communication through education sessions, redesigning the current whiteboards and an overall culture change. This study will look to see what effect the study had on patient experience scores for patients discharged from the unit.

**Objective:** The hypothesis for this study is that there will be a positive effect on satisfaction scores from patients in the experimental group for selected questions from HCAHPS and Press Ganey surveys after the start of the initiative (6/6/2016) compared to those in the control group (two other general medicine units at Rush). These questions will be ones that relate to communication of the staff.

**Methods:** This study is a quasi-experimental design that will be using patient satisfaction surveys from patients discharged from general medicine units at RUMC (6/6/2014 - 12/31/2016). The descriptive statistics used will be top box scores from HCAHPS patient surveys and mean scores from Press Ganey patients surveys. (Study also has IRB approval)

**Results:** Initial results have seen the pilot unit increased HCAHPS scores for nurse communication from 44th percentile prior to the initiative to the 79th percentile since the start of the initiative while physician communication scores went from the 9th percentile to 90th percentile.

**Conclusion:** Patient satisfaction scores are becoming more important with the shift away from fee-for-service reimbursement and success in the pilot group could lead to more units in the medical center redesigning whiteboards or focusing on effectively utilizing them.

**Significance:** Results could also help guide similar implementation efforts in the future.

## Effect of Alcohol Binge on Circadian Rhythm of Leukocyte Subset Trafficking to the Proximal Colon

**Primary Author:** Eve Grumish, M.S. Candidate

**Introduction:** Alcohol use is considered to be the cause of 4.5% of all disease and 4% of worldwide death and binge drinking is becoming increasingly popular. Alcohol is known to affect 24h circadian rhythms in physiology that are synchronized to external time cues known as Zeitgebers (ZT). Recent studies identified the circadian clock as a crucial mediator of digestive disease and immune response, however alcohol's interaction with circadian rhythm is not understood. In this study we investigate the effects of alcohol binge on the circadian rhythm of leukocyte subset trafficking to the proximal colon.

**Objective:** The primary objective of this study was to determine the effect of alcohol binge at different times of the day on the gastrointestinal immune response.

**Methods:** Chow fed, C57BL/6 mice (n=60) were binged with 6g/kg alcohol or PBS control per day for 3 consecutive days at 6 different ZT (n=5 per ZT). Fixed proximal colon tissue samples were evaluated for CD3, Foxp3, GATA-3, T-bet and RORgt T cell markers and CD68 monocyte marker using immunofluorescence and immunoperoxidase staining. Independent, blinded observation performed using ImageJ (SciJava), Biopix iQ (Biopix AB) and statistical significance ( $p=.05$ ) determined using Graphpad Prism (Graphpad Software, Inc.) and R (R Foundation).

**Results:** Alcohol binge produced an inflammatory immune response in the proximal colon, marked by significantly decreased T-regulatory cells also significantly varied by binge time. Th1 cells dominated Th2 cells in the colon 10-60 fold, with a marked decrease in Th2 cells in the alcohol binged groups. These results will be correlated with increased trafficking of Th17 cells and macrophages in the alcohol binged mice in future investigations.

**Conclusion:** These data will provide novel insights into the mechanisms through which binge drinking may affect the natural rhythm of immune response in the GI tract.

## B Cell Immunoaging

**Primary Author:** Allison Nipper, BS

**Contributors:** Alan Landay, PhD (Rush)

**Introduction:** While age-related changes in B cells have been extensively studied in mice, human studies have not progressed as extensively.

**Objective:** We examined differences between B-cells from young (<45 years) and aged (>65 years) individuals in an attempt to identify hallmarks of immune senescence utilizing multiparameter flow cytometry.

**Methods:** Flow cytometry was used to characterize peripheral B cells of young and aged individuals.

**Results:** Phenotypic characterization of PBMCs demonstrated a significant increase in the frequency of atypical memory B cells (CD10-CD20+CD21-CD27-) with age ( $p=0.0039$ ). We next examined expression of B-cell receptor (BCR) inhibitory molecules associated with this subset, and found expression of CD72 decreased significantly with age ( $p=0.0024$ ). While phosphorylation following BCR stimulation was similar between age groups, aged individuals had decreased phosphorylation of multiple kinases prior to stimulation. Additionally, in examining regulators of terminal differentiation, we observed reduced expression of PAX5 in mature peripheral B cells with age ( $p=0.0002$ ).

**Conclusion:** B cells of aged individuals possess a unique phenotype characterized by reduced expression of PAX5 and members of its gene regulatory network.

**Significance:** Taken together, these observations may be indicative of age-related changes to B cells, which may serve as markers of immune senescence.

## Spontaneous Necrotizing Fasciitis in a Case of Pediatric Acute Lymphoid Leukemia

**Primary Author:** Stephen Dvorak, MFA

**Contributors:** Antonio DC Logan (Rush) Jeff Ording (Rush) Paul Kent MD (Rush)

**Introduction:** Necrotizing fasciitis (NF) is a secondary life and limb-threatening infection of the fascial layer; NF in immuno-compromised children is rare. Though symptoms may include pyrexia, tachycardia, edema, erythema with or without crepitus, sepsis, and swelling of entry point, the differentiating factor in diagnoses is extreme pain out of proportion to clinical findings. Expeditious diagnoses via frozen-section biopsy and surgical debridement are critical to maximizing the patient's outcome.

**Objective:** This case report is to serve as a clinical reminder to pediatric oncologists that, NF should be kept in mind for a secondary infection during chemotherapy and that pain out of proportion with clinical findings is the differentiating factor.

**Methods:** A comprehensive literature search was conducted (using pubmed mesh terms 'necrotizing fasciitis' and 'Acute Lymphoid Leukemia') through the pediatric population for all reported cases of pediatric ALL patients who had an NF infection during treatment with Chemotherapy. Additionally, the most recent ALL protocols for the COG were searched to find any other mention of occurrences of NF while on protocol.

**Results:** Our patient presented without any portal of entry or trauma, which was otherwise unreported in pediatric ALL cases. The only early sign of NF was the patient's excruciating pain. Our patient had no crepitus in the area of infection throughout its progression, and both CT and MRI scans showed no subcutaneous gas, the 'standard' for soft-tissue infection. Ultimately the only definitive method to diagnose NF is frozen section biopsy.

**Conclusion:** Pain out of proportion is the differentiating factor in the diagnoses of NF versus cellulitis. Though CT and MRI scans are useful, they are not foolproof. Our case is an excellent example. Despite its rarity, pediatric oncologists should keep NF on the differential diagnosis (including pain, fevers, erythema, edema, and subcutaneous gas) of possible secondary infection, especially in patients who are severely immune-compromised.

**Significance:** This case, though very rare, is an excellent reminder for clinicians of the importance of these diagnostic factors when treating ALL patients undergoing chemotherapy. In this case, a timely diagnosis and excellent work by all the physician's involved resulted in a limb-saving operation, and excellent recovery for the patient.

## **Resistance Mechanisms and Factors associated with Plasmid-Mediated Fluoroquinolone Resistant (PMFQR) Enterobacteriaceae (Ent) Infections in Children**

**Primary Author:** Rachel Medernach, MD

**Contributors:** Jared R. Rispens, MD, Steven H. Marshall, MS, Andrea M. Hujer, BS, T. Nicholas Domitrovic, BA, Susan D. Rudin, BS, Xiaotian Zheng, MD, PhD, Nadia K. Qureshi, MD, Mary K. Hayden, MD, Robert A. Weinstein, Robert A. Bonomo, MD, and Latania K. Logan, MD

**Introduction:** Fluoroquinolones (FQs) are not commonly prescribed in children, yet the increasing incidence of multidrug resistant (MDR) gram-negative infections in this population often reveals linked resistance to FQs.

**Objective:** We sought to define the epidemiology of MDR GNs in children to devise more effective treatment and prevention strategies.

**Methods:** A case-control study of children (0-21 y) cared for by 3 Chicago area hospitals during 2011-14 was performed. Cases were 53 children diagnosed with 3rd generation cephalosporin (3GC) and/or carbapenem-resistant (CR) Ent infections. PCR amplification, DNA sequencing, and DNA microarray analysis (Check-Points®) assessed for bla genes and PMFQR. Rep-PCR, MLST, and phylogenetic grouping were also performed. Controls were 131 children with 3GC and carbapenem susceptible Ent infections matched by hospital. Demographics; comorbidities; device, antibiotic, and healthcare exposures; and the impact of location of patient residence were evaluated. Race categories were white, black, Hispanic, and other. Multivariable logistic regression was used to explore associations between predictors and PMFQR infection. Data were analyzed in SAS 9.4.

**Results:** Of 169 G3CR Ent and CR Ent isolates, 85 were FQR; 56 (66%) contained PMFQR genes, and of those, 53 (95%) were analyzed. Median age was 6 years. The predominant organism was *E. coli* 40/53 (76%). PMFQR gene mutations included aac 6'1b-cr, oqx A/B, qepA, and qnr A/B/D/S in 83%, 15%, 13% and 11% of isolates, respectively. PMFQR was found with gyrA and/or parC mutations in 43/49 (88%). The most common bla gene was blaCTX-M-1 group in 76%, followed by blaSHV ESBL in 11%. One isolate harbored a blaKPC gene. Several isolates contained >1 bla/PMFQR gene. Children with PMFQR Ent infections were more likely to be diagnosed in an outpatient clinic (OR 2.2, CI 1.5-3.2) and of race 'other' (OR 1.7, CI 1.1-2.7) vs. controls. Residents of Southwest Chicago were 7 times more likely to have a PMFQR Ent infection than controls (OR 6.9, CI 2.1-22.4); while residence in Central Chicago was associated with a 91% decreased risk (OR 0.09, CI 0.1-0.7). Significant differences in other demographics; comorbidities; invasive devices; antibiotic use; or recent healthcare were not found.

**Conclusion:** Environmental influences may contribute to acquisition of MDROs showing FQR. Regional differences associated with PMFQR Ent are observed. A significant number of PMFQR strains are found in the community, which may reflect linkage to blaCTX-M harboring plasmids which are endemic in some communities.

## Impact of Wnt 7A on monocyte differentiation

**Primary Author:** Jennillee Wallace, MS

**Contributors:** Lena Al-Harthi, PhD (RUMC)

**Introduction:** Monocytes infiltrate tissue for pathological and/or homeostatic purposes and differentiate into proinflammatory (M1), alternative (M2) macrophages, or a variation of intermediate phenotypes. In HIV infection macrophage/microglia phenotype has been shown to correlate with neuropathological events. One such example is the increased expression of the CD163 scavenger receptor with increasing HIV encephalitic lesion size. Published data from our lab illustrates that beta-catenin; a protein primarily regulated by a family of morphogenetic glycoproteins known as Wnts, is a restrictive factor for productive HIV infection of monocytes. Beta-catenin decreases as monocytes mature, rendering monocyte derived macrophages (MDMs) more susceptible to infection.

**Objective:** Our objective is to further evaluate the impact of Wnts on macrophage phenotype and function.

**Methods:** in vitro, in vivo experiments; flow cytometry, IF, ELISAs, q RT-PCR.

**Results:** Culturing monocytes with Wnts 1, or 7a recombinant human proteins revealed that Wnt7a inhibited the expression of CD14+CD16-, CD14+CD16+, and CD163 relative to M1 and M2 MDMs. Wnt7a also inhibited secretion of IL-1b and DKK1 compared to M1 and M2 MDMs.

**Conclusion:** These data suggest that Wnt7a influences MDM phenotype; ongoing studies continue to assess the phenotype and functionality of Wnt7a treated MDMs. Ultimately, this study will provide a better understanding of how Wnts influence the phenotype and function of MDMs.



## **Resistance mechanisms and Factors associated with *Klebsiella pneumoniae* carbapenemase (KPC)-producing Enterobacteriaceae infections in children**

**Primary Author:** David Nguyen, MD

**Contributors:** Felicia A. Scaggs, MD (Cincinnati Children's Hospital); Angella Charnot-Katsikas, MD (University of Chicago); Allison Bartlett, MD, MS (University of Chicago); Xiaotian Zheng, MD, PhD (Ann & Robert H. Lurie Children's Hospital of Chicago, Northwestern University); Nadia K. Qureshi, MD (Loyola), Robert A. Weinstein, MD (Cook County Health and Hospital Systems) and Latania K. Logan (Rush University)

**Introduction:** Carbapenem-resistant (CR) Enterobacteriaceae (Ent) are multidrug-resistant organisms (MDRO) associated with significant morbidity and mortality. The prevalence of CR-Ent infections is increasing in U.S. children; however, multi-centered pediatric data is lacking.

**Objective:** 1) Identify resistance mechanisms and factors associated with pediatric KPC-producing Ent infections; 2) Assess outcomes.

**Methods:** We conducted a case-control study of patients (0-22 years) at 3 medical centers in Chicago, 2008-2014. Cases had infections due to CR-Ent isolates phenotyped as KPC-producers (blaKPC); whereas controls had carbapenem-susceptible Ent infections matched by age, source, and location. Analysis was performed (Student's t-test). Rep-PCR, DNA Microarray (Checkpoints<sup>®</sup>), DNA sequencing, and multi-locus sequence typing were performed on available isolates (4).

**Results:** We identified 17 KPC-producing Enterobacteriaceae infections. Median age was 17.4 years; 29% were African-American; 71% were ICU patients, while 18% resided in long-term care facilities. The predominant organism was *Klebsiella pneumoniae* (94%) and common sources were blood (23.5%), respiratory (23.5%), and urine (17.5%). Cases were more likely to have had previous MDRO infection (65% vs 12%,  $p<0.001$ ), gastrointestinal (76% vs 45%,  $p=0.05$ ), hematologic-oncologic (64% vs 25%,  $p=0.01$ ), and/or  $>3$  comorbidities (71% vs 37%,  $p<0.04$ ) vs. controls. Though not significant, cases were often ventilated (41% vs 17%,  $p=0.09$ ) and had  $>1$  foreign bodies (82% vs 58%,  $p=0.11$ ) vs. controls. The average LOS after infection was 33.7 vs 22.5 days ( $p=0.34$ ) with no difference in mortality (12% vs 17%,  $p=0.67$ ). Of four isolates available for analysis (3 *K. pneumoniae*, 1 *E. coli*), 1 isolate was ST258 harboring a blaKPC-3, and 3 isolates were non-ST258 and harbored blaKPC-2.

**Conclusion:** Potential factors associated with KPC-Ent infections in children include previous MDRO infection, GI and hematologic-oncologic comorbidities, and/or having multiple comorbidities. LOS and mortality in children with KPC-Ent infections were similar to controls, and most isolates harbored blaKPC-2, which differs from regional reports in adults.

**Significance:**

## **SICKLE CELL TRAIT: THE RISKS FOR ATHLETIC PARTICIPATION**

**Primary Author:** Anil George, MD

**Contributors:** Paul Kent, MD (RUMC); Antonio Logan, BS (RUMC); and Mindy Simpson, MD (RUMC)

**Introduction:** Sickle cell trait (SCT) is an inherited blood disorder that affects 1 to 3 million people in the United States and more than 100 million people worldwide. Previous studies have suggested that having sickle cell trait increases one's risk of exertional rhabdomyolysis and subsequent death. A number of these cases highlighting several high-profile deaths have been reported in both television and newspaper media and attributed death to SCT. A recent study published in the New England Journal of Medicine reported that SCT was not associated with a higher risk of death than absence of the trait. None of the medical experts in the National Institutes of Health (NIH), American Academy of Pediatrics (AAP), or Centers for Disease Control and Prevention (CDC) advise against participation in competitive sports. We performed a retrospective review of both newspaper and television media to determine if television and newspaper media opinion used evidence-based guidelines in accurately depicting the risks associated with SCT.

**Objective:** To highlight the discrepancy between the evidence-based guidelines in the medical community with the depiction of SCT-associated risks in national television and newspaper media.

**Methods:** Sixteen media outlets were included in this review. This included the 6 most viewed television news networks based on the 2015 Nielsen ratings and the top 10 newspaper outlets according to circulation in the United States. The search engines on each of the respective media websites were used to identify stories reporting about sickle cell trait, whether these stories quoted evidence-based guidelines and whether they quoted the NCAA policy pertaining to athletic participation.

**Results:** Three of the 6 television networks and 9 of the 10 newspaper outlets reported stories relating to SCT, however 1 of the 6 television networks and 3 of the 10 newspaper outlets referenced evidence-based guidelines. Additionally just 1 of the 6 television networks and 2 of the 10 newspaper outlets quoted the NCAA policy pertaining to athletic participation.

**Conclusion:** The absolute risks of SCT are known to be low, but not well described by the mainstream media. More accurate risk estimates are needed, as well as continued research into contributing factors. Widespread dissemination of universal precautions for exertion-related illness and a consistent positive message of SCT participation in athletics may lead to less discrimination of SCT individuals and an overall reduction morbidity and mortality.

## The Role of Childhood Sexual Abuse in Predicting Distress for Pregnant Trauma Survivors

**Primary Author:** Linzy Wagner, BS

**Contributors:** Natalie Stevens, Ph.D. (RUMC) , Alyson K. Zalta, Ph.D. (RUMC), Teresa Lillis, Ph.D. (RUMC) & Stevan Hobfoll, Ph.D. (RUMC)

**Introduction:** While it has been established that women with histories of abuse are more likely to experience perinatal psychological distress (e.g. pregnancy-related anxiety, posttraumatic stress disorder (PTSD), and depression) as compared to their non-trauma-exposed counterparts, little work has been done to differentiate rates of perinatal distress based on the type of trauma exposure. In particular, childhood sexual abuse (CSA) may play a significant role in affecting distress as the women may have concerns about their child facing similar experiences of abuse.

**Objective:** Determine whether age at the time of trauma or type of trauma impacts the amount of distress experienced during pregnancy.

**Methods:** As part of a pilot study of trauma-sensitive care for pregnant women, 43 low-income women ages 18-45 were recruited from an inner-city OB-GYN clinic. Women were accepted if they had a history of trauma and at least one symptom of PTSD. Prior to starting the program, they completed the following self-report measures: Childhood Trauma Questionnaire (CTQ); PTSD Symptom Checklist-Civilian Version (PCL-C); Pregnancy-Related Anxiety Questionnaire (PRAQ) to assess worry/concern for their pregnancy; and the Patient Health Questionnaire (PHQ-9) to evaluate depressive symptoms. Rush University Medical Center's IRB approved this study and informed consent was obtained.

**Results:** More than half of the women (55.81%) reported a history of CSA. Independent-samples t-tests were conducted to compare psychological distress for those with CSA versus those who had experienced other types of trauma. Although no significant differences were found for anxiety or PTSD symptoms, there were significant differences for depression  $t(41) = 2.07, p = .045$ . Specifically, women with CSA ( $M = 10.63, SD = 6.52$ ) were 1.5 times more likely to be depressed than those without CSA ( $M = 7.00, SD = 4.45$ ).

**Conclusion:** Although a history of CSA did not impact pregnancy-related anxiety or PTSD symptoms as expected, these findings suggest that CSA confers additional risk to developing depression during the perinatal period.

**Significance:** Our preliminary findings suggest interventions aiming to screen for and reduce depression in pregnancy should consider the impact of histories of abuse, with particular attention paid to reports of childhood sexual abuse.

## The Significance of Trauma as it Relates to PTSD

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**Contributors:** Dr. Frances Aranda, PhD, MPH, (RUMC); Dr. Steven Hobfoll, PhD, (RUMC); John Burns, PhD (RUMC); Yanina Purim-Shem-Tov, M.D., (RUMC); Linzy Wagner, B.S. (RUMC); Brittany Nguyen, B.A. (RUMC); Sara Tamizuddin, B.S. (RUMC); Mary Kennedy B.S. (RUMC)

**Introduction:** Many individuals from lower socioeconomic status (SES) report experiences with trauma and Post Traumatic Stress Disorder (PTSD). This is particularly true among African American women who tend to have frequent encounters with crime/violence and sexual/physical abuse compared to other racial/ethnic groups which is commonly associated with the development of PTSD. In many African American communities, PTSD is often under-reported due to lack of awareness and/or misdiagnosed.

**Objective:** We examined the relationship between trauma and PTSD among inner city African American women.

**Methods:** Women ages of 18-40 years were recruited from Rush University Medical Center's (RUMC) Emergency Department. Eligible women participated in 7-interviews, three in-person and four by phone, within a six-month time frame. This study was approved by RUMC's Institutional Review Board and informed consent was obtained. Measures included life experiences, health, and pain data which were analyzed using SPSS v23.

**Results:** Of the 183 women who completed a baseline interview, more than half were African American (65%). Of this sample, 40% had a high school diploma/GED or less and about 25% were unemployed. Additionally, 31.1% of the women reported sexual abuse and 41% physical abuse. 53% reported experiencing a crime (with/without a weapon), and the mean reported for PTSD was 7.20 (SD 5.69; range 0-20). Women who reported experiencing either sexual and/or physical abuse were more likely to report PTSD.

**Conclusion:** There was no significant difference in reporting by race/ethnicity among the women for having PTSD but there were significant differences for those who reported sexual/physical abuse and PTSD compared to those who did not report abuse.

**Significance:** Both sexual and physical type-traumas were significant factors reported among these participants which were positively associated with PTSD. Perhaps this population can benefit from prevention education and/or intervention services.

## PTSD and Pain Sensitivity: A Real Relationship?

**Primary Author:** Sara Tamizuddin, BA

**Contributors:** Frances Aranda, Ph.D. M.P.H. (RUMC); Brittany Nguyen, B.A. (RUMC); Linzy Wagner, B.S. (RUMC); Mary Kennedy, B.S. (RUMC); De'Andra Robertson (RUMC); John Burns, Ph.D. (RUMC); Yanina Purim-Shem-Tov, M.D. (RUMC); Stevan Hobfoll, Ph.D. (RUMC).

**Introduction:** The comorbidity of the physiology of posttraumatic stress disorder (PTSD) with pain conditions remains unclear. Previous findings show mixed results concerning pain sensitivity among participants with PTSD and a theory unifying biological knowledge and experimental evidence is lacking. This study explores the relationship between PTSD and thermal pain sensitivity in women presenting to the Rush University Medical Center (RUMC) Emergency Department in Chicago, IL.

**Objective:** This research hypothesizes a negative relationship between somatic thermal pain sensations and PTSD among women. The majority of research supports this hypothesis, though some studies with war veterans have found contradictory evidence.

**Methods:** RUMC's Institutional Review Board approved the study and 182 participants provided informed consent. PTSD was assessed using the PTSD Checklist 5 (PCL-5), which evaluated participants' reactions to their most stressful life experiences. Somatic pain threshold and tolerance were assessed using a Medoc TSA-II NeuroSensory Analyzer. A heat probe was strapped to each participant's ventral non-dominant forearm to determine pain threshold and maximum pain tolerance, with the average of four trials reported for each. A bivariate, one-tailed, Pearson correlation was calculated for PTSD symptoms and pain sensitivity.

**Results:** The average provisional score on the PCL-5 was 7.21 (SD .438; Range 0-20). The pain threshold average was 43.58°F (SD 3.19), and pain tolerance was 46.86°F (SD 1.59). PTSD symptoms were not significantly correlated to either pain threshold or tolerance at  $p < .05$ .

**Conclusion:** PTSD is a multifaceted condition that can affect many aspects of an individual's health. The women in this study do not exhibit increased pain sensitization with PTSD symptoms as expected. Previous conclusions based on smaller samples, different quantitative measures of pain, or more extreme cases of PTSD may not be generalizable to the public.

**Significance:** This knowledge is useful for future assessments of pain conditions and PTSD as researchers investigate the association between various pain conditions and PTSD.

## Accurately identifying anger: a treatment target for schizophrenia

**Primary Author:** Samantha Schoeneman, BA

**Contributors:** Abhishek Saxena (Department of Psychiatry, Rush University), Erin Guty (Department of Psychology, Penn State University; Department of Psychology, Harvard University), David Dodell-Feder (Department of Psychology, Harvard University), Mor Nahum (Posit Science Corporation; Hebrew University of Jerusalem, School of Occupational Therapy), and Christine I. Hooker (Department of Psychiatry, Rush University, Department of Psychology, Harvard University)

**Introduction:** Schizophrenia patients have facial emotion recognition deficits, associated with poor social functioning, that appear early in the disease, making it an optimal treatment target. Although antipsychotics, the standard treatment, do not improve cognitive deficits, recent studies show that computerized cognitive training improves cognitive skills in many populations including schizophrenia patients; however, little work has been done on whether such training can specifically improve social cognition in patients or healthy adults. In this study we evaluate social cognition performance malleability in healthy adults to eventually develop an intervention for schizophrenia patients. We hypothesize that such training can improve social cognitive skills, such as facial emotion recognition.

**Objective:** To evaluate whether targeted social cognitive training can improve facial emotion recognition.

**Methods:** All subjects gave informed consent to participate in this IRB-approved study. We used an internet-based social cognition training program, 'Socialville' by Posit Science, designed to improve social cognition using games targeting social skills. Fifty-six healthy adults were asked to complete 10 hours of training over two weeks using either Socialville or commercially-available computer games. Before and after training all subjects completed the Penn ER40 assessment during which they assigned emotions (i.e. happy, angry, sad, fearful, and neutral) to 40 faces. Multivariate repeated measure and paired t-tests were used to compare general and specific emotion recognition accuracy before and after training within each group.

**Results:** Although both groups performed at equivalently high accuracy levels, making training-related improvement difficult to detect, the experimental group significantly improved in their ability to identify angry faces as angry instead of neutral.

**Conclusion:** SocialVille improved subjects' ability to distinguish between anger and neutrality. As anger-neutrality confusion is associated with poor social functioning in schizophrenia, SocialVille could benefit schizophrenia patients. Further research needs to evaluate whether SocialVille can help schizophrenia patients distinguish between anger and neutrality and consequently improve their social functioning.

**Significance:** SocialVille has the potential to treat deficient anger recognition in schizophrenia patients, a deficit predictive of a poor prognosis which antipsychotics cannot treat.

**Poster #: 134**

Withdrawn by Author.

## The Relationship between Traumatic Experiences and Chronic Pain Related Factors in Women

**Primary Author:** Mary Kennedy, B.S.

**Contributors:** John Burns, Ph.D. (RUMC); Yanina Purim, M.D.(RUMC); Frances Aranda, Ph.D.(RUMC); Linzy Wagner, B.S.(RUMC); Brittany Nguyen, B.A.(RUMC); Sara Tamizuddin, B.A.(RUMC); De'Andra Robertson, B.A.(RUMC); Steven Hobfoll, Ph.D.(RUMC)

**Introduction:** Chronic pain is a growing public health issue amongst women. Women are also at a high risk for experiencing traumatic events. Little is known about how the total number or types of traumatic experiences and age during first traumatic experience affect related factors (pain catastrophizing and acute pain intensity) for developing chronic pain.

**Objective:** The current study predicts a positive relationship between the total number and types of traumatic experiences and pain catastrophizing and acute pain intensity in women. Additionally, it predicts a negative relationship between age during first traumatic experience and pain catastrophizing and acute pain intensity in women.

**Methods:** This study includes 183 women, ages 18-40, experiencing acute pain and recruited from Rush University Medical Center's (RUMC) Emergency Department (ED). Participants completed a survey-interview within two weeks of their ED visit. The Traumatic History Questionnaire was used to assess women's exposures to trauma; the Pain Catastrophizing Scale was used to measure pain catastrophizing; and a past month pain intensity item was used to assess acute pain intensity. This study was approved by RUMC's Institutional Review Board and informed consent was obtained at the interview.

**Results:** Bivariate correlations showed there was a positive significant relationship between the total number of traumatic experiences and acute pain intensity  $r(182)=.20, p=.01$ . Additionally, there was a positive significant relationship between the number of types of traumatic experiences and acute pain intensity  $r(183)=.16, p=.04$ . There was no significant relationship between the age during first traumatic experience and acute pain intensity or between the total number, types of traumatic experiences, and the age during first traumatic experience and pain catastrophizing.

**Conclusion:** These findings suggest an increased number of traumatic experiences and types of traumatic experiences are related to increased acute pain intensity in women. A limitation of the study is a lack of longitudinal data.

**Significance:** Future studies should seek to identify additional related factors for developing chronic pain associated with traumatic events using longitudinal data. This will incentivize patients to disclose information about traumatic events and allow clinicians to provide additional preventative care.



## **'S.O.S.' Support Our Staff: Responding to Distress with Care and Compassion**

**Primary Author:** Judy Friedrichs, DNP, RN

**Contributors:** Cally McKinney MS, APN, PMHCNS-BC (Rush University Medical Center)

**Introduction:** For patients, their families and healthcare professionals, hospitals are places of healing as well as distress. While striving to create the healing environments required for safer, higher quality and compassionate patient care, staff move from patient to patient, bearing witness to painful, debilitating and life threatening situations, often without the time and place needed to reflect on and attend to the distress.

**Objective:** To create a safe space to acknowledge staff distress

**Methods:** A team member requests a 'SOS (delayed debriefing) ALL staff touched by the event or dilemma are invited. A pre-SOS survey is sent with the invitation. Facilitated discussion lasts 60-90 minutes Ending with a review of agreed upon actions. Post survey is sent to staff after the discussion.

**Results:** In 2005 the bereavement support coordinator recognized staff distress was often avoided, leading to dissatisfaction, emotional exhaustion, and the potential for detachment. As detachment has been shown to diminish compassion, quality and satisfaction for all, a structure to provide a safe place to address distress was developed. 'SOS' (Support Our Staff) occurs on all units and can be called by anyone. The bereavement support coordinator, psych liaisons, chaplain and other disciplines as needed, are part of the support team. The interdisciplinary team is invited and the facilitated discussion lasts 60-90 minutes. The structure of the discussion includes introductions, a thumb-nail sketch of the patient's history, the event and a series of discussion points. All are encouraged, and no one is compelled, to identify feelings, thoughts and wishes for the future without the need to explain. As colleagues own how this event affected them, they begin to open up, instead of avoiding the emotional conversations. The discussion ends with a review of actions agreed upon and a post-survey is sent to staff attending the discussion.

**Conclusion:** There have been 15-30 SOS discussions each year. The findings suggest the more frequently a unit holds an SOS the better appreciation the team has for one another. Data collected over the past year shows it was useful to share recurrent thoughts (78%); having an opportunity to share unexpected feelings put things into perspective (93%); staff felt it was helpful that concerns around procedures, processes and rules were voiced and heard (95.7%); and they felt satisfied that the actions will result in a positive change (96%). Communication occurs in many ways and when people are emotionally impacted by an experience, face to face compassionate communication is critical. Just as healthcare professionals are charged with creating a culture of purposeful communication and connection for better patient care and outcomes, they also need the time and place to engage in meaningful communication, sharing experiences of the work they do.

## A Wearable Morning Light Therapy for Pst-Traumatic Stress Disorder

**Primary Author:** Zerbrina Valdespino-Hayden, BA

**Contributors:** A. Zalta (RUMC), E. Lewis (RUMC), M. Pollack (RUMC), H. Burgess (RUMC)

**Introduction:** Sleep disturbance is among the most treatment resistant and distressing symptoms of posttraumatic stress disorder (PTSD). Evidence suggests that later circadian timing may exacerbate PTSD-related sleep disturbance. Additionally, research suggests that some circadian photoreceptors project directly to the amygdala, which is implicated in PTSD.

**Objective:** Thus, morning light treatment may be an efficacious adjunctive strategy for reducing PTSD symptoms. We are testing a novel wearable light treatment device, the Re-timer®. We also created a placebo device by dimming the light intensity with neutral density filters. The goal of this ongoing pilot study is to determine the feasibility, acceptability and efficacy of wearable light treatment in a sample of individuals experiencing PTSD.

**Methods:** Individuals with probable PTSD are randomized to self-administer a 4 week, daily 1-hour morning light treatment or placebo. Weekly visits are conducted to assess outcome measures (PTSD Checklist for DSM-5 [PCL], Patient Health Questionnaire - 9 [PHQ-9], Pittsburgh Sleep Quality Index [PSQI], Insomnia Severity Index [ISI]) and adherence to the light treatment using actigraphy.

**Results:** Two participants (P1 & P2) have completed all study visits to date. Based on actigraphy data, P1 (placebo) completed 15 of 28 days of treatment and received an average of 51 minutes per treatment day; P2 (active) completed 9 of 28 days of treatment and received an average of 47 minutes per treatment day. P1 (placebo) demonstrated no improvement from pre- to post-treatment on the PCL (44 pre, 44 post), PHQ-9 (14 pre, 17 post), PSQI (7 pre, 14 post) and ISI (13 pre, 17 post). By contrast, P2 (active) showed meaningful reductions from pre- to post-treatment on the PCL (21 pre, 6 post), PHQ-9 (13 pre, 3 post), PSQI (12 pre, 8 post) and ISI (10 pre, 5 post). P2 reported higher subjective benefit (a lot) from the light therapy than P1(somewhat).

**Conclusion:** Our very preliminary evidence suggests that wearable light therapy may be potentially efficacious for individuals with probable PTSD but that adherence may be a challenge. Data on the full sample of randomized participants will be presented upon availability.

## Predictors of Expressed Anger in a Treatment-Seeking Sample of Veterans and Service Members

**Primary Author:** Randy Boley, BA

**Contributors:** Philip Held, PhD (RUMC) Niranjan Karnik, MD, PhD (RUMC) Mark Pollack, MD (RUMC)  
Alyson Zalta, PhD (RUMC)

**Introduction:** Research on posttraumatic stress disorder (PTSD) and anger in veterans has demonstrated a strong positive relationship between these variables. While studies have identified PTSD severity as a significant predictor of anger, less is known about the impact of other predictors that have been shown to be associated with anger independent of PTSD.

**Objective:** The goal of the present study was to examine whether PTSD severity would remain a significant predictor of anger while accounting for other potential predictors including demographics, the number of lifetime traumatic events, depression, anxious arousal, chronic tension, pain, self-compassion, perceived social support, and alcohol use.

**Methods:** Data were collected from a sample of 227 treatment-seeking veterans at a non-VA outpatient mental health clinic. At intake, veterans completed self-report measures assessing all variables for the present study. We included variables that significantly correlated with anger at the bivariate level as predictors in the multiple regression analysis.

**Results:** In this sample, 62.2% endorsed clinically significant symptoms of PTSD and 56.8% endorsed notable anger dyscontrol problems. Bivariate analyses demonstrated that anger was significantly positively correlated with increased PTSD, depression, anxious arousal, chronic tension, pain, and the number of lifetime traumas. Additionally, anger was significantly negatively correlated with self-compassion and perceived social support. A multiple regression analysis revealed that only self-compassion ( $\beta = -.24$ ,  $p = .035$ ) and the number of lifetime traumatic events ( $\beta = .28$ ,  $p = .002$ ) significantly predicted anger ( $R^2 = .47$ ,  $p = .045$ ). Interestingly, in the presence of the included predictors, PTSD severity did not significantly predict anger ( $\beta = .10$ ,  $p = .425$ ).

**Conclusion:** The present study supports the need to address anger in conjunction with the treatment of trauma-related psychopathology. Additionally, these results support the need to examine lifetime trauma history in the treatment of veterans and service members who report struggling with anger. Future research should examine whether interventions focused on enhancing self-compassion might be helpful in reducing anger in veterans.

## Phase Advancing Teens with Different Durations of Weekend Morning Bright Light

**Primary Author:** Stephanie Crowley, PhD

**Contributors:** Lameese D. Akacem, PhD & Charmane I. Eastman, PhD (RUSH)

**Introduction:** The majority of teens experience chronic sleep restriction due in part to a dissonance between delayed circadian timing and early school start times. Morning bright light advances circadian timing and may be used to increase sleep duration on school-nights; however, the most effective light duration to advance rhythms remains unknown in this age group.

**Objective:** To quantify phase advances in response to two durations of morning bright light in teenagers.

**Methods:** Thirty-seven adolescents aged 14-17 years ( $16.41 \pm 1.04$  years; 21 females) slept unrestricted at home for 3 weeks before living in the lab for a weekend. On Friday evening, participants completed a baseline dim light melatonin onset (DLMO) assessment. Salivary melatonin samples were collected in 30-min intervals in dim light ( $<5$  lux). Participants received 1.5h bright light ( $n=11$ ;  $\sim 6,000$  lux; three 30-min exposures), 2.5h bright light ( $n=13$ ; three 50-min exposures) or room light ( $\sim 100$  lux; control group;  $n=13$ ) upon waking on Saturday and Sunday mornings. Bright light started 1h after weekend midsleep time (MST) on Saturday and at weekend MST on Sunday. The sleep/dark episode advanced on Saturday night. A final DLMO was measured on Sunday evening. Phase shifts were the difference between baseline and final DLMO.

**Results:** Room light, 1.5h, and 2.5h of bright light resulted in  $0.56 \pm 0.40$ h,  $0.66 \pm 0.53$ h, and  $1.04 \pm 0.44$ h phase advances, respectively (between group effect:  $F(2,34)=4.14$ ,  $p=0.03$ ). Post-hoc analyses revealed that 2.5h bright light produced greater phase shifts than both 1.5h bright light ( $p=0.04$ ) and room light ( $p=0.01$ ). 1.5h of bright light did not produce larger phase shifts than room light ( $p=0.60$ ).

**Conclusion:** Findings demonstrate that 2.5h of bright light on two weekend mornings, is necessary to advance circadian rhythms of teens by 1h, and 1.5h of morning bright light was no more effective than room light when timed to begin just after weekend MST. Our adolescent phase response curve to light predicts maximum phase advances 2-6h after MST, which may explain why the longer stimulus produced the largest phase shift.

**Significance:** These findings inform methods to phase advance teenagers to facilitate earlier sleep onset and increase school-night sleep duration.

## The Stability of Circadian Variables over Months

**Primary Author:** Charmane Eastman, Ph.D.

**Contributors:** Victoria A. Tomaka, BA (RUMC), Stephanie J. Crowley, PhD (RUMC)

**Introduction:** We conducted two studies that were similar for the first 10 days. In both studies, we determined each subject's morningness-eveningness score (MEQ), Mid-sleep on Free Days (MSF) from the Munich Chronotype Questionnaire (MCTQ), baseline dim light melatonin onset (DLMO), phase angle of entrainment, and free-running circadian period.

**Objective:** To examine the reproducibility of these circadian variables.

**Methods:** Ten African-Americans (6F, 4M) and 8 European-Americans (2F, 6M) participated in two IRB-approved studies with informed consent separated by 9 to 33 months (mean $\pm$ SD = 16 $\pm$ 7). Subjects slept in the lab on a fixed 8-hour sleep schedule similar to their usual sleep schedule for 4 days, followed by a circadian phase assessment to calculate baseline DLMO. Phase angle was the interval from DLMO to bedtime. There were 3 days of ultradian LD cycles producing forced desynchrony and thus free-running. Circadian period was determined from phase assessments before and after the days of free-running. For each circadian parameter, we made scatter plots with identical x and y axes and lines of unity to show when the variable would be exactly the same in both studies. We also calculated Pearson correlations.

**Results:** The MEQ score differed by less than 10 points between the two studies; MSF by 1 hour or less, except for 2 subjects; baseline DLMO by 1 hour or less except for 3 subjects; phase angle by 2 hours or less; and circadian period by 0.3 hours or less except for 2 subjects. All correlations were significant ( $p < 0.0001$ ): MEQ  $r = .85$ , MSF  $r = .78$ , baseline DLMO  $r = .81$ , phase angle  $r = .80$ , circadian period  $r = .78$ . A longer time between the two studies did not produce more variability. In this small sample, there were no differences between the sexes or between ancestry groups in the stability of these variables.

**Conclusion:** Circadian variables were relatively stable over months.

**Significance:** These circadian variables, which determine whether an individual is a morning-type person (lark) or an evening-type person (owl), are relatively stable over months.

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## Does Sleep/Wake Schedule Variability Affect the Circadian System of Adolescents?

**Primary Author:** Stephanie Crowley, PhD

**Contributors:** Ali Norwood, BS(RUMC); Lameese Akacem, PhD(RUMC); Charmane Eastman, PhD(RUMC)

**Introduction:** A well-established literature demonstrates a circadian phase delay during adolescence. Despite this delay in circadian timing, adolescents must wake early for school and typically sleep later on weekends resulting in irregular sleep/wake timing.

**Objective:** To examine whether sleep-wake timing variability was associated with circadian phase in high-school students during the school year.

**Methods:** Forty-six adolescents aged 14-17 years ( $16.2 \pm 1.1$  years; 29 females) who reported late bedtimes ( $>23:00$  on school nights;  $>00:00$  on non-school nights) and short school-night sleep duration ( $<7.5$  h) completed the study. Participants slept on their usual sleep schedules for 15 days at home before a dim light melatonin onset (DLMO) assessment (light  $<5$ lux), in which saliva was sampled every 30 minutes. DLMO was the time when salivary melatonin levels exceeded 4pg/mL. Nocturnal sleep timing and duration were quantified from wrist actigraphy (11-15 nights;  $14.5 \pm 1.1$  nights). Interquartile ranges (IQR) for sleep onset time, midsleep time, wake-up time, and sleep duration were computed and used as measures of sleep variability. Frequency of daytime naps were also examined.

**Results:** Average ( $\pm$ SD) school-night bedtime, midsleep time, and wake time were  $00:23 \pm 0:56$ ,  $03:28 \pm 0:34$  and  $06:27 \pm 0:31$ , respectively. School-night nocturnal sleep duration averaged  $6.1 \pm 1.0$ h. Average non-school night bedtime, midsleep time, and wake time were  $01:21 \pm 0:58$ ,  $05:28 \pm 0:54$  and  $09:37 \pm 1:13$ , respectively. Weekend nocturnal sleep duration averaged  $8.3 \pm 1.3$ h. Frequency of naps ranged from 0 to 9 during the 2 weeks. On average, bedtimes were  $1.0 \pm 0.1$ h later, wake times were  $3.2 \pm 0.2$ h later, and sleep durations were  $2.2 \pm 0.2$ h longer on non-school nights compared to school nights. Variability in bedtime, midsleep time, sleep duration, and nap frequency were not associated with DLMO phase. A trend emerged, however, for more variable wake times to be associated with later DLMOs ( $r=.28$ ,  $p=.06$ ).

**Conclusion:** These data suggest that irregular sleep timing does not predict a later circadian phase, nor does a later circadian phase lead to more variable sleep patterns in this group of older adolescents. The only exception may be irregular wake-up times; sleeping late on weekends may be more likely in adolescents with a later circadian phase or sleeping late on weekends delays the clock.

## **Mindfulness-Based Relapse Prevention Program for Substance Use and Co-occurring Mental Health Disorders**

**Primary Author:** Luke Swift, MSN, RN

**Introduction:** Substance use disorder and co-occurring mental health disorders are growing issues in today's healthcare system. Mental health disorders significantly increase the risk of relapse among individuals with a substance use disorder.

**Objective:** Use of mindfulness-based Interventions have shown to be effective in preventing relapse in the substance use disorder population with co-occurring disorders. Mindfulness-Based Interventions focus on the experiences of craving and negative affect and teach alternative responses to lessen the conditioned response of craving.

**Methods:** The Mindfulness-Based Relapse Prevention Program was developed and initiated on the Men's Integrated Treatment unit at a substance abuse treatment center in the Chicago Metropolitan area. The program was designed to teach important components of mindfulness skills, such as awareness of triggers and craving, mindful breathing, and observing thoughts. The 45-minute program was offered to all clients three days per week. The participants were asked to complete The Five-Facet Mindfulness Questionnaire (39-items) to assess their mindfulness skills at their first and last sessions. The clients were also asked to complete a brief program evaluation survey at the last session. A brief staff interview was conducted to assess the perceived benefit of the program.

**Results:** A total of 50 participants completed the pre-session questionnaire and 40 participants completed the post-session questionnaire. The pre-session questionnaire data showed low levels of mindfulness and acting with awareness and high levels of judging and impulsive reacting. The post-session questionnaire data showed significant improvement in levels of self-awareness and non-reactivity. The program evaluation and the staff interview suggest general satisfaction with the program and potential value of the program in preventing relapse.

**Conclusion:** The Mindfulness-Based Relapse Prevention Program is an inexpensive and feasible way to teach mindfulness skills among individuals struggling with a substance use disorder and their co-occurring mental health disorders. Follow-up monitoring of the discharged clients is necessary to assess the impact of the intervention in reducing relapse.

**Significance:** Substance use disorders and co-occurring mental health disorders are growing issues in the healthcare system, affecting an estimated 21.5 million people nationwide. Mental and substance use disorders will surpass all physical diseases as a major cause of disability worldwide by 2020. Despite current treatment options, 40-60% of individuals with a substance use disorder eventually relapse.

## Examining the Relationship between Veteran and Offspring Psychopathology

**Primary Author:** Crissy Glover, BA

**Contributors:** Philip Held, PhD (Rush), Randy Boley, BS (Rush), Niranjan Karnik, MD, PhD (Rush), Mark Pollack, MD (Rush), Alyson Zalta, PhD (Rush)

**Introduction:** It is established that children in military families have higher rates of internalizing and externalizing symptoms than civilian children. Moreover, PTSD in veteran parents has been linked to PTSD, depression, and anxiety in offspring. However, studies have failed to investigate the range of trauma-related pathology in veterans.

**Objective:** This research aims to explore how different expressions of veteran pathology associate with different psychological symptoms in offspring.

**Methods:** Data were collected from an IRB-approved data repository of 170 veterans seeking mental health services at a non-VA outpatient clinic. Veterans completed self-report measures assessing PTSD, depression, anxious arousal, chronic stress, alcohol use, and explosive anger. Veterans with a child aged 4-17 reported on their children's internalizing, externalizing, and attentional problems. Bivariate correlations were drawn between individual veteran pathologies and symptomology in offspring.

**Results:** 39 veterans were a parent of a child aged 4-17, and reported on children's internalizing, externalizing, or attentional problems. 30% (n=12) of veterans reported a child with at least one of these problems at a clinically significant level. Veteran report of child internalizing symptoms was significantly positively correlated with their own PTSD ( $r=0.43$ ,  $n=39$ ,  $p=0.006$ ), depression ( $r=0.34$ ,  $n=39$ ,  $p=0.031$ ), anxiety ( $r=0.35$ ,  $n=39$ ,  $p=0.029$ ), and stress ( $r=0.39$ ,  $n=39$ ,  $p=0.013$ ). There was a positive trend in the relationship between veteran stress and children's attentional problems ( $r=0.31$ ,  $n=39$ ,  $p=0.051$ ). There was a significant negative correlation between veterans' risky alcohol use and reported children's attentional problems ( $r=-0.42$ ,  $n=33$ ,  $p=0.014$ ).

**Conclusion:** Findings suggest that offspring psychopathology is common in samples of veterans with PTSD, depression, anxiety, and chronic stress. Findings counterintuitively demonstrate that higher rates of alcohol use in veterans were associated with fewer attentional problems in children. This could be because children become hypervigilant to avoid threat when parents are drinking. It could also showcase limitations of using self-report measures in samples endorsing probable alcohol abuse.

**Significance:** Findings support use of routine mental health screening of children of veterans with distress. Future research should explore mechanisms by which veteran distress is associated with offspring psychopathology to develop effective interventions for this population.



## Using Mindfulness to Manage Moral Distress

**Primary Author:** Elizabeth Vaclavik, DNP

**Contributors:** Beth A. Staffileno, PhD, FAHA, RN (Rush); and Elizabeth Carlson , PhD, RN (Rush)

**Introduction:** Moral distress was identified among oncology nurses, and of concern are the unfavorable correlations between moral distress and staff engagement.

**Objective:** The purpose of this quality initiative was to minimize moral distress by implementing a bundle of mindful interventions.

**Methods:** This initiative involved a convenience sample of 54 nurses on a 32 bed oncology unit. The 21-item Moral Distress Scale-Revised (MDS-R) was administered pre and post intervention to assess: 1) if staff experienced moral distress, and 2) whether moral distress could be alleviated using a bundle of mindful interventions. Nurses received an email describing the purpose of the survey and a direct link to Survey Monkey was available over a 2 week period. The bundle of mindful interventions were tailored to the identified stressor in the MDS-R. The bundle of mindful Interventions included: critical debriefs and support groups within 72 hours of a patient death or code; a memory tree of deceased patients on a wall in the break room; yoga sessions led by staff; and Code Lavendar bags containing a café beverage gift card, chocolate, tissues, aromatherapy and an inspirational message from the leadership. The final portion of the bundle was a six week program on mindfulness. Three months following implementation of the bundle, the MDS-R was again administered to the same 54 nurses. Analysis of results calculated a percentage decrease in the frequency staff experienced distress.

**Results:** All 27 respondents had a BSN degree or higher. Healthcare providers giving false sense of home was the most frequently reported morally distressful situation (81%). Results reflected a 46% decrease in frequency of distress from 81% pre-test to 44% post-test .

**Conclusion:** This quality initiative identified the presence of moral distress among oncology nurses and the positive impact of supportive and mindful interventions. Communication and mindfulness are important to enhance a healthy work environment.

**Significance:** This quality initiative responded to the presence of moral distress among hematology nurses by implementing a bundle of mindful interventions. These mindful interventions were not aimed at changing other's behaviors such as providing a sense of hope to patients, but at the nurse's perception of their environment, providing resilience to their environment.

## Neural Changes in Emotion Recognition Following Cognitive Training in Individuals at Risk for Psychosis

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**Contributors:** Abhishek Saxena, BA (RUMC); Hong Yin, PhD (Harvard University), David Dodell-Feder, MA (Harvard University), Sarah Hope Lincoln PhD (Harvard University), Matcheri Keshavan MD (Beth Israel Deaconess Medical Center), Larry Seidman PhD (Harvard University), Mor Nahum PhD (University of Jerusalem) Christine Hooker, PhD (RUMC)

**Introduction:** Deficits in social cognition are a prominent feature of schizophrenia that are present prior to the onset of frank psychotic symptoms and help predict long-term functional outcome, thus presenting a potential target for intervention in individuals at clinical high risk (CHR) for psychosis. Performance deficits in social cognition are associated with alterations in functional neural networks, including those that support abilities such as emotion recognition.

**Objective:** This study investigates how targeted social cognitive training alters activity and connectivity of functional networks engaged in facial emotion processing in CHR individuals.

**Methods:** 14 CHR subjects (7 male, mean age = 21.9) showing attenuated psychotic symptoms were included in the study and 14 matched healthy control subjects (HC) were included as a comparison group for functional neuroimaging. CHR subjects completed 40 hours (8 weeks) of targeted cognitive and social cognitive training. fMRI was acquired before and after training during performance of an emotion recognition task. Changes in emotional face processing network functional connectivity was evaluated using seed-based connectivity analyses and psychophysiological interaction (PPI) in regions involved in facial emotion perception, especially the amygdala and superior temporal sulcus (STS).

**Results:** CHR individuals showed significant improvements on measures of social cognition, including the emotion recognition task. Prior to training, CHR individuals demonstrated hyperactivity in the left orbitofrontal cortex, posterior cingulate cortex and amygdala that was reduced somewhat after training. CHR individuals also showed differences from HC in amygdala connectivity with the temporal and fusiform gyrus as well as reduced STS connectivity with prefrontal, temporal and posterior cingulate cortex that normalized following training.

**Conclusion:** These results suggest that targeted cognitive training may be effective in altering functional network connectivity in networks associated with psychosis risk and may be a useful tool for prevention or early intervention in individuals at risk for psychotic disorders.

## How Does Resource Loss Relate to Pain Interference?

**Primary Author:** Brittany Nguyen, BA

**Contributors:** Dr. Frances Aranda, PhD, MPH (RUMC); Linzy Wagner, BS (RUMC); Sara Tamizuddin, BS (RUMC); De'Andra Robertson, BA (RUMC); Mary Kennedy, BS (RUMC); Dr. Stevan Hobfoll, PhD (RUMC); Dr. John Burns, PhD (RUMC); Dr. Yanina Purim-Shem-Tov, MD (RUMC)

**Introduction:** Lifetime prevalence rates for anxiety disorders in women (30.5%) are higher than men (19.2%). Anxiety can stem from resource loss, which refers to personal, social, and/or material resources. Resource loss as it relates to anxiety can exacerbate pain interference—a term which refers to the consequence of pain on a person's ability to function in daily life. However, additional research is required to understand the relationships among resource loss, anxiety, and pain interference.

**Objective:** This study evaluates the impact of resource loss on pain interference in inner-city women by examining the role of anxiety. It is hypothesized that there will be a positive relationship among resource loss, anxiety, and pain interference.

**Methods:** 192 women, ages 18-40, experiencing acute pain within targeted areas were recruited from Rush University Medical Center's (RUMC) Emergency Department (ED). Women participated in a face-to-face survey-interview within two-weeks of their ED visit. The measures used were two based on Patient Reported Outcomes Measurement Information Systems (PROMIS) and Resource Loss. The study was approved by RUMC's Institutional Review Board and informed consent was obtained. A three-step hierarchical regression analysis was conducted to examine pain interference and the effects of demographic controls, resource loss, and anxiety.

**Results:** In Step-2, resource loss ( $\beta = 0.21$ ,  $p < 0.05$ ) significantly predicted past-week pain interference which accounted for 6.9% of the variance. In Step 3, anxiety ( $\beta = 0.37$ ,  $p < 0.001$ ) was significant in predicting past-week pain interference, accounting for 11% of the variance above and beyond the previous steps. The full model significantly accounted for 17.9% of the variance in past-week pain interference.

**Conclusion:** As hypothesized, resource loss was positively related to past-week pain interference. However, when anxiety was added to the model, resource loss was no longer significant.

**Significance:** Resource loss is an important risk factor to consider when evaluating pain interference among inner-city women. Perhaps providing service recommendations to off-set the type of losses reported or mental health services for anxiety can potentially ameliorate the inability to function in their daily lives.

## Clinical Outcomes of Arthroscopic Capsular Release for Idiopathic Adhesive Capsulitis in the Lateral Decubitus Position

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**Introduction:** Idiopathic glenohumeral adhesive capsulitis impairs patient motion and function. Arthroscopic capsular release is classically performed in the beach-chair position with incomplete capsule release and manipulation under anesthesia.

**Objective:** The purpose of this study is to report outcomes following arthroscopic 360-degree capsular release in lateral decubitus position. We hypothesized that patients would have improvements in range of motion (ROM) and function with low rate of complications.

**Methods:** A retrospective case series of patients undergoing arthroscopic capsular release in the lateral decubitus position for idiopathic adhesive capsulitis with minimum 2-year follow-up was conducted. Patient demographics, preoperative ROM, postoperative ROM, postoperative outcome scores, complications, and reoperations were recorded. Paired t-tests were used to compare preoperative and postoperative ROM, with  $p < 0.05$ .

**Results:** Overall, 43 patients were identified, of which 10 were excluded due to posttraumatic etiology. Of the remaining 33 patients, 27/33 (81.8%) completed a minimum follow-up of 2-years. The mean age was  $54.8 \pm 7.4$  years and 73% female, with duration of symptoms  $16.2 \pm 21.0$  months (range 2 to 125). Hypothyroidism was present in 6% and diabetes present in 33%. Pre-operatively, patients had  $1.8 \pm 1.1$  preoperative corticosteroid injections (range 0-5). Active forward flexion improved from  $115.0 \pm 21.9$  degrees to  $156.2 \pm 16.1$  degrees at final follow-up (mean difference 41.2, 95% confidence interval [33.7, 48.7],  $p < 0.001$ ). Active external rotation with the arm adducted improved from  $28.1 \pm 16.3$  degrees preoperatively to  $56.8 \pm 15.7$  degrees at final follow-up (mean difference 27.7, 95% confidence interval [19.1, 36.3],  $p < 0.001$ ). Significant range of motion improvements were seen even as early as 2-weeks postoperative (Figure). Overall, final outcomes were excellent, including VAS pain of  $0.2 \pm 0.5$ , SANE  $96.3 \pm 4.9$ , SST  $11.3 \pm 1.2$ , and ASES  $97.0 \pm 4.7$ . There were no revision surgeries and no complications.

**Conclusion:** Arthroscopic 360-degree capsular release in the lateral decubitus position for idiopathic adhesive capsulitis results in a significant early and lasting improvement in range of motion, excellent functional outcomes, and low revision and complication rates.

**Significance:** By performing capsular release in the lateral position, it has the potential to allow 360-degree capsular release and eliminate the need for manipulation and the potential complications that are commonly attributed to manipulation under anesthesia such as humeral fracture.

## **Ablation of IGF-1R Signaling in Osteochondroprogenitor Cells Induces a Substantial and Persistent Attenuation of Skeletal Development**

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**Introduction:** The type 1 insulin-like growth factor ligand and receptor (IGF-1/IGF-1R) both have key anabolic roles in postnatal skeletal development. However, their associated signaling network remains poorly understood because IGF-1/IGF-1R knockouts (KO) mice die prenatally for systemic complications.

**Objective:** Recent reports have suggested a key role for periosteal cells in skeletal development, and as such, periosteally-localized IGF-1/IGF-1R KO mice present a viable means to investigate this pathway without systemic complications. As we have previously identified and traced a population of periosteally-localized Prx1+ progenitor cells, we generated a new line of mutant mice in which the entire Prx1+ cell lineage was IGF-1R deficient (IGF1KO). To test the hypothesis that IGF-1R signaling in osteochondroprogenitors (OCP) is essential for normal bone development and homeostasis, we characterized the skeletal ontogenesis of IGF1KO mice.

**Methods:** Specifically, we generated IGF1KO mutant mice by crossing Prx1-Cre+ mice with igf1r-floxed gene and characterized their hind-limbs from postnatal day 1 (P1) to 12 weeks (W). In vivo, we first evaluated skeletal growth by longitudinally measuring the tibial length of IGF1KO mice and their control littermates. Next, we evaluated skeletal growth by labeling the developing bone front with injections of calcein (day 2) and alizarin red (day 7). For post-mortem studies, tibiae from P1 to 12W mice were harvested and fixed in 4% PFA. For histology, samples were decalcified, embedded in paraffin, sectioned, and stained for H&E. For structural measurements, fixed tibiae were evaluated by mCT at 8W and 12W.

**Results:** From P1 to P10, IGF1KO tibiae were shorter than controls (30%,  $p=0.05$ ). This relative deficiency was reduced to 15% at 12W. As measured by post-mortem bone histomorphometry analysis, IGF1KO mice had decreased mineral apposition rate (28%) and bone formation rate/bone volume (50%) compared to controls. At all times, IGF1KO mice had a thicker, hypercellular periosteum and porous cortical bone compared to controls. At both times, IGF1KO mice were skeletally deficient compared to controls: they had a reduced bone volume fraction (17%,  $p=0.059$ ) in the trabecular bone region and a reduced cortical thickness (20%,  $p=0.05$ ) in the diaphysis.

**Conclusion:** Together, our results suggest that IGF-1R signaling derived from periosteally-localized OCP cells is essential for normal skeletal development. Studies are in progress to further characterize the nature of such mechanisms.

## Biomechanical Analysis of All-Suture Suture-Anchor Fixation for Biceps Tenodesis

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**Introduction:** Interference screws and conventional suture anchors have commonly been described for fixation of the long head of the biceps tendon (LHBT) to the end of the humerus. Recently, all-suture suture-anchor (ASSA) constructs have been introduced as an alternative for soft-tissue to bone fixation.

**Objective:** The purpose of this study was to determine the biomechanical properties of ASSA fixation for LHBT fixation during biceps tenodesis.

**Methods:** Twenty-two fresh-frozen human cadaveric shoulders (average age  $55.45 \pm 6.19$  years; 100% male) were randomized into 3 subpectoral biceps tenodesis treatment groups: ASSA (N=7), conventional suture anchor (CSA, N=7), and interference screw (IS, N=8) (Smith & Nephew, Andover, MA). Each construct was cyclically loaded from 5 to 70N for 500 cycles at 1Hz, and then pulled to failure at 1mm/s. Cyclic displacement at 500 cycles, maximum load during pull-to-failure testing, and failure mode were recorded. The groups were compared with a one-way ANOVA and post-hoc Bonferroni analysis, with  $p < 0.05$  considered significant.

**Results:** During cyclic testing there were no failures in the ASSA or CSA groups, and 3 tendon tear failures at the tendon-screw interface in the IS group. The IS group had significantly lower displacement ( $7.19 \pm 2.98\text{mm}$ ) at cycle 500 compared to the ASSA ( $11.80 \pm 2.38\text{mm}$ ,  $p = 0.019$ ) and the CSA ( $14.41 \pm 2.25\text{mm}$ ,  $p < 0.001$ ) groups. There was no statistically significant difference in displacement between the ASSA and CSA groups ( $p = 0.204$ ). There were no significant differences in maximum load between the groups ( $p = 0.503$ ), with mean maximum loads of  $230.61 \pm 55.08\text{N}$ ,  $192.33 \pm 66.58\text{N}$ ,  $219.45 \pm 61\text{N}$  for the ASSA, CSA, and IS groups, respectively.

**Conclusion:** The use of ASSA results in maximum loads similar to conventional methods including CSA and IS for biceps tenodesis, with a low overall failure rate.

**Significance:** Clinical failures following biceps tenodesis are uncommon but when they occur, they are devastating for the patient. By determining the optimal soft-tissue to bone fixation construct, the clinical outcomes in patients undergoing the biceps tenodesis for LHBT pathology may improve. The data from this study demonstrate ASSA biomechanical properties are similar to traditional fixation devices with regard to ultimate failure load.

## Age-Dependent Cortical Bone Geometric and Mechanical Property Phenotype in CD26 Deficient Mice

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**Introduction:** CD26 (dipeptidyl peptidase IV [DPP-IV or DPP-4]) is a protease that cleaves circulating chemokines, which is of particular interest in bone physiology because animals deficient in CD26 have impaired osteoclast development.

**Objective:** To test the hypothesis that CD26 KO mice have higher bone mass compared to WT mice, we measured bone length, cortical geometry, whole bone mechanical, cortical bone material, cortical bone matrix composition and trabecular architecture of CD26 KO and WT mice, taking into account the possibility of age-related effects.

**Methods:** A total of n=43 intact CD26 KO and WT male mice aged 1, 3 and 6 months were analyzed. Left femurs were fixed and right femurs were frozen. Bones were  $\mu$ CT scanned and two regions of interest were analyzed: 1) midshaft for cortical bone geometry and 2) distal growth plate to 30% of the total femoral length for trabecular bone architecture. Mechanical and Fourier Transform Infrared Imaging were completed. All results are reported as means  $\pm$  standard deviation.

**Results:** The main results showed a significant interaction between genotype and age for femoral length as KO mice had ~1% longer femurs at 1 and 3 months, but ~2% shorter femurs at 6 months than WT mice ( $p = 0.05$  genotype and age, 2-way ANOVA). Cortical thickness and cortical area also varied in the two genotypes as a function of age ( $p = 0.011$  and  $p = 0.031$ , respectively, genotype and age interaction). KO mice had consistently 8% larger medullary area than WT mice (Fig. 1,  $p = 0.022$ , genotype).

**Conclusion:** We determined that CD26 KO mice have a mild age-dependent, post-natal developmental bone phenotype. These differences were found mainly in the cortical bone compartment. Despite having only modest effects on the overall bone phenotype, our findings suggest that CD26 affects the endocortical surface more than the periosteal surface.

## Specific ablation of Prx1Cre-expressing cells results in impaired long bone fracture healing

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**Introduction:** Despite substantial advances in orthopedic care and surgical technology, fracture nonunion remains a clinically important problem. The use of mesenchymal stromal cells (MSC) in fracture repair has been receiving special attention due to their potential role in tissue regeneration. Paired-related homeobox protein family is implicated to regulate MSC fate. Our preliminary data in Prx1CreER;ROSA26 reporter mice demonstrated Prx1-enhancer-driven expression of LacZ in periosteum of postnatal tibias, as well as rapid accumulation of chondrocytes, osteoblasts, and perivascular cells derived from Prx1-lacZ expressing cells into the callus of fractured tibias.

**Objective:** The purpose of this study is to verify whether multipotent Prx1-expressing cells are essential in fracture healing.

**Methods:** The role of Prx1 was evaluated using a tibial fracture-healing model in 10-12 week old Prx1CreER;R26DTAfl/+ male mice, in which Prx1-expressing cells were ablated when tamoxifen was administered. 4-OH-tamoxifen was injected intraperitoneal 0.5mg/mouse/day for 6 days started two days before fracture. Mice were euthanized and the tibias were dissected 7 and 14 days after fracture for micro-CT analysis. Callus samples were fixed and decalcified, and subjected to frozen sections and histological staining. Immunofluorescence studies were performed to characterize the phenotype of the cells involved in the formation of fracture callus.

**Results:** Micro-CT revealed that the total volume of callus and volume of soft tissue was significantly decreased in Prx1CreER;R26DTAfl/+ mice compared to their control littermates. Histology analysis showed that, at day 7 after fracture, the fracture gap was filled with cartilage and newly-formed woven bone. Safranin O/Fast-green staining indicated that cartilage formation was reduced in Prx1CreER;R26DTAfl/+ mice. Sox9, an important transcription factor in the chondrogenic commitment of the progenitors during fracture healing, was less expressed in the soft callus of Prx1 mutant mice.

**Conclusion:** In conclusion, these findings provided evidence that Prx1-expressing cells may play a crucial role in promoting fracture healing by serving as multipotent progenitors.

**Significance:** These findings may provide a novel insight into the molecular mechanisms regulating fracture healing, and help develop new potential therapeutic targets for accelerating bone repair.



## Factors Influencing Patient Selection of an Orthopaedic Sports Medicine Physician

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**Introduction:** The rise in consumer-centric health insurance plans has increased the importance of patients in choosing a provider. Hence, understanding the process of physician selection may allow physicians to better satisfy patient expectations.

**Objective:** To evaluate factors that patients consider when choosing an orthopaedic sports medicine physician.

**Methods:** 1,077 patients who sought treatment by three sports medicine physicians were administered an anonymous questionnaire. The questionnaire included 19 questions asking respondents to rate the importance of specific factors regarding orthopaedic sports medicine physician selection on a 1 to 10 scale, with 10 being designated as 'Very important'. The remaining 6 questions were multiple-choice questions regarding the following criteria: physician age, appointment availability, clinic waiting room times, travel distance, and medical student/resident involvement.

**Results:** Of 1,077 consecutive patients administered the survey, 382 (35%) responded. Of these 59% (n=224) were male and 41% (158) female. In rating the 19 criteria in terms of importance, patients rated board certification ( $9.12 \pm 1.88$ ), being "well-known" for a specific area of expertise ( $8.27 \pm 2.39$ ), and in-network provider status ( $8.13 \pm 2.94$ ) as the three most important factors. Radio, television, and internet advertisement were rated by patients as the least important. Regarding physician age, 63% of patients would consider seeking a physician who is younger than 65 years. 78% of patients would consider seeking a different physician if no appointments were available within 4 weeks.

**Conclusion:** Our results suggest that board certification, being 'well-known' for a specific area of expertise, and health insurance in-network providers may be the most important factors influencing patient selection of an orthopaedic sports medicine physician. Advertisements were of least importance to patients. Patient preferences varied regarding ideal physician age, clinic appointment availability, student/resident involvement, and travel distance. In the context of healthcare delivery and reimbursement become increasingly consumer-centered, understanding the process of provider selection is important.

**Significance:** In the context of healthcare delivery and reimbursement become increasingly consumer-centered, understanding the process of provider selection is important.

## Outcomes of Latarjet for Recurrent Anterior Shoulder Instability in Females

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**Introduction:** A variety of bone grafts have been described for reconstruction of glenoid bony deficiency in the setting of recurrent anterior shoulder instability. While the Latarjet procedure has been described with excellent outcomes, most studies contain cohorts that are >90% male, and clinical outcomes following Latarjet in females are poorly understood.

**Objective:** To assess the clinical patient reported outcomes of female patients with recurrent anterior shoulder instability treated with the Latarjet procedure.

**Methods:** Consecutive female patients with a minimum 15% glenoid bone loss with recurrent anterior instability undergoing anterior glenoid bone reconstruction via the Latarjet technique were analyzed. Male patients, as well as patients with generalized hyperlaxity or neurologic injury were excluded. Patients completed preoperative and postoperative surveys containing the VAS, ASES, SANE, SST, and WOSI index at a minimum of two years. Statistical analysis was performed with T-tests, with  $P < 0.05$  considered significant.

**Results:** A total of 16 female patients (average age  $33 \pm 12.5$  years) with an average follow-up of 40 months (range, 23-101) were included. Postoperatively, there were statistically significant improvements in VAS (4.3 to 2.1,  $P = 0.003$ ), ASES (49 to 78,  $P = 0.008$ ), SANE (36.5 to 76,  $P = 0.01$ ), SST (4.6 to 9.4,  $P < 0.001$ ), and WOSI (28% to 78%,  $P = 0.02$ ). One patient (6.25%) developed arthrosis and flattening of the medial aspect of the humeral head and underwent a total shoulder arthroplasty 6 months following the Latarjet procedure, which was unsuccessful and revised to a reverse total shoulder arthroplasty 3 months after.

**Conclusion:** At an average follow-up of over 3 years, the Latarjet procedure for recurrent anterior shoulder instability results in a clinically stable joint with excellent clinical outcomes that are comparable to historical controls of male patients undergoing this procedure.

**Significance:** This information can be used to counsel female patients who are considering the Latarjet procedure for reconstruction of glenoid bony deficiency in the setting of recurrent anterior shoulder instability.

## **Hypertrophy of the Anterior Coracoacromial Ligament as an Etiology of Shoulder Pain in the Young Overhead Athlete**

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**Introduction:** Shoulder pain in young, overhead athletes is commonly thought to result from instability and SLAP pathology. However, we encountered a series of young, overhead athletes with shoulder pain due to primary subacromial space pathology. All had pain at the anterolateral (AL) corner of the acromion and a thickened anterior Coracoacromial ligament (CAL).

**Objective:** We report the clinical characteristics, pathology, and results of treatment of this previously unreported association.

**Methods:** 92 young (mean age 19 [13-26 years]) overhead athletes presented with shoulder pain unresponsive to conservative treatment. All underwent EUA and arthroscopy. Patient demographics, return to sport, physical exam findings, ASES, SST, and VAS scores are reported.

**Results:** Of the 92 patients (42 males, 38 females), 76% had pain at the AL acromial corner; 71% had pain with an overhead arc of motion from Abd/ER to Abd/IR position; and 53% had SLAP-type physical exam findings, but none had instability symptoms. Patients most commonly participated in: Baseball (39%), Swimming (16%), Softball (15%), and Volleyball (11%). At average follow-up of 2.2 years (1-5), all had returned to the former level of overhead sport activity. Average return to sport was 5 months (3-8). Average pre-op scores: ASES= 60, SST= 7.5, and VAS pain= 4.3 and post-op scores: ASES= 98, SST= 11.7, VAS= 0.3. There were no complications, re-operations, or occult instability revealed.

**Conclusion:** Symptomatic, hypertrophic anterior CAL is a variant of impingement, most likely due to overuse in the younger, overhead athletic population. Although instability, SLAP lesion, and labral injury are recognized as overuse injuries in this patient population, primary subacromial pathology is thought to exist primarily in older patients.

**Significance:** The clinical significance in this series represents a primary, subacromial space pathology resulting from overuse. Clinicians should maintain a high index of suspicion for this pathology when evaluating young, overhead athletes.

## **Transarterial Chemoembolization for Hepatocellular Carcinoma using Doxorubicin Eluting Beads with or without Ethiodized Oil: A Review of Explant Histology in Patients Bridged to Liver Transplantation**

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**Introduction:** Transarterial Chemoembolization (TACE) using Doxorubicin-Eluting Beads (DEB-TACE) is a widely accepted locoregional treatment for Hepatocellular Carcinoma (HCC). Comparisons between DEB-TACE and Conventional TACE (C-TACE) have shown mixed results in tumor response and patient survival. Some authors have attributed the absence of ethiodized oil (EO) in DEB-TACE regimens as a potential reason for its lack of superiority to C-TACE.

**Objective:** The purpose of this study is to compare liver explant histology of patients undergoing DEB-TACE versus those undergoing DEB-TACE with ethiodized oil (EDEB-TACE) for HCC.

**Methods:** All patients with HCC that underwent TACE at our institution between 1/2010 and 6/2016 were reviewed. Those within Milan criteria and bridged to liver transplantation were identified. Patients were excluded if they underwent alternative loco-regional tumor therapy. Treatment parameters and patient demographics/disease characteristics were evaluated. Pathologist reports for explant tumor histology and percent tumor necrosis were reviewed as endpoints. Liver related complications using SIR guidelines were studied.

**Results:** 117 patients with HCC underwent TACE, of which 48 were within Milan criteria and bridged to liver transplantation. 16 were excluded due to prior/subsequent alternative tumor therapy. Explant histology for 26 patients (34 tumors) undergoing DEB-TACE and 6 undergoing EDEB-TACE were reviewed. Mean number of treatment sessions was 2.3 in the DEB-TACE group and 2 in the EDEB-TACE group. The mean time from treatment to transplant for the DEB-TACE and EDEB-TACE groups was 91.2 days and 153.6 days respectively ( $p=0.34$ ). No significant differences between the groups regarding doxorubicin dose, age, sex, BCLC staging, portal vein invasion, liver function (Child-Pugh) or tumor grading. The mean percent tumor necrosis at explant for the DEB-TACE group was 74.7% (range 5-100%, STD 32.3) and for the EDEB-TACE 93% (range 70-100%, STD 11)  $P=0.18$ . There was no significant difference in treatment related liver toxicity.

**Conclusion:** Adding ethiodized oil to existing DEB-TACE regimens is safe and showed a trend towards increased tumor necrosis at explant histology. More studies with larger sample sizes are necessary to further evaluate this hypothesis and demonstrate a statistically significant response.

**Significance:** Although this difference in percent tumor necrosis is not yet significant between the two groups due to small sample size, the trend is encouraging. Institutions across the country should consider adding ethiodized oil to existing DEB-TACE regimens to maximize tumor necrosis at time of transplant and thus improve patient outcomes.

## Effect of swelling and loading on stiffness in articular cartilage: a microindentation study

**Primary Author:** Catherine Yuh, MS

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**Introduction:** Tissue swelling and stiffness loss may compromise cartilage function. The current understanding of how tribological stress on cartilage affects mechanical and swelling properties remains unclear. Proteoglycans play a role in osmotic swelling of cartilage, contributing to its load-bearing function. Experimentally, by using different saline concentrations in the lubricant, cartilage swelling conditions can be altered.

**Objective:** In this study, we performed microindentation tests to analyze the change in stiffness of cartilage explants after ex vivo articulation under various contact loads and lubricant salinity concentrations.

**Methods:** Five cartilage explants from a freeze-thawed 24-week-old bovine stifle joint were placed in 1X PBS at 4°C. Following equilibrium, two explants were placed in each PBS concentration group (0.1X, 10X). All the explants were articulated against a 32mm CoCr ball for 1hr in a tribological joint simulator. In each PBS group of two explants, one explant was loaded at 20N, while the other was loaded at 60N during articulation. One explant was loaded at 40N in 1X PBS concentration to obtain a center-point for statistical analysis. Microindentation was performed with a 20um-spherical indenter to measure cartilage surface stiffness before and after articulation, in the explants' respective PBS concentrations. The data was analyzed using ANOVA.

**Results:** An increase in compressive load significantly increased stiffness in the articulated region. The results indicate that stiffness was influenced more by load than salinity (Load  $p < 0.0001$ , Log[Salinity]  $p = 0.0032$ ). At high load, the cartilage significantly stiffened after articulation, regardless of salinity, although the effect increased with salinity. At low load, there was significant softening (0.1X) or no change in stiffness (10X) on the cartilage following articulation.

**Conclusion:** In contrast to clinical observations of stiffness loss following cartilage degeneration, our results demonstrated that cartilage surface stiffness increases with increasing ex vivo articulation load. Limitations of this study include low sample size and the use of freeze-thawed tissue.

**Significance:** This study suggests that a stiffening response may be a precursor to cartilage softening. Cartilage stiffening may promote damage, resulting in secondary cartilage softening during cartilage degeneration in diseases such as osteoarthritis. Understanding the short-term responses of cartilage wear can provide novel perspectives of mechanisms of cartilage degeneration.

## Contributors to Knee Load Redistribution using Flexible Footwear

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**Introduction:** Flexible footwear reduces knee loads such as the knee adduction moment (KAM) in patients with knee osteoarthritis (OA), but the specific mechanisms underlying these reductions are not clear. Foot-mediated biomechanical interventions such as modified footwear work from the ground up to reduce KAM, and these reductions may be associated with alterations in ankle kinetics and stride length.

**Objective:** The primary aim of this study is to test the hypothesis that a decrease in KAM from walking with flexible footwear is associated with reduced ankle kinetics due to a reduction in stride length.

**Methods:** Participants with medial knee OA (KL 2/3) underwent 3-D gait analysis, completing five walking trials in their 'own shoes' and in flexible shoes. The primary outcomes of interest were the KAM during the first (KAM1) and second (KAM2) halves of the stance phase, stride length, and 3D ankle kinetics.

**Results:** When walking in the flexible shoe, thirty-nine individuals (31F, 60.2±8.7yrs, 30.0±4.2kg/m<sup>2</sup>) reduced their stride length ( $p=0.014$ ) and lowered their KAM1 5.37% ( $p=0.004$ ) and KAM2 3.0% ( $p=0.020$ ) despite walking at similar speeds ( $p=0.188$ ). This reduction was associated with a reduction in the plantarflexion moment ( $r=0.397$ ,  $p=0.012$ ) moment as well as stride length ( $r=0.380$ ,  $p=0.017$ ). The reduction in stride length was associated with a reduction in the plantarflexion moment ( $p=0.397$ ,  $p=0.003$ ). Only the change in stride length remained in the backwards multiple regression model ( $p=0.022$ ) during the first half of stance.

**Conclusion:** Flexible footwear reduces stride length without affecting speed, lowering the KAM during early stance but not later in stance. The reduction in stride length, reduced ankle plantarflexion moments, and a downward trend in the dorsiflexion moment suggests collinearity of stride length and sagittal plane ankle moments with respect to KAM. Stride length, but not speed, may greatly impact overall loading throughout the lower extremity.

## Dynamic 3D Mapping of Isometric Anterior Cruciate Ligament Attachment Sites on the Tibia and Femur

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**Introduction:** Positioning of the anterior cruciate ligament (ACL) at the most isometric position is essential to limit the degree of stress and strain on the graft. The intra-articular distances from the medial wall of the lateral femoral condyle (MWLFC) to the tibial plateau vary with knee flexion. Thus, identifying the graft orientation such that the intra-articular length change is the least throughout knee range of motion will reduce stress on the graft.

**Objective:** Utilizing 3D models of the knee, the objective of this study was to determine intra-articular length change throughout knee range of motion, thereby mapping the isometric regions and determining the most isometric point for ACL reconstructions.

**Methods:** 3D CT point-cloud models of 5 cadaveric knees were obtained at multiple flexion angles from 0° to maximum flexion. A 60-69 point grid was placed on the MWLFC of each knee and a 20 point grid was placed on the tibial plateau over the ACL footprint. Intra-articular lengths were then calculated from the tibial points to each point on the MWLFC at each of the flexion angles. The length changes were normalized and compared with respect to 4 groupings of points on the MWLFC.

**Results:** Throughout full range of motion, the ranges of normalized length change represented as a percentage of the maximum intra-articular length from the tibial center point were as follows: the area encompassing the anteromedial bundle of the ACL changed 21% of the normalized length; the area representing the posterolateral bundle changed 27%, the area slightly anterior to these changed 15%, and the most anterior area changed 32%.

**Conclusion:** From 0° to 40° of flexion, length changes are minimal compared to 40° to maximum flexion. The most isometric region appears to encompass the anterior portion of the AM bundle footprint in addition to some of the area just anterior to this region.

## Cell-Induced Corrosion Is Associated with a Column-Like Damage Pattern in Wrought CoCrMo Modular Head Tapers

**Primary Author:** Deborah Hall, BS

**Introduction:** Corrosion damage modes within modular head-neck junctions of total hip replacements are diverse, resulting in different damage patterns. One damage pattern within head tapers is that of columns of parallel troughs that run perpendicular to the initial machining marks in the proximal to distal direction. Cells have been observed on column damage surfaces. It is possible that the presence of cells and the occurrence of column damage are related.

**Objective:** The purpose of this study was to determine the prevalence and extent of column damage among head tapers with moderate to severe corrosion, and whether cell-induced corrosion is associated with the occurrence of column damage.

**Methods:** 776 retrieved CoCrMo femoral heads were studied. Corrosion damage was evaluated under a stereo-microscope and scored for damage severity. 165 retrieved heads had either moderate corrosion (n=57) or severe corrosion (n=108). The presence column damage was recorded. Replicas of the head tapers were measured with a non-contact 3D profiler. Selected heads were sectioned to visualize damage patterns in a scanning electron microscope.

**Results:** Column damage was observed in 28% of moderately to severely corroded head tapers and stretched proximal to middle within the taper. The troughs exhibited no material pile-up on the sides, had an etched surface and were often filled with organic residue. The trough profile was oddly shaped, with a depth of 20-40µm. Three tapers had clear evidence of preserved cells adherent to the column damage. Based on morphology and size, the cells appeared similar to macrophages. Etching trails exposing crystallographic features were associated with the cells.

**Conclusion:** Column damage is a prevalent occurrence, covering a large surface area and reaching a depth of 40µm, thus being an important contributor to material loss. Column damage is (electro)chemical in nature, as the troughs start proximally, occur independent of contact with the stem taper, and have an etched appearance. Etching trails were associated with preserved cells. Further analyses are warranted to determine whether column damage is primarily the result of cell-induced corrosion or whether cells are secondarily attracted to these sites.

**Significance:** It is imperative to minimize total hip replacement failures due to corrosion and subsequent adverse tissue reactions. This study provides a representative in depth analysis of an important damage mode contributing to material loss. This study will help to enable appropriate counter measures.



## 90-Day Complications Following the Latarjet Procedure

**Primary Author:** Michael O'Brien, MA

**Contributors:** Rachel M. Frank, MD (RMC); Bonnie Gregory, MD (RMC); Eamon Bernardoni, MS(RMC); Nikhil N. Verma, MD(RMC); Brian J. Cole, MD MBA (RMC); Gregory P. Nicholson, MD(RMC); Anthony A. Romeo, MD(RMC)

**Introduction:** The utilization of the Latarjet procedure for the treatment of anterior shoulder instability has increased exponentially over the past two decades. Relatively little data on short-term complication rates following Latarjet is available, though some authors have reported complication rates as high as 25%.

**Objective:** The purpose of this study was to describe the rate and type of complications occurring within 90-days following the Latarjet procedure for anterior glenohumeral instability.

**Methods:** total of 146 consecutive patients underwent the Latarjet procedure for anterior glenohumeral instability by fellowship-trained surgeons from a single institution between 2007-2016. Indications for Latarjet included primary or recurrent anterior instability with clinically significant anterior glenoid bone loss and/or failed prior arthroscopic stabilization. Patients undergoing Latarjet after prior glenoid bone grafting were excluded. All complications that occurred within 90 days of surgery were analyzed.

**Results:** Eight patients were lost to follow-up within 90 days of surgery, while two patients were excluded for prior bone graft procedures, leaving 136 patients (average age  $28.3 \pm 11.8$  years, 76% male) available for analysis, for an overall follow-up rate of 92%. There were 10 total complications within 90 days of surgery, for an overall short-term complication rate of 7.4%. Five of these complications required subsequent surgery, including 2 for recurrent instability (1.5%), 2 for infection (1.5%) and 1 for a musculotaneous nerve palsy (<1%). The remaining 5 complications were transient, resolving with non-operative treatment. No cases of hardware failure or graft osteolysis were reported.

**Conclusion:** The overall 90-day complication rate following Latarjet for anterior shoulder stabilization is 7.4%, substantially lower than the previously described rate of 25%. In 5 cases, complications led to subsequent surgery, including 2 conversions to arthroplasty, while in the remaining 5 cases, the complications were transient and resolved with non-operative treatment.

**Significance:** This information can be used to counsel patients on the risks of early complications following Latarjet.

## **Long-Term Clinical Outcomes After Microfracture of the Glenohumeral Joint: Minimum 8-Year Follow-up**

**Primary Author:** Kevin Wang, BS

**Contributors:** Eric Cotter, BS(Rush); Rachel Frank, MD(Rush); Annabelle Davey, BS(Rush); Charles Hannon, MD(Rush); Timothy Leroux, MD(Rush); Anthony Romeo, MD(Rush); Brian Cole, MD/MBA(Rush)

**Introduction:** Microfracture is an effective, minimally-invasive surgical treatment for full-thickness cartilage defects of the knee; however, little is known regarding outcomes following microfracture in the shoulder.

**Objective:** The purpose of this study is to present long-term clinical outcomes of patients undergoing microfracture of full-thickness articular cartilage defects of the glenohumeral joint.

**Methods:** Sixteen consecutive patients (17 shoulders) who underwent arthroscopic microfracture of the humeral head and/or glenoid surface between 2001 and 2008 were retrospectively reviewed. All patients completed preoperative and postoperative surveys containing the visual analog scale (VAS), American Shoulder and Elbow Surgeons (ASES) score, and simple shoulder test (SST). Complications and reoperations were analyzed. Failure was defined by reoperation, including conversion to arthroplasty.

**Results:** Of the original 16 patients (17 shoulders), 14 shoulders in 13 patients (6 males, 7 females) were available for follow-up at an average  $10.2 \pm 1.9$  years following microfracture (range, 8.5 to 15.8 years), for an overall clinical follow-up rate of 82%. The patients had an average age of  $36.1 \pm 12.9$  years at time of microfracture. The average size of humeral and glenoid defects was 5.07 cm<sup>2</sup> (range, 1.0-7.8 cm<sup>2</sup>) and 1.66 cm<sup>2</sup> (range, 0.4-3.8 cm<sup>2</sup>), respectively. Three patients (3 shoulders - 21.4%) progressed to shoulder arthroplasty at an average 5.7 years (range, 0.2 to 9.6 years) after microfracture. For the remaining patients there were statistically significant improvements in VAS ( $p < 0.001$ ), ASES ( $p < 0.001$ ) and SST ( $p = 0.002$ ) compared to preoperative values, and there was no significant change in VAS, SANE, or ASES between short-term follow-up (2.3 years) and final follow-up (10.2 years).

**Conclusion:** The management of full-thickness symptomatic chondral defects of the glenohumeral joint is challenging. For some patients, microfracture can result in enduring improved function and reduced pain, however, in this small series, 21.4% of patients required conversion to arthroplasty less than 10 years following the index microfracture procedure. Additional studies with larger patient cohorts are needed.

**Significance:** To date, little is known regarding long-term clinical outcomes of glenohumeral microfracture. This study presents a small, retrospective case series that provides valuable data on this important topic.

## Randomized Prospective Analysis of Arthroscopic Suprapectoral and Open Subpectoral Biceps Tenodesis

**Primary Author:** Brian Forsythe, MD

**Contributors:** William Zuke, BA (Indiana University School of Medicine), Beatrice Go, BS (UIC), Adam Yanke, MD (MOR), Nikhil Verma, MD (MOR), Anthony Romeo, MD (MOR)

**Introduction:** Surgical treatment for biceps pathology can include tenotomy or various forms of tenodesis. Techniques for osseous tenodesis include suprapectoral osseous fixation or subpectoral osseous fixation.

**Objective:** It is unclear if there is a clinical or surgical benefit of performing an open subpectoral biceps tenodesis (OBT) versus arthroscopic suprapectoral biceps tenodesis (ABT). This randomized clinical trial assesses these two techniques.

**Methods:** Patients diagnosed with biceps tendinopathy who met the inclusion criteria were randomized into the ABT or the OBT group. Prior to surgery, patients were asked a series of questions regarding their anterior shoulder pain and underwent a subsequent shoulder exam. Follow-up was completed at 3 months, 6 months, and 1 year time points, during which a shoulder exam or patient questionnaires were completed.

**Results:** A total of 38 patients were enrolled, 18 ABT and 20 OBT. The demographics and concomitant surgical procedures did not differ between the two groups. The surgical time for the ABT group,  $20.0 \pm 11.3$  minutes, was significantly greater than the OBT group,  $11.5 \pm 4.6$  ( $p < 0.01$ ). One patient was converted from the ABT group to the OBT group due to sheering of a severely attenuated tendon preventing an ABT. No significant difference ( $p > 0.05$ ) was found in strength or anterior shoulder pain. Additionally, no significant difference ( $p > 0.05$ ) was found in the American Shoulder and Elbow Surgeons score at 6 months and 1 year. No revisions were required in either group.

**Conclusion:** This randomized clinical trial suggests there is no clinical difference between the two techniques. Additionally, while the arthroscopic procedure requires more surgical time, the revision rates are not different. Besides the cosmetic concern for an additional scar, we recommend decisions to be made based on surgeon preference and experience.

## Estimating Bone Loss using a Best-fit Circle on Glenoid 3D CT

**Primary Author:** Kevin Wang, BS

**Contributors:** Eamon Bernardoni, MS(Rush); Drew Lansdown, MD(Rush); Anthony Romeo, MD(Rush); Nikhil Verma, MD(Rush)

**Introduction:** Glenoid bone loss is seen in the setting of recurrent shoulder instability and contributes to failure of soft tissue stabilization procedures. A best-fit circle estimation of glenoid morphology is most frequently used in the clinical setting, but this method has not been rigorously validated. The purpose of this study is to validate the use of the best-fit circle method in 3D CT models to estimate bony loss in the glenoid.

**Objective:** The purpose of this study is to validate the use of the best-fit circle method in 3D CT models to estimate bony loss in the glenoid.

**Methods:** Sixty-nine healthy 3D CT glenoid scans were retrieved from a previously compiled, de-identified database of cadaveric CT scans. Scans from donors >65 years old and those demonstrating bone loss were excluded. Thirty-one CT models were included in the final analysis. Three independent reviewers placed eleven points along the rim of the inferior half of the glenoid, at 3 o'clock, 6 o'clock, and 9 o'clock with the others spaced evenly between. Using ImageJ, a best-fit circle for the inferior glenoid (BFC-IG) was generated from these points. The 6 anterior and 6 posterior points, each including the 6 o'clock point, were then used to create anterior-based and posterior-based circles which were then compared to each BFC-IG.

**Results:** The calculated area and centers for each BFC-IG from each rater were analyzed and demonstrated excellent inter-rater reliability with an intra-class correlation coefficient of 0.94 for area, 0.98 for X-center, and 0.98 for Y-center. On average, the area of the anterior-based circles were  $92.4 \pm 17.4\%$  of the area of the BFC-IG. The area of the posterior-based circles were  $110.6 \pm 21.3\%$  of the BFC-IG. The area estimates based on the posterior- and anterior-fit circles were significantly different from each other ( $p < 0.001$ ).

**Conclusion:** The clinically-utilized method of estimating glenoid bone loss using the unaffected hemisphere may result in an inaccurate determination of glenoid bone loss. In the setting of anterior bone loss, the posterior-based circle would over-estimate the actual amount of bone loss, while in posterior bone loss, the anterior circle would under-estimate actual bone loss. Future efforts should be directed towards determining a more accurate method to quantify glenoid bone loss.

**Significance:** Our model demonstrates that the current clinically-utilized method of estimating glenoid bone loss - a best-fit circle method - does not provide a valid estimation. This is likely because the morphology of the glenoid varies significantly between individuals, often having an ellipsoid rather than circular morphology. By taking this into account, we can better understand and adjust for the limitations of the best-fit circle model in estimating glenoid bone loss.

## Hamstring Activation during the Baseball Pitch

**Primary Author:** Antonia Zaferiou, PhD

**Contributors:** Brandon Erickson, MD (RUMC) Peter Chalmers, MD (University of Utah) Philip Malloy, PT (RUMC, Marquette University) Nikhil Verma, MD (RUMC) Anthony Romeo, MD (RUMC)

**Introduction:** During UCL reconstruction performed on pitchers, surgeons typically harvest a graft from the semimembranosus/semitendinosus (SMST). However, little is known about how pitchers recruit their hamstrings throughout the baseball pitch.

**Objective:** We hypothesized that the back-leg biceps femoris (BF) would be recruited most during the drive phase (context: back-leg single-leg support with hip external rotation and hip extension), back-leg SMST would be recruited most as the back-leg leaves the ground, and that both front-leg hamstrings would be recruited most during the braking phase (context: front-leg single leg support while decelerating hip flexion and hip internal rotation to prevent loss of balance).

**Methods:** Pitchers (16 males) provided informed consent and performed five pitches while SMST and BF activation were monitored using electromyography (EMG, Noraxon, 1200Hz). Pitch subphases were defined: drive phase (single leg stance on the back-leg after the front-leg reached maximum height), double-support phase, and braking phase (back-leg off the ground). EMG data were filtered via butterworth filter (100-400Hz) and quantified using root mean squared values in 20ms average bins, normalized to the maximum bin during manual muscle tests (MMT). The sum, median, and time above 20%MMT of muscle activity for each hamstring were compared across pitching phases using Kruskal-Wallis and post-hoc sum rank test.

**Results:** The sum activation, and time above 20%MMT for all four hamstrings were significantly greater during the braking phase vs. during other phases ( $p < .001$ ). The median back-leg SMST was least activated during the drive phase vs. during other phases ( $p < .001$ ). Back-leg BF ( $p = .018$ ), front-leg BF ( $p = .001$ ), and front-leg SMST ( $p = .001$ ) had the largest median activation during the braking phase vs. other phases.

**Conclusion:** These findings are consistent with the fact that the braking phase was shorter than the accelerating phases of the pitch and, therefore, would impose a greater mechanical demand to neutralize the body rotation and translation previously generated.

**Significance:** Similar EMG analyses may assist surgeons decide which hamstring to harvest a graft from an individual pitcher during UCL surgery performed on pitchers to ease lower extremity rehabilitation before returning to pitching.

## **Development of a Novel Time Dependent Polyethylene Cross Shear and Wear Model for use in the Computational Analysis of Total Knee Replacements**

**Primary Author:** Steven Mell, BS

**Contributors:** Markus A. Wimmer, PhD(Rush); Hannah J. Lundberg, PhD(Rush)

**Introduction:** Preclinical testing of TKRs is primarily done using mechanical knee simulators, however such testing can be both time consuming and costly. Finite element analysis (FEA) combined with computational wear modeling offers a potential solution to this problem. However, current wear models are limited in their ability to predict wear under differing contact conditions. This could be due to a lack of consideration of polyethylene fibril realignment.

**Objective:** In this study, we propose a computational model of polyethylene wear, including a time dependent cross shear and polyethylene fibril realignment model, for use alongside finite element analysis (FEA) and suitable for use in a variety of contact conditions.

**Methods:** Using results from experimental tests, we developed a computational model of polyethylene fibril realignment and combined it with a frictional energy based model of polyethylene wear. Development was done using Scientific Python(SciPy). Optimization was used to fit the model constants to the experimental data. The fibril realignment model and the wear model were then coupled to FEA models of the experiments. Experimental results were compared to both the SciPy and FEA models.

**Results:** After optimization, the model fit the experimental data with an r-squared of 0.99. The FEA implementation compared well to both the experimental results and the SciPy model. Wear was highest following a 90° turn during testing, but quickly tapered off as the fibril direction reoriented.

**Conclusion:** The optimization fit the model to the experimental results. The model was able to translate well into the FEA models. Current limitations include the lack of validation against other experimental tests. Studies have shown that the wear rates for a pin on a square sliding path is a function of the number of cycles, not the total sliding distance. This behavior can be explained by the highest wear rates following a 90° turn, which the model duplicates.

**Significance:** A polyethylene wear model capable of predicting wear under a variety of contact conditions, run in parallel with an FEA contact model, could prove a valuable tool in the analysis and preclinical testing of TKRs and other orthopedic implants which use polyethylene as a bearing surface.

## In Vivo Three-Dimensional Analysis of the Facet Joint Alignment of the Lumbar Spine

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**Introduction:** A diverse range of spine diseases are caused by a pathological orientation of the facet joint (FJ). It is of interest to know the position of the FJ in relation to the vertebral body when understanding load transmission in healthy and diseased states.

**Objective:** The aim of this study was to test the hypothesis the FJ plane is oriented in a parallel lattice formation to the posterior wall.

**Methods:** Subjects underwent supine lumbar CT scans in this IRB approved study. 3D models of vertebral body, facet joint surface and VB posterior wall were created. Local coordinate system of VBs, FJ centroids, PWs, and FJ center planes was defined. Angles between the facet plane normal vector and Y-axis, sagittal, and transverse planes; as well as intra-facet joint plane were calculated. Subgroup analysis was performed to evaluate level, age, and gender effects.

**Results:** The mean angle between the PW and FJ plane was 3.033° in females and 5.377° in males. By age, the average angle in the 20yrs cohort was 2.722°, 30yrs 4.926°, 40ys 6.524°, and 50yrs 5.515°. Significant differences were observed between the 20yrs and all other cohorts, and 30yrs vs 40yrs cohort. By level, average angles were L1 4.532°, L2 5.336°, L3 3.993°, L4 3.789°, and L5 5.355°. A significant difference was observed between L2 vs L4, and L4 vs L5. Level by age, older cohorts had increased angles indicative of more departure from the posterior wall.

**Conclusion:** Our study proposed a new concept of 'facet alignment' in relation with the PW sagittal alignment. We observed the facet plane declined by 3.0 to 5.4 degrees in female and male, respectively. Gender, age and level differences were subtle and likely due to subjects lacking structural pathology. Future studies including structural abnormalities are needed to demonstrate relevance of the proposed concept of the facet joint alignment.

**Significance:** This study proposed a novel concept of the 3D facet joint alignment. It may provide important information for better understanding of load transmission through the facet joints and spinal disorders involving 3D deformity of the posterior element of the spine.

## Clinical Outcomes of Patellofemoral Osteochondral Allograft Transplantation: A Prospective Analysis

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**Introduction:** The use of osteochondral allograft transplantation (OAG) for chondral defects of the knee is increasing, particularly for defects involving the femoral condyles. A paucity of literature exists regarding the utility of OAG for treatment of chondral lesions in the patellofemoral compartment

**Objective:** The purpose of this study was to prospectively evaluate the clinical outcomes for patients undergoing patellofemoral OAG for symptomatic chondral lesions.

**Methods:** Consecutive patients undergoing OAG for full-thickness patella and trochlear lesions between 2007 and 2014 by two senior surgeons were analyzed. Pre- and post-operative patient reported outcomes scores were collected, with a minimum 21-month follow-up. Patient demographics, preoperative clinical data including information on prior ipsilateral knee surgeries, and intraoperative details were analyzed for all patients. Complications, reoperations, and conversion to total knee or patellofemoral arthroplasty were recorded. Statistical analysis was conducted with student's T-tests, with  $P < 0.05$  considered significant.

**Results:** A total of 14 patients (10 females, 4 males) with an average age of  $32.8 \pm 7.5$  years (range, 20-48) were identified for inclusion with an average follow-up of  $3.6 \pm 1.8$  years (range, 1.8-7.8) (Table 1). The average body mass index was  $27.5 \pm 6.9$  kg/m<sup>2</sup>. Patients experienced an average  $5.4 \pm 4.2$  years of symptoms prior to OAG and 100% of patients had undergone previous ipsilateral knee surgery with an average  $4.1 \pm 3.5$  prior procedures before undergoing patellofemoral OAG. The average defect size on the patella was 855mm<sup>2</sup> while that on the trochlea was 322mm<sup>2</sup>. At the time of OAG, 6 (43%) patients received trochlear grafts, 6 (43%) received patellar grafts, and 2 (14%) received bipolar grafts. Nine patients (64%) received a single allograft, 3 (21%) received 2 allografts to 2 separate lesions, and 2 (14%) received grafts to 4 separate lesions. At final follow-up, there were significant improvements in Lysholm, IKDC, KOOS, WOMAC, and SF-12 Physical outcomes scores; no significant improvements were found in the SF-12 Mental subscale (Figure 1). Two patients (both female, ages 27 and 41) were considered failures as they had converted to knee arthroplasty at an average 2.7 years following OAG. Both of these patients had received allografts to the patella with lesion sizes of 506mm<sup>2</sup> and 1800mm<sup>2</sup>, respectively.

**Conclusion:** Osteochondral allograft transplantation of the patellofemoral joint can be considered a viable restorative procedure for patients with symptomatic chondral lesions to the trochlea and patella. At an average follow-up of 3.6 years, the majority of patients will experience significant improvements in nearly all outcomes scores, with an arthroplasty conversion rate of 14%. Additional information on this difficult-to-treat patient population, including a better understanding of risk factors for failure, prognostic factors for success, and long-term outcomes, is needed.



**Significance:** Chondral lesions of the patellofemoral compartment are relatively common and can be difficult to manage. In recent years, other investigators have begun evaluating the utility of osteochondral allograft transplantations as a salvage treatment for these lesions. This study is a multicenter collaboration demonstrating significant clinical improvement at a minimum 2-year follow-up after OAG to the patellofemoral compartment as either a primary or salvage procedure.

## Do Outcomes Differ for Osteochondral Allografts of the Knee for Osteochondritis Dissecans Based on Patient Age

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**Contributors:** Kevin C. Wang BS, (Rush); Rachel M. Frank, MD (Rush); Sarah Poland, BS (Rush); Max A. Meyer, BS (Rush); Brian J. Cole, MD MBA (Rush)

**Introduction:** Osteochondritis dissecans (OCD) is not an uncommon disease process, especially in the knee joint. While it is most commonly seen in children and adolescents, it may manifest in adults. Osteochondral allograft (OCA) has emerged in recent years as a viable treatment option for OCD.

**Objective:** The purpose of the current study was to investigate the differences in outcomes following osteochondral allograft for a diagnosis of osteochondritis dissecans based on patient age.

**Methods:** Consecutive patients who underwent OCA by a single surgeon between 10/1/2002 and 11/1/2014 for a diagnosis of OCD with >2 years of clinical follow-up were included. The patient cohort was divided into 2 study groups based on age. Group 1 included patients less than 21 years of age at the time of OCA, while Group 2 included patients greater than 21 years of age at the time of OCA. Preoperative and final follow-up patient reported outcomes (PROs) were statistically compared between groups, including Lysholm, IKDC, KOOS, WOMAC, and SF-12. In addition, the minimal clinically important difference (MCID) and minimal detectable change (MDC) scores were analyzed as appropriate.

**Results:** A total of 48 patients (31 males, 17 females) with a diagnosis of OCD treated with OCA were included. A total of 39 patients (81%) with an average age of  $24.8 \pm 9.0$  years were available for clinical follow-up at an average  $5.5 \pm 2.7$  years following surgery. The entire cohort had an undergone an average of  $2.0 \pm 1.3$  previous ipsilateral knee surgeries, with 94% undergoing at least 1 prior surgery. The average time between previous surgery and OCA was  $2.0 \pm 2.7$  years (range 0.3-15.7 years). Group 1 included 21 patients (15 male, 5 female, average age  $31.5 \pm 8.1$ ) and Group 2 included 19 patients (9 male, 10 female, average age  $17.9 \pm 1.7$ ). There were significant improvements in all PROs for both groups ( $P < 0.05$  for all) other than SF-12 Mental (Table 1). Both groups met MCID and MCD thresholds where appropriate. There were no significant differences between Group 1 and Group 2 in terms of preoperative, postoperative, or magnitude of change for all PROs (Figure 1). Patients in Group 1 required 6 reoperations (29%) at an average of  $3.5 \pm 2.4$  years following OCA, with 1 failure at 1.63 years resulting in OCA removal and microfracture. Patients in Group 2 required 6 reoperations (32%) at an average of  $3.4 \pm 2.9$  years with 2 failures at an average of  $6.2 \pm 3.8$  years resulting in 1 revision OCA and 1 conversion to unicompartmental knee arthroplasty.

**Conclusion:** OCA is a successful surgical treatment for OCD of the knee and leads to significant and clinically meaningful improvements in PROs regardless of patient age. While reoperation may be common following OCA, failure rate is low at mid-term follow-up.

**Significance:** If OCD fails conservative management, it is usually treated initially with fixation of the chondral flap. However, many patients fail this treatment and require further intervention due to

persistent pain. OCA has emerged as a viable treatment option. The results of this study demonstrate that osteochondral allograft transplantation is an effective treatment method regardless of patient age.

## Does ACL Retention Affect Muscle Recruitment in Total Knee Replacement?

**Primary Author:** Jacqueline C. Simon, BS

**Contributors:** Craig J. Della Valle, MD (Rush University Medical Center, Department of Orthopedic Surgery); Markus A. Wimmer, PhD (Rush University Medical Center, Department of Orthopedic Surgery)

**Introduction:** Posterior-cruciate retaining (PCR) total knee replacements (TKRs) are linked to altered muscle patterns compared with healthy knees. Bicruciate-retaining (BiCR) TKRs were designed to improve implant performance.

**Objective:** The goal of this study is to compare muscle activity during level walking, downhill walking, and stair ascent for patients with BiCR and PCR TKRs.

**Methods:** Motion and electromyography (EMG) data were collected simultaneously for 11 subjects (3/8 m/f, 63±11 years, 31.0±7.6 BMI, 6/5 right/left) with BiCR TKRs and 13 subjects (6/7 m/f, 67±8 years, 30.8±5.4 BMI, 4/9 right/left) with PCR TKRs during level walking, downhill walking, and stair ascent using the point cluster marker set and surface electrodes placed on the vastus medialis obliquus (VMO), rectus femoris (RF), biceps femoris (BF), and semitendinosus (ST) muscles.

**Results:** For level walking, there were no significant differences between groups in knee kinematics, kinetics, and EMG patterns. During downhill walking, subjects with BiCR implants showed significantly lower peak muscle activity in the VMO (69.4±43.6 %RVC vs. 107.0±20.7 %RVC;  $p=0.037$ ) and RF (89.1±23.4 %RVC vs. 114.0±18.5 %RVC;  $p=0.027$ ) and lower muscle activity overall from 39-52 % stance phase in the ST ( $p=0.002$ ), while PCR subjects displayed a peak abduction moment (1.01±0.50 BW\*HT) that is borderline significantly larger compared to the BiCR group (0.64±0.26 BW\*HT;  $p=0.055$ , Cohen's  $d=0.93$ ). BiCR subjects had borderline significantly greater peak muscle activity in the VMO (361±199 %RVC vs. 171±100 %RVC;  $p=0.053$ ) during stair climbing, but the PCR group had a significantly larger abduction peak (0.79±0.26 BW\*HT vs. 0.57±0.16 BW\*HT;  $p=0.038$ ), as well as a trending larger adduction peak (2.71±0.50 BW\*HT vs. 2.27±0.60 BW\*HT;  $p=0.07$ , Cohen's  $d=0.85$ ).

**Conclusion:** Retention of the ACL may lead to 'normal' muscle recruitment in BiCR subjects, while PCR subjects may use quadriceps and hamstring muscles to compensate for knee stability. BiCR subjects appear better able to recruit the VMO during extensor-driven activities.

## Visual event-related potentials as a disease-specific biomarker in Fragile X Syndrome and Phelan-McDermid Syndrome.

**Primary Author:** Alan Siegel, BS

**Contributors:** Elizabeth M. Berry-Kravis, MD, PhD (RUMC)

**Introduction:** Fragile X Syndrome (FXS) and Phelan-McDermid Syndrome (PMS) are both single-gene disorders that have been associated with autism spectrum disorder (ASD), and in which glutamate signaling in neurons is affected. Targeted treatments in animal models exist for both FXS and PMS. Identification of a central nervous system biomarker is a crucial next step in the translation of these pharmacological interventions to humans. Currently, drug trials rely on parent-report measures which suffer from problems with consistency and strong placebo effects.

**Objective:** We propose that visual event-related potentials (VEP) can be used as a biomarker to provide feedback on target engagement and effectiveness of pharmacological interventions in differentially targeting abnormal cortical processing of visual signals in FXS and PMS.

**Methods:** An EvokedX system was used for stimulus (standard contrast-reversing checkerboard) presentation and data recording. Our sample included 22 participants: 4 participants with FXS (4 males, mean age= 19.5 years, SD= 9.61), 8 participants with PMS (5 males, mean age= 11 years, SD= 4.41), and 10 healthy controls (7 males, mean age= 19.2 years, SD= 5.96). All procedures received IRB approval and participants signed informed consents or assents as appropriate. We compared amplitude values at two critical VEP components.

**Results:** The mean P60-N75 amplitude was  $-3.3 \pm 8.02$  (control),  $-5.28 \pm 3.3$  (PMS,  $p = 0.27$  compared to control), and  $-3.13 \pm 11.92$  (FXS,  $p = 0.49$  compared to control,  $p = 0.39$  compared to FXS). The mean N75-P100 amplitude was  $13.55 \pm 7.01$  (control),  $11.43 \pm 5.58$  (PMS,  $p = 0.27$ ), and  $24.57 \pm 12.79$  (FXS,  $p = 0.15$ ,  $p = 0.26$ ).

**Conclusion:** The small sample size limited significance and we will continue to collect more data. Our initial data suggests that VEPs can be used to assess visual functioning in patients of all ages with ASD and may be sensitive to differences in cortical processing between PMS and FXS.

**Significance:** We believe that VEPs will one day be useful as a biomarker to assess the efficacy of novel interventions and cater treatments to individual patients.

## Upregulation of BPOZ-2 by PPAR-alpha: Implications for Lewy body disease

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**Introduction:** Formation of Lewy body inclusions (LBs) in the substantia nigra (SN) is a very well-characterized pathological hallmark of Parkinson's disease (PD). LBs are aggregates of many biologically inactive proteins including structural elements, alpha-synuclein (asyn)-binding proteins, synphilin-1-binding proteins, and components of the ubiquitin-proteasome system, proteins implicated in cellular responses, proteins associated with phosphorylation and signal transduction, cytoskeletal proteins, cell cycle proteins, cytosolic proteins and many more. So far almost 76 proteins have been found to be associated with the formation of LBs (Beyer et al., 2009). Deposition of LBs in the cell bodies and neurites often leads to the metabolic impairment and eventually the death of dopaminergic (DA) neurons. Therefore, lowering the burden of LBs is a potential challenge to restore the health and function of DA neurons. The most important strategy for minimizing the accumulation of LBs is preserving mitochondrial homeostasis. In a healthy neuron, mitochondrial biogenesis (mitogenesis) is required for the production of ATP, neurotransmitter release, calcium buffering, and augmentation of synaptic strength. However, during neurodegenerative condition, increased mitogenic response might bring opposite effect as it leads to the production of more depolarized mitochondria, reactive oxygen species (ROS), different inflammatory mediators including p38MAPK, Ras, Raf; and eventually the development of LB pathology. Therefore, tight regulation between mitochondrial biosynthesis and its breakdown is critical for the maintenance of neuronal health and function (Palikaras and Tavernarakis, 2014). Recently, our lab has delineated the role of a novel ankyrin-rich, BTB domain containing protein BPOZ-2 or ABTB2 in LB disease (Roy et al., 2016), which can also be a crucial regulator of mitochondrial quality control process.

**Objective:** The regulation of BPOZ-2 has not been studied so far. Interestingly, we observed that the expression of BPOZ-2 had been strongly down-regulated in Peroxisome Proliferator Activation Receptor-alpha knock-out (ppara-null) animals. Therefore, our objective is to investigate the role of PPAR-alpha in the expression of BPOZ-2.

**Methods:** 1. Semi-quantitative RT-PCR, realtime PCR analyses were adopted to study the mRNA expression of bpoz-2 gene. 2. Immunohistochemistry analyses were performed in striata and nigra to compare the level of BPOZ-2 between Wt and ppara-null animals. 3. Promoter analyses of bpoz2 gene by Qiagen promoter analyses tool followed by Chromatin-immunoprecipitation (ChIP) assay were performed in vivo in nigral tissue of 6-8 weeks old mouse brain.

**Results:** 1. mRNA expression analyses revealed that there was a strong downregulation of bpoz-2 mRNA in the absence of ppar-alpha suggesting that the expression of bpoz-2 gene was regulated by PPAR-alpha. 2. Similarly, a dual immunohistochemical analyses of tyrosine hydroxylase (TH; dopaminergic neuronal marker) and BPOZ-2 clearly indicated that BPOZ-2 expression was strongly downregulated in TH-ir neuron of nigra in the absence of PPAR-alpha. 3. Finally, the recruitment of PPAR-alpha in the promoter of bpoz-2 has been shown by ChIP assay.

**Conclusion:** PPAR-alpha has been shown to be recruited in the promoter of bpoz-2 gene. PPAR-alpha positively regulates the transcription of bpoz-2 gene.

**Significance:** A crosstalk between PPAR-alpha and BPOZ-2 could be important for the amelioration of Lewy body pathology in nigra.

## **Objective inertial sensor based gait outcome measures for efficacy of cyclodextrin treatment in Niemann-Pick Type C1 (NPC1): Preliminary analysis**

**Primary Author:** Joan O'Keefe, PhD, PT

**Contributors:** Erin Robertson, BA (RUMC) Andrew McAsey, BA (RUMC) Jamie Chin, BS (RUMC) Medha Parulekar, BS (RUMC) Elizabeth Berry-Kravis, MD, PhD (RUMC)

**Introduction:** Traditional gait outcome measures frequently lack sensitivity to detect clinically meaningful changes in clinical trials.

**Objective:** To longitudinally evaluate the efficacy of hydroxypropyl- $\beta$ -cyclodextrin (HP- $\beta$ -CD) treatment on ambulatory function in NPC1

**Methods:** Three patients with NPC were treated biweekly with HP- $\beta$ -CD intrathecally through an expanded access IND. Disease course for ambulation was tracked every 2 to 3 months for 30 to 36 months with an inertial sensor system (MobilityLab/APDMTM). An instrumented two minute walk test was used in 2 patients and a 7 meter Timed Up and Go (i-TUG) was used in the third. Percent of scores improved by >10%, changed by <10% (unchanged/stable), and worsened by >10% from baseline to present was quantified for each gait/turn parameter.

**Results:** Subject 1 (age 17) presented with cerebellar ataxia. 6/13 variables improved (stride velocity 20%, cadence 16%, double support time 14%, gait variability for stride length 29%, velocity 20%, and frontal plane trunk ROM(FPTROM) 36%), 5/13 stayed the same and 2/13 worsened (FPTROM 29%; number of steps to turn 15%). Subject 2 (age 15) presented with normal gait except for slightly increased gait variability and double support time. 1/13 variables improved (double support 24%), 8/13 stayed the same, and 4/13 worsened (FPTROM 19%, gait variability for stride length 97%, velocity 57%, cadence 27%). Subject 3 (age 14) presented with a clumsy, slow gait, severe cognitive dysfunction and intractable seizures. 6/15 variables improved (frontal plane trunk ROM 37%, turn duration 15%, turn to sit velocity 26.5% and duration 38%), 5/15 remain unchanged and 4/15 worsened (stride lengths 21%, gait variability for stride length 22%, velocity 82%, and FPTROM 52%).

**Conclusion:** The use of the MobilityLab inertial sensor gait analysis system is feasible to determine efficacy of pharmaceutical interventions in neurological populations. HP- $\beta$ -CD treatment appears to have stabilized or improved the majority of gait outcomes in this NPC1 cohort.

**Significance:** The use of promising portable inertial sensor technologies to measure treatment effects in clinical populations is important for detecting clinically meaningful gait outcome measures.



## **Excitability of mPFC pyramidal neurons is abnormally increased in older HIV-1 transgenic rats and associated with reduced K<sup>+</sup> channel function**

**Primary Author:** Lihua Chen, PhD

**Contributors:** Christina E. Khodr, PhD (Rush); Lena Al-Harthi, PhD (Rush); and Xiu-Ti Hu, MD PhD (Rush)

**Introduction:** HIV-associated neurological and psychological deficits are associated with dysfunction of the medial prefrontal cortex (mPFC), a key regulator of cognition. These deficits still occur even with combinations antiretroviral therapy, and may worsen as the HIV+ population ages. Our previous studies demonstrated that the excitability of mPFC pyramidal neurons is abnormally-increased in adolescent (~7-week-old) and young adult (~6-month-old) HIV-1 Tg rats compared to age-matched non-Tg rats. Such dysregulation is associated with over-activation/expression of the voltage-gated Ca<sup>2+</sup> channels (VGCCs).

**Objective:** To evaluate the impact of HIV and age on mPFC, we use HIV-1 Tg rats as an animal model of such comorbid conditions.

**Methods:** In the present study, we assessed excitability of mPFC neurons in 12-month-old (12-mo) HIV-1 Tg rats to elucidate mechanisms driving the neuronal dysfunction in old HIV-1 Tg rats. Whole-cell patch-clamp recordings were conducted to evaluate HIV-induced alterations in K<sup>+</sup> channel function.

**Results:** We found that evoked firing of mPFC neurons was significantly increased in 12-mo HIV-1 Tg rats compared to non-Tg rats. This dysfunction was associated with an increased input resistance (reflecting decreased K<sub>2P</sub> channel activity), reduced voltage-gated K<sup>+</sup> efflux (indicating reduced K<sub>v</sub> channel activity during membrane depolarization), and attenuated inward rectification (suggesting decreased K<sub>ir</sub> channel activity during membrane hyperpolarization) (all p<0.05). The reduced K<sub>2P</sub>/K<sub>v</sub> channel activity induced a consequential reduction of the rheobase and increased firing. The attenuated K<sup>+</sup> influx via K<sub>ir</sub> channels could elevate extracellular K<sup>+</sup> levels, which also could contribute to the mPFC neuronal hyperactivity. Meanwhile, our parallel studies (Khodr et al., 2016) presented in this meeting show unchanged Ca<sup>2+</sup> influx through VGCCs in mPFC neurons of 12-mo HIV-1 Tg rats.

**Conclusion:** Together, these novel findings suggest that the mPFC neuronal hyper-excitation in older HIV-1 Tg rats is mediated predominately by reduced function of K<sup>+</sup> channels, which may be a potential target for treating HIV+ patients during aging.

## Primary intraventricular hemorrhage: clinical characteristics and outcomes

**Primary Author:** Rachel Weinstein, BA

**Contributors:** Kathryn Ess, MD; Bilaal Sirdar, MD; Sarah Song, MD, MPH; Shawna Cutting, MD, MS

**Introduction:** Primary intraventricular hemorrhage (IVH), defined as a nontraumatic intracranial hemorrhage confined to the ventricular system and immediate parenchymal ependymal lining, is a rare and poorly understood neurological disease. Unlike the more commonly seen secondary IVH, which occurs as a consequence of intraparenchymal or subarachnoid hemorrhage into the ventricular system, primary IVH accounts for only 3.1% of all nontraumatic central nervous system hemorrhages. Due to the rarity of primary IVH, the etiology, treatment and prognosis still remain unclear.

**Objective:** In this retrospective review study, we sought to better define the clinical characteristics of primary IVH in order to provide insight into the risk factors and prognosis of this high-risk, poorly understood disease.

**Methods:** Consecutive patient records with a diagnosis of intracerebral hemorrhage admitted between May 2009 and June 2014 at a tertiary care center were retrospectively reviewed. Subjects were included in study cohort if all neurologists and the radiology report agreed that the subject had an isolated IVH. Patients with intraparenchymal hemorrhage, subarachnoid hemorrhage, malignancy with hemorrhagic components, and hemorrhagic transformation of ischemic stroke were excluded. The electronic medical record, imaging report, and imaging studies were reviewed. A literature review was also conducted to identify all prior publications of patients with intraventricular hemorrhage, using the key words 'primary intraventricular hemorrhage' and excluding articles written in a language other than English and those with 5 cases or less. This review was conducted using Ovid, Scopus, and PubMed.

**Results:** Of 1692 cases reviewed, 33 (1.9%) had primary IVH. Most common presenting symptoms included altered mental status (48.5%), headache, (39.4%), and nausea (24.2%). In 36.3%, hypertension was found to be a contributing factor; 27.2% were attributed solely to hypertension. Vascular abnormalities were the primary etiology in 21.3% of patients. When observing outcomes, 61.8% were discharged home or to rehab, while 20.5% died or were placed in hospice care. A higher Graeb score was associated with an increased likelihood of death or hospice (8 vs 5,  $p=0.02$ ).

**Conclusion:** This study is one of few to describe the etiology, contributing factors, and outcomes of primary IVH. As in prior studies, hypertension was a contributing factor, and vascular lesions were less common than expected. More research is necessary to further define the course and characteristics of this rare type of intracerebral hemorrhage.

**Significance:** From the time it was first described in the late 1800's by Sanders, intraventricular hemorrhage has been associated with poor outcomes, mainly sudden onset of coma without recovery. Half a century later, Gordon and colleagues qualified primary IVH by coma with absence of hemiplegia, paraplegia or pathologic reflexes. Gordon also observed hyperextension of muscles, hyperthermia, and myoclonic and tetanic contractions. Since the pioneering works of Sanders and Gordon, there have only been a handful of studies investigating primary intraventricular hemorrhage. Our study provides a

detailed report of the risk factors, etiology, clinical symptoms and outcomes of primary intraventricular hemorrhage patients. As such, our study helps to fill the existing knowledge gaps in the literature and contributes to a better overall understanding of primary IVH.

## **PROBABILISTIC SUBTRACTED POST-ICTAL DIFFUSION TENSOR IMAGING TO IDENTIFY ICTAL TRANSIENT DIFFUSION CHANGES IN WHITE MATTER FOR DIRECT BRAIN STIMULATION THERAPY**

**Primary Author:** Diego Garibay-Pulido, BS

**Contributors:** Leopoldo Cendejas-Zaragoza, BS (RUSH, IIT); Marvin A. Rossi, MD (RUSH, IIT)

**Introduction:** Functional imaging techniques predominantly address the detection of epileptogenic foci in grey matter for focal-onset epilepsy. However, few techniques assess the degree of ictal-associated connectivity in the epileptogenic cortex through white matter (WM) pathways, overlooking a crucial step to understand epileptic networks. Probabilistic Subtracted Post-Ictal Diffusion Tensor Imaging (pspi-DTI) is a novel technique that identifies transient water diffusion changes in such pathways.

**Objective:** Measurements of Fractional Anisotropy (FA) and Trace (Tr) provide information about the structural integrity of axonal pathways and cell hydration, respectively. By comparing the inter- and post-ictal states following stereotypic dyscognitive seizures through Diffusion Tensor Imaging (DTI), activated axonal bundles connecting epileptogenic zones can be identified.

**Methods:** A post-ictal and inter-ictal DTI were acquired for each patient. Imaging parameters consisted of 2mm slices in 60 directions with  $b=900$  s/mm<sup>2</sup> in a 3T MRI scanner. Eddy current and motion corrections were applied using TORTOISE. Tensor reconstruction was performed using FSL. Tensor registration was applied using DTI-TK. Statistically significant differences ( $p<0.01$ ) in FA and Tr were identified by performing a voxel-wise one-tailed unpaired t-test. Results were co-registered to a SPGR MRI for anatomical localization.

**Results:** Our sample consisted of 5 responsive neurostimulation (RNS) therapy candidate patients. Regions with statistically significant decreases in FA and increases in Tr were detected. A spatial correlation between ictal SPECT and pspi-DTI was found in all patients.

**Conclusion:** Pspi-DTI can identify ictal-associated propagation pathways involved in the epileptogenic network. This information can be later used to predict optimal implant sites for RNS therapy in order to modulate the maximal extent of the epileptogenic network.

**Significance:** Pspi-DTI is a novel technique that addresses the problem of evaluating meaningful connectivity between ictal-onset zones for direct brain modulation therapy.

## **Inertial sensor based normative spatiotemporal gait and postural sway parameters in typically developing children and young adults**

**Primary Author:** Medha Parulekar, BS

**Contributors:** Alexandra Berry (Rush Medical College); Colleen Huml (Rush University Medical Center); Keith Kravis (Northwestern University); Chris D. Arca (Rush Medical College); Andrew McAsey (Rush University Medical Center); Anna DeSonia (Rush University Medical Center); Elizabeth Berry-Kravis, MD-PhD (Rush University Medical Center); Joan A O'Keefe, PhD (Rush University Medical Center)

**Introduction:** The use of inertial sensors to analyze gait and balance is increasingly popular due to their portability, relatively low cost and ability to be used in the clinic or community. One widely-used system is MobilityLab (APDM™). However, normative data using this system has not yet been established in children or young adults and is essential to compare with data obtained in clinical populations.

**Objective:** To establish a normative database of gait and balance parameters in children and young adults for use by clinicians and researchers.

**Methods:** We collected gait, turning and balance data from an instrumented self-selected and fast paced 2 minute walk (i-WALK) and i-SWAY in typically developing children and healthy young adults between the ages of 5 and 30 years of age (n=95). Data was stratified into the following age group 5-6 (n=14); 7-8 (n=16), 9-10 (n=7), 11-13 (n=13), 14-21 (n=9), and 22-30 (n=36) years

**Results:** There were no differences between male and female metrics; therefore data was combined for analysis. Cadence decreased significantly from 5 yrs. to those greater than 14 yrs., gait speed achieved adult values by 8 yrs. and gait variability decreased from age 5 to adulthood. Swing/stance/double support times did not differ between groups. Absolute stride length increased with increasing age but when expressed as % height did not. Turn duration was longer in those 22-30 yrs. compared to 5-8 yrs. but the number of steps to turn did not vary between groups. Children aged 5-8 had increased postural sway measures on many i-SWAY conditions (eyes closed, on foam, tandem) compared to older age groups.

**Conclusion:** Normative data from this study may be useful to clinicians and researchers using the MobilityLab system to analyze gait and balance in children and young adults. Further validation of this system with gold standard methods is needed in children.

## **A dual-hit model of methamphetamine-induced vulnerability for Parkinson's disease**

**Primary Author:** Isadora Daphne Calma, MS

**Contributors:** Amanda Persons, PhD (RU), Matthew Kase, BS, and T. Celeste Napier, PhD (RU)

**Introduction:** Methamphetamine (meth) abusers are at risk for developing Parkinson's disease (PD). We revealed that rats self-administering (SA) meth exhibit an abstinence time-dependent reduction in striatal and nigral tyrosine hydroxylase (TH) (Kousik et al., JPET 351:432,2014).

**Objective:** These findings led to our hypotheses that (i) meth initiates a pathological trajectory that may result in PD and (ii) the meth-compromised state would be vulnerable to a secondary dopaminergic insult. To test these hypotheses, we administered a subthreshold dose of rotenone, a dopaminergic toxin, to meth-SA rats and controls; we measured brain and behavioral markers of PD.

**Methods:** Male Sprague-Dawley rats (n=64) self-administered meth (0.1mg/kg/0.1mL infusions) or were saline-yoked for 14 days, 3h per day. After the last operant session, rats were randomly assigned to receive vehicle or rotenone (1mg/kg/day) via subcutaneous osmotic minipumps for 6 days. Rats were sacrificed 1 or ~56 days after the rotenone treatment. PD-like motor assessments (forelimb akinesia, rearing) were performed throughout the study. Biomarkers for PD-like pathology were assessed in the striatum using immunohistochemistry (TH) or immunoblotting (VMAT-2) at 1 and ~56 days post-treatment. Statistical analyses were performed using GraphPad 6.

**Results:** Behavioral and biochemical markers were not altered by saline+rotenone. In the meth-SA rats, rearing was not altered, but by 36 days, akinesia developed ( $p=0.0002$ ). By 50 days, meth+rotenone rats exhibited greater akinesia ( $p<0.0001$ ). None of the treatment groups showed changes in VMAT-2, but there was a 50% TH reduction in meth-SA rats compared to saline-yoked rats 56 days after rotenone ( $p=0.02$ ), but was not exacerbated in meth+rotenone rats.

**Conclusion:** Thus, a subthreshold dose of rotenone was sufficient to exacerbate the emerging akinesia effects of meth-SA, but not dopamine terminal markers.

## Effects of Chronic Pramipexole on AMPA Receptor Trafficking and Akt/GSK-3 $\beta$ Signaling in a Rat Model of Parkinson's Disease

**Primary Author:** Matthew Kase, BS

**Contributors:** A.L. Persons, PhD(RMC); T.C. Napier, PhD(RMC)

**Introduction:** The D2/D3 receptor-preferring agonist pramipexole (PPX) is an effective treatment for motor symptoms in Parkinson's disease (PD). However, non-motor symptoms associated with limbic systems emerge with chronic PPX. We previously demonstrated that acute PPX strengthens glutamatergic synapses (i.e., surface expression of AMPA receptors (AMPA)) in the limbic system via the Akt/GSK-3 $\beta$  pathway, but the effects of chronic PPX on this pathway remain unknown.

**Objective:** Here we tested the hypothesis that chronic PPX can increase AMPAR trafficking in limbic brain regions.

**Methods:** 6OHDA was injected bilaterally into the dorsolateral striatum of rats to model PD; controls were injected with vehicle. Twenty-one days post-lesion, rats were subcutaneously implanted with osmotic minipumps containing vehicle or PPX (1.2 mg/kg/day). The forelimb adjusted step task was used to confirm PD-like behavior and PPX efficacy in lesioned rats. After 14 days of PPX treatment, brain tissue was harvested. Modified Western blot protocols determined surface and intracellular levels of GluA1 (an AMPAR subunit) and Akt and GSK3 $\beta$ .

**Results:** In the nucleus accumbens, there was no effect of chronic PPX on Akt or GSK-3 $\beta$ . In the medial prefrontal cortex, the ratios of pAkt/Akt and pGSK-3 $\beta$ /GSK-3 $\beta$  were significantly increased in PPX-treated, PD-like rats (ANOVA;  $p=0.0161$  and  $p=0.0119$ , respectively), but surface/intracellular GluA1 was unchanged.

**Conclusion:** Thus, while acute PPX promotes AMPAR function, AMPAR appear to normalize with chronic PPX.

**Significance:** As excitatory synapses are also regulated by GSK-3 $\beta$ -linked changes in NMDAR, we also are considering that NMDAR may contribute to PPX-induced non-motor symptoms.

## **Feasibility of utilizing the NIH Toolbox to assess neurological function in moderate to advanced disease Parkinson's disease (PD) subjects with bilateral subthalamic nucleus deep brain stimulation**

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**Introduction:** The CAPSIT-PD protocol (REF) recommends a series of neuropsychological measures which have poor tolerability in PD patients undergoing DBS (REF). A novel assessment tool, the NIH Toolbox cognition battery (REF), has been developed to serve as a brief, convenient set of measures that provides a 'common currency' among researchers for comparisons across a wide range of studies and populations. Though the NIH Toolbox cognition battery was released in 2012 and is listed as one of the 'common data elements,' its use has only been described in PD patients with mild disease and it has not been utilized in the DBS population.

**Objective:** To determine the feasibility of utilizing the NIH Toolbox in moderate to advanced disease Parkinson's disease (PD) subjects with bilateral subthalamic nucleus deep brain stimulation (STN-DBS).

**Methods:** We enrolled 14 PD subjects with bilateral STN-DBS. Subjects were administered the NIH Toolbox cognition battery in the ON-medication, ON-stimulation state. Additional data collected included basic demographic information, Montreal Cognitive Assessment (MoCA), and Unified Parkinson's disease Rating Scale (UPDRS). The NIH Toolbox cognition battery fully-corrected t-scores were analyzed which have a normative mean of 50 with an SD of 10, and are corrected for age, education, sex, and race.

**Results:** Fourteen PD subjects were enrolled with a mean age of  $63.9 \pm 6.5$ , mean disease duration of  $12.8 \pm 7.1$  years, and 78.6 percent were men. All subjects had bilateral STN-DBS with a mean of  $1.7 \pm 1.1$  years of DBS duration. Mean UPDRS-III score was  $16.6 \pm 8.2$  years and mean MoCA score was  $24.9 \pm 5.1$ . All but one subject (13/14) completed the full range of cognitive measures. Subjects performed in the average to above average range in nearly all measures except for processing speed where individuals performed significantly below average. Overall cognitive function was in the average to above average level based on the toolbox composite scores [table 1]. There was a moderate correlation between the NIH Toolbox global cognitive measures and MoCA scores, with the cognitive function composite score having the strongest correlation with MoCA [table 2].

**Conclusion:** The NIH Toolbox cognition battery is feasible to administer to moderate to advanced PD patients with bilateral STN-DBS and has modest correlation with the MoCA, a widely used assessment tool in PD. Further studies are needed to validate the NIH Toolbox in the PD population.



## Potential preclinical gait and balance markers for developing Fragile X-Associated Tremor/Ataxia Syndrome (FXTAS)

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**Introduction:** Carriers of a premutation size 55-200 CGG repeat expansion in the fragile X mental retardation 1 (FMR1) gene are at risk for developing FXTAS, a disorder marked by ataxia, balance deficits, and cognitive impairment. Risk factors for FXTAS are not completely understood and preclinical detection methods are needed.

**Objective:** Therefore, we conducted gait and balance 'stress' tests using dual-task (DT) cognitive interference, which we hypothesized would reveal early motor impairments in asymptomatic FMR1 premutation (PM) carriers.

**Methods:** PM carriers without FXTAS (n=14;  $62.4 \pm 9.4$  yrs), PM carriers with FXTAS (n=9;  $67.1 \pm 10.1$  yrs) and controls (n=22;  $60.0 \pm 10.8$  yrs) underwent gait/balance testing using a 2 minute walk test and postural control test (i-SWAY) with an inertial sensor system (APDM; Oregon). Gait analysis was performed at a self-selected and fast pace and a DT condition. Stance, vision, surface stability, and cognitive demand were varied to modulate postural challenge on the i-SWAY. DT conditions included a verbal fluency task.

**Results:** During fast paced gait, PM carriers without FXTAS demonstrated reduced total distance traveled ( $p = 0.03$ ) and cadence ( $p = 0.04$ ), and longer turn step time ( $p = 0.046$ ). They also had slower stride velocities during DT walking ( $p < 0.0001$ ) and their DT cost for total distance walked was higher than controls ( $p < 0.05$ ). PM carriers with and without FXTAS exhibited worse balance on the i-SWAY than controls, with more difficult conditions yielding the most highly significant results ( $p = 0.04$  to  $< 0.0001$ ).

**Conclusion:** PM carriers demonstrate worse gait at fast speeds and under DT conditions and worse balance under challenging conditions. This suggests that these quantitative measures may be sensitive to produce at risk markers for FXTAS. Identification of preclinical motor signs in FXTAS will provide an early intervention window for preventative rehabilitation strategies and disease modifying drugs.

## **Aging in the context of HIV infection differentially alters Ca<sup>2+</sup> influx through voltage-gated Ca<sup>2+</sup> channels in cortical neurons.**

**Primary Author:** Christina Khodr, PhD

**Contributors:** Lihua Chen, PhD (Rush); Lena Al-Harthi, PhD (Rush),; Xiu-Ti Hu, MD, PhD (Rush)

**Introduction:** HIV-Associated Neurocognitive Disorders (HAND) is characterized by deficits in executive function, attention, and working memory. Despite combined antiretroviral therapies (cART), mild forms of HAND are still prevalent and are expected to increase with the aging HIV+ population. The medial prefrontal cortex (mPFC), which regulates cognition, is altered in HIV+ patients. Mechanisms driving neuronal injury in HAND are multifaceted. Even in the era of ART, HIV proteins and/or persistent CNS inflammation may perturb neuronal Ca<sup>2+</sup> homeostasis.

**Objective:** We studied the effects of HIV on voltage-gated Ca<sup>2+</sup> channel (VGCC) function in mPFC pyramidal neurons, using the HIV-1 transgenic (Tg) rat model. Previously, we demonstrated that Ca<sup>2+</sup> influx through VGCCs is abnormally enhanced in young HIV-1 Tg rats (~7wks-old), and associated with mPFC neuronal hyper-excitation. Further, we showed that mPFC neurons remain hyper-excitable in adult (6 months, mo) and older HIV-1 Tg rats (12mo). In the current study, we evaluated VGCC activity in mPFC neurons in 12mo-old HIV-1 Tg rats.

**Methods:** Whole-cell current-clamp recordings were performed in brain slices under blockade of Na<sup>+</sup> and K<sup>+</sup> channels, and excitatory and inhibitory inputs, to assess Ca<sup>2+</sup> spikes (representing Ca<sup>2+</sup> influx through VGCCs).

**Results:** We found that neurons in 12mo-old HIV-1 Tg rats required stronger rheobase (the minimal excitatory stimulation) to elicit Ca<sup>2+</sup> spikes than age-matched non-Tg rats. There was no significant difference in the Ca<sup>2+</sup> spike duration/area, but Ca<sup>2+</sup> channel protein levels were significantly reduced in mPFC from HIV-1 Tg rats compared to non-Tg rats.

**Conclusion:** These findings indicate that VGCC function is differentially affected by aging in the context of HIV infection. Our parallel studies suggest that the increased mPFC neuronal firing in 12mo-old HIV-Tg rats is mediated by K<sup>+</sup> channel alterations. Together, our current/previous studies demonstrate that aging in the context of HIV affects the nature of Ca<sup>2+</sup>/K<sup>+</sup> channel function, which cooperatively mediate mPFC neuronal dysfunction.

## **Cranial nerve contrast in fluorescence-guided neurosurgery improved by paired-agent imaging with nerve-specific fluorophores**

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**Introduction:** Nonspecific uptake of contrast make identification of critical structures, such as cranial nerves, in fluorescence-guided neurosurgery difficult. A paired-agent imaging approach has been proposed to address this problem, but no optimal protocol for this method has been established.

**Objective:** To develop a paired-agent imaging protocol that can enhance identification of cranial nerves in fluorescence-guided neurosurgery.

**Methods:** Following IRB approval, either of two myelin-targeting agents (Oxazine 4 (Ox4), Rhodamine 800 (Rh800)) and a control agent (indocyanine green (ICG)) were co-administered onto the ventral surface of 10 excised adult rat brains ( $n = 5$  per targeted agent). Staining was performed for 10 min followed by three repeated flushes with PBS. In an additional five rats, intravenous administration of Ox4 and ICG 4 h prior to euthanasia and brain excision was performed. Fluorescence imaging of the rat brains was performed ex vivo by an in-house developed wide-field multichannel fluorescence imaging system. Paired-agent ratiometric data analysis was used to determine preferential retention of the nerve-targeted agents over nonspecific retention. In all groups, nerve contrast was evaluated using nerve-to-brain ratio (NBR) and contrast-to-noise ratio (CNR) for targeted agent signal alone and paired-agent ratiometric signal.

**Results:** The paired-agent approach yielded higher nerve contrast in all groups for both metrics ( $p < 0.05$ ) except CNR for the Rh800 Direct group ( $p > 0.1$ ). A corollary simulation study demonstrated CNR more accurately assessed image quality, measured by the area under a receiver operating characteristic curve. For the average of all nerves, direct application of Ox4 provided significant improvement ( $p < 0.05$ ) in CNR over the other groups for both single ( $5.5 \pm 2.2$ ) and paired-agent imaging ( $3.0 \pm 2.0$ ).

**Conclusion:** The paired-agent ratiometric method resulted in a 3-times greater improvement in identification of cranial nerves over brain tissue. Thus, this method demonstrates potential to improve cranial nerve contrast and, consequently, surgical outcome.

**Significance:** The results of this study underscore the importance of accounting for nonspecific delivery and retention of targeted imaging agents in fluorescence guided neurosurgery and demonstrates that paired-agent imaging is a potential method for doing so. Future studies will test various staining, rinsing, and imaging protocols to optimize contrast enhancement and will evaluate the contrast achievable over cancerous tissues.

## The Role of PPAR- $\alpha$ ) in the Up-regulation of BPOZ-2 in the Basal Ganglia of Mouse Brain; Implications for Parkinson's Disease

**Primary Author:** Eric Abello, B.S.

**Contributors:** Avik Roy, PhD (Rush)

**Introduction:** Ankyrin-rich BTB/POZ domain containing protein 2, or BPOZ2, has recently been shown to be involved in the amelioration of nigral alpha-synuclein pathology in a53t-transgenic mouse model of Parkinson's Disease. However, the molecular mechanism of bpoz-2 expression is not known so far. Here we demonstrate that PPAR $\alpha$ , a lipid lowering transcription factor, regulates the expression of BPOZ-2.

**Objective:** The goal of our research is to explore the transcriptional regulation of BPOZ-2, with the anticipation that through control of BPOZ-2 expression, levels of alpha-synuclein could thus be controlled and reduced. Interestingly, promoter analysis indicated that there was a conserved peroxisome proliferator-activated receptor alpha (PPAR- $\alpha$ ) binding site in the BPOZ-2 promoter. Peroxisome proliferator-activated receptor alpha (PPAR- $\alpha$ ) is a nuclear receptor protein and transcription factor with major roles in lipid metabolism, anti-inflammation, immune-modulation, and anti-oxidation. However, its role has not been explored in the basal ganglia, especially in reference to BPOZ-2. This research project investigates the role of PPAR- $\alpha$  in the up-regulation of BPOZ-2, specifically in the substantia nigra, striatum, and hippocampus regions of mice brain.

**Methods:** First, bpoz2 mRNA in the basal ganglia of ppara-null mice was monitored by semi-quantitative and quantitative PCR assay. Second, immunofluorescence analyses of BPOZ-2 protein in vivo in mouse brain were performed. Finally, we detected PPAR $\alpha$  responsive element (PPRE) in the promoter of bpoz2 gene followed by a PCR-based chromatin immunoprecipitation analyses.

**Results:** Tables and Figures will be presented on poster.

**Conclusion:** Marked downregulation of bpoz2 mRNA in the basal ganglia of ppara-null mice was monitored by semi-quantitative and quantitative PCR assay, which indicated that PPAR $\alpha$  could be involved in the expression of BPOZ-2. Through our immunofluorescence analyses we further validated that the absence of PPAR $\alpha$  is crucial for the downregulation of BPOZ-2 protein in vivo in mouse brain. The detection of PPAR $\alpha$  responsive element (PPRE) in the promoter of bpoz2 gene followed by a PCR-based chromatin immunoprecipitation analyses have demonstrated that PPAR $\alpha$  directly recruits to the promoter and therefore regulates the transcription of bpoz-2 gene.

**Significance:** Current treatment for PD is directed toward symptomatic relief, but there are potential therapeutic opportunities involving alpha-synuclein, including limiting the formation of the aggregates and/or completely removing them. Through the transcriptional regulation of BPOZ-2 expression, we hope this research can indicate that levels of alpha-synuclein could thus be controlled and reduced leading to alternative therapies for control and treatment of PD.

## Interest in Genetic Testing in Parkinson's disease patients with Deep Brain Stimulation

**Primary Author:** Avram Frait, MD

**Contributors:** Gian Pal, MD, MS (Rush University Medical Center); Courtney Timms, BS (Rush University Medical Center); Eric Tam (Rush University Medical Center); Radha Bhavsar, MD (Rush University Medical Center); Leo Verhagen, MD, PhD (Rush University Medical Center)

**Introduction:** Nearly 27% of patients with early-onset PD carry a mutation in one of three genes: glucocerebrosidase (GBA), leucine-rich repeat kinase 2 (LRRK2), and parkin (PRKN). Phenotypes which are unique to each mutation may inform disease progression, which patients may benefit from or develop side effects due to DBS, and which surgical targets may be optimal. As it becomes more accessible, it is important to understand whether or not patients would opt for genetic testing, and what factors may predict or influence their decisions.

**Objective:** To determine interest in genetic testing among Parkinson's disease (PD) patients with deep brain stimulation (DBS).

**Methods:** A Genetic Attitude Questionnaire (GAQ) was administered at Rush Medical Center to non-demented PD patients with DBS who were unaware of their mutation status. Fifty-eight subjects had genetic testing for GBA, LRRK2, and PRKN and were unaware of their genetic mutation status. All subjects completed the GAQ, indicating their genetic knowledge, desire for testing, and reasons why they would or would not want testing. Interest in genetic testing was dichotomized - subjects who were definitely or probably interested in testing were considered one group, and subjects who definitely or probably did not want testing were a second group. A third group of patients were undecided. Models were adjusted for age, disease duration, family history, UPDRS-III score, and mutation status.

**Results:** Average age of patients was  $63.22 \pm 8.39$  and 74.1% were men. Approximately 26% reported a family history of PD. Of these, 53% believed PD is hereditary, 13% believed it is not hereditary, and 33% were unsure. At the present time, twelve subjects (20.7%) definitely wanted genetic testing, fifteen (25.9%) probably wanted genetic testing, eight (13.8%) definitely did not want genetic testing, three (5.2%) probably didn't want genetic testing, and twenty (34.5%) were undecided. Though there was a trend toward higher UPDRS-III scores and desire to obtain genetic testing, this did not reach statistical significance. Fifty-seven percent of subjects would want genetic testing to determine if they would benefit from surgical intervention.

**Conclusion:** PD patients are interested in genetic testing, and are more likely to obtain genetic testing if results could predict response to surgical treatment. Further studies are needed to understand the factors that influence a patient's desire for genetic testing.

## Genotyping Functional Movement Disorders

**Primary Author:** Emily Tharp, BS

**Contributors:** Maura Walsh, MD(IU); Bryan Bernard, PhD(Rush); Bichun Ouyang, PhD(Rush); Elizabeth Berry-Kravis, MD, PhD(Rush); Deborah Hall, MD, PhD(Rush)

**Introduction:** The diagnosis of a functional movement disorder (FMD) rests on the presence of incongruence and inconsistency. Few studies focused on genetic susceptibility factors have been performed FMDs. Expansions of FMR1 and polymorphisms of COMT and BDNF have each been associated with a variety of neuropsychiatric symptoms. Due to the phenotypic overlap of these groups and FMDs, we hypothesized that women with FMDs would have a higher rate of val/met polymorphisms in COMT and BDNF and expansions in the FMR1 gene.

**Objective:** To determine the prevalence of FMR1 expansions, COMT and BDNF polymorphisms, and the association of these polymorphisms with neuropsychological scales in women with functional movement disorders.

**Methods:** FMR1, COMT, BDNF PCR was performed on women recruited through the Rush Movement Disorders Clinic with a consensus diagnosis of a FMD. Each FMD woman was asked to bring an unaffected friend to serve as a control. Evaluation of each participant included diagnostic criteria for somatoform disorders (SCID-1), neuropsychological scales, a measure of hypnotizability, and a neurological exam.

**Results:** The mean age of the subjects was  $39.7 \pm 2.7$  yrs (FMDs) vs.  $39.3 \pm 3$  yrs (controls), with 95% white non-Hispanic, 7.5% Asian, and 5% reporting more than one race. Sixty percent of the FMDs met criteria for somatization disorder ( $p < 0.0001$ ) and 25% for undifferentiated somatoform disorder ( $p = 0.047$ ) compared to none of the controls. Two FMR1 premutation carriers were identified: one FMD and one control, with the FMD carrier subsequently having a fragile X child diagnosed. COMT ( $p = 0.14$ ) and BDNF ( $p = 0.53$ ) polymorphisms were not significantly increased in the FMDs. Among the FMD subjects, COMT nor BDNF polymorphisms were associated with hypnotizability scales, anxiety, nor depression.

**Conclusion:** This pilot study did not show an increased prevalence of FMR1 expansions nor COMT or BDNF polymorphisms in FMD patients. FMD women also had difficulty in recruiting friends for controls and most were recruited from the general populations.

## The Effect of Anxiety on Cognition in Parkinson's Disease

**Primary Author:** Jennifer Goldman, MD, MS

**Contributors:** Sharlet Anderson, PhD (RUMC), Glenn T. Stebbins, PhD (RUMS), Bryan Bernard, PhD (RUMC), Alyce Negron (RUMC)

**Introduction:** Anxiety is common in Parkinson's disease (PD), along with cognitive impairment and in later stages, dementia. The relationship between anxiety and cognition in PD is unknown.

**Objective:** Our study examined the effect of anxiety on cognition in Parkinson's disease (PD) patients without cognitive impairment, mild cognitive impairment and dementia.

**Methods:** Neuropsychological data were collected from 119 PD patients and 27 healthy controls. PD patients underwent comprehensive neuropsychological evaluation (attention/working memory, executive function, language, memory, and visuospatial function domains) and were classified according to Movement Disorder Society (MDS) diagnostic criteria. Forty-two patients were classified as having no cognitive impairment, 51 with mild cognitive impairment, and 26 with dementia. Anxiety was measured with the Beck Anxiety Inventory (BAI). One-way ANOVAs, Pearson correlations, and multiple regression analyses were conducted.

**Results:** Mental Status Exam scores were similar in controls and PD patients without cognitive impairment, but significantly lower in PD mild cognitive impairment and PD dementia groups. PD cognitive groups' BAI scores were significantly higher than controls', but not significantly different among the PD subgroups (PD-NCI, PD-MCI and PDD). Among PD patients, BAI score was negatively correlated with attention/working memory and visuospatial function domain scores. After controlling for age, education, and gender, BAI score was a significant independent predictor of attention/working memory and visuospatial function composite scores.

**Conclusion:** PD patients have higher levels of anxiety than controls. Anxiety has a modest, inverse correlation to cognitive function. Anxiety negatively influences scores on tests of visuo-spatial functioning and attention/working memory in PD patients.

**Significance:** Targeting anxiety in treatment may not only improve mood, but also some aspects of cognitive functioning in patients with PD.

## **Alteration in markers of neuronal activity and plasticity in the limbic brain of HIV-1 Tg rats revealed by methamphetamine self-administration**

**Primary Author:** Michael Ohene-Nyako, BSc, MHS

**Contributors:** Amanda L. Persons, PhD (RU) and T. Celeste Napier, PhD (RU)

**Introduction:** Methamphetamine (meth) abuse co-occurs with HIV infection, and the comorbid condition presents a greater pathology than either condition alone. Extracellular signal-regulated kinase (ERK), a mitogen-activated protein kinase (MAPK), and the downstream transcription factor  $\Delta$ FosB, play vital roles in activity-dependent neuronal plasticity associated with chronic exposure to psychostimulants, including meth. Meth alters MAPK signaling in limbic brain regions and pathological studies suggest that HIV has a strong predilection for subcortical brain regions such as those affected by meth. However, little is known about the comorbid effects of HIV-1 proteins and meth in these brain regions.

**Objective:** This study seeks to evaluate markers of neuronal activity and plasticity in limbic regions of the comorbid brain.

**Methods:** We studied young adult Fischer 344 HIV-1 transgenic (Tg) and non-Tg rats that self-administered meth (0.02-0.04mg/kg/0.05ml iv infusion) 2hr/day for 21 days or served as saline-yoked controls (n=10rats/group). One day following the last operant session, the rats were killed and the nucleus accumbens (NAc) and ventral pallidum (VP) were dissected out and prepared for immunoblotting.

**Results:** ERK data was calculated as ratio of phosphoERK/ERK. Meth increased ERK1 in the NAc of Tg rats relative to their saline controls and increased ERK2 and  $\Delta$ FosB in the NAc of both Tg and non-Tg rats ( $p < 0.05$  ANOVA). We observed an interaction between genotype and meth for ERK1 in the NAc. Ongoing studies of the VP indicate that ERK and  $\Delta$ FosB are not altered by meth or genotype.

**Conclusion:** These results suggest a region-specific activation of ERK and increased  $\Delta$ FosB expression induced by HIV and meth that may underlie activity-dependent maladaptations associated with the comorbid brain state.



## Gender differences in motor and non-motor features across the Parkinson's disease spectrum

**Primary Author:** Therese Dunne, BA, MA

**Contributors:** Glenn T. Stebbins, PhD; Rush Medical Center Christopher G. Goetz, MD; Rush Medical Center Shen Luo, PhD; University of Texas Health Science Center at Houston Jennifer G. Goldman, MD, MS; Rush Medical Center

**Introduction:** There is evidence of male predominance in PD, however less is known about the role of gender in the clinical presentation of PD. The Movement Disorder Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) provides a uniform way to capture PD features.

**Objective:** To examine how gender differences influence motor and non-motor features across the Parkinson's disease (PD) spectrum.

**Methods:** We examined MDS-UPDRS Parts I-IV administered in a large cohort (n=1321) drawn from the MDS-UPDRS Clinimetric testing program (CTPS), the Rush PD-Cognitive Behavioral Imaging study (PD-CBI), and the Parkinson's Progression Markers Initiative (PPMI). Using published MDS-UPDRS factor structures (Goetz, 2008), we examined gender differences in tremor dominant/postural instability gait disorder (TD/PIGD) phenotype using Chi-square statistic and individual factors using a multivariate general linear model controlling (MANCOVA) for age and disease duration.

**Results:** The cohort was 64.8% male and 35.2% female, with mean (SD) age of 68.71 (10.91) and 68.86 (12.08) years and disease duration 6.44 (6.31) and 6.54 (8.22) years, for men and women respectively. PD onset age and disease duration differed by gender, while TD/PIGD classifications did not. Males scored worse on MDS-UPDRS Part II Factor 1 (fine motor functions) ( $p < 0.0005$ ), Part III Factors 3 (rigidity) ( $p = 0.003$ ) and 6 (upper extremity tremor) ( $p = 0.012$ ), while females scored worse on Part I Factor 2 (depression, anxiety, apathy) ( $p = 0.011$ ), Part II Factor 3 (dressing, hygiene, walking, balance, freezing) ( $p = 0.024$ ), Part III Factors 5 (upper extremity bradykinesia) ( $p = 0.019$ ) and 7 (lower extremity bradykinesia) ( $p = 0.010$ ).

**Conclusion:** Gender may affect certain aspects of motor and non-motor features and experiences of daily living in PD. Recognition of worse fine motor functions, rigidity, and upper extremity tremor in males and worse mood, dressing ability and bradykinesia in females may influence treatments in PD.

## **Rare toxicities associated with chronic phenytoin and phenobarbital usage: A case report and review of the literature**

**Primary Author:** Adam Hood, PharmD

**Contributors:** Monika Gil, PharmD (RUMC); Cicely Moreno, MD (RUMC)

**Introduction:** Phenobarbital and phenytoin are older agents used in treating and preventing seizures in patients of all ages. Phenobarbital, a barbiturate, has been available since 1912 where it was originally used as a sedative. Phenobarbital activates the GABA-A receptor, which acts as an inhibitor of signal propagation by maintaining the opening of the chloride channel. Phenytoin has been available since 1938 when it was found to bind the sodium channel on neurons which decreased the frequency of action potentials during abnormal firing. Long term use of phenytoin and phenobarbital has been cited as possible etiologies of pseudolymphoma, liver dysfunction, anemia and hemophilia.

**Objective:** To describe a case of rare toxicities associated with chronic phenytoin and phenobarbital usage, and review literature on cases to identify the epidemiology and mechanism of the toxicity.

**Methods:** A case reviewed of a 78 year old male who was diagnosed with seizures at the age of 18 and has been seizure free for 35 years on phenobarbital and phenytoin. Consent obtained from case subject. A literature search was performed using the following key words: phenytoin, phenobarbital, lymphoma, pseudolymphoma, toxicity, liver, dysfunction, hemophilia, anemia, and withdrawal.

**Results:** The patient has a past medical history significant for seizure disorder, recurrent gastrointestinal bleeds and hemothorax with pleural effusion requiring blood and FEIBA, hyperbilirubinemia, cholangitis, choledocholithiasis, cholecystitis, hepatic cirrhosis with ascites, b-cell lymphoma, febrile neutropenia, anemia, and chronic steroid use. Drug therapy consisted of phenytoin ER 100 mg 3 times daily, phenobarbital 32.4 mg 3 times daily, amiloride daily, ursodiol two times daily, furosemide daily, acyclovir two times daily, pantoprazole two times daily, carvedilol two times daily, prednisone daily, ferrous sulfate, and folic acid. Literature search found cases of rare toxicities with long term use of phenobarbital and phenytoin.

**Conclusion:** This case report demonstrates rare toxicities associated with chronic phenytoin and phenobarbital usage.

## **FXTAS, PD, and ET subjects demonstrate distinct gait, balance and tremor deficits under normal, environmentally challenging, and dual-task conditions**

**Primary Author:** Alexandra Bery, BS

**Contributors:** Erin Robertson, Deborah A. Hall, Andrew McAsey, Maija Swanson, Colleen Huml, Elizabeth Berry-Kravis, Joan A. O'Keefe

**Introduction:** Fragile X-associated tremor/ataxia syndrome (FXTAS), a neurodegenerative disease that affects carriers of a 55-200 CGG repeat expansion in the fragile X mental retardation 1 gene, may be misdiagnosed as PD or ET due to overlapping motor symptoms. It is critical to characterize distinct phenotypes in FXTAS compared to PD and ET to improve diagnostic accuracy. Environmentally challenging and dual-task (DT) paradigms can reveal subtle gait and balance impairments, and tremorography has been shown to correlate with clinical tremor rating scale scores.

**Objective:** To compare FXTAS, PD, ET and controls using quantitative measures of gait, balance, and tremor.

**Methods:** Subjects with FXTAS ( $n = 10$ ;  $69.7 \pm 6.8$  yrs), PD ( $n = 15$ ;  $70.9 \pm 8$  yrs) and ET ( $n = 9$ ;  $69.6 \pm 7.4$  yrs) and controls ( $n = 12$ ;  $64.4 \pm 7.1$  yrs) underwent gait and balance testing with an inertial sensor system (APDM; Oregon). Instrumented Timed Up and Go (i-TUG) and 2-minute walk (i-WALK) tests were used to test gait, and the i-SWAY to test balance. DT conditions included a verbal fluency task. Subjects also underwent tremorography using the ETSense<sup>TM</sup> system (Kinesia HomeView<sup>TM</sup>; Great Lakes NeuroTechnologies Inc.).

**Results:** On the i-TUG, FXTAS subjects had increased sit-to-stand peak velocity compared to PD subjects ( $p=0.04$ ). On self-selected speed and DT i-WALKs, they had increased stride length ( $p=0.03$  and  $0.04$ , respectively), and during self-selected and fast i-WALKs they had reduced cadence ( $p=0.03$  and  $0.04$ , respectively) compared to PD subjects. On the i-SWAY, both FXTAS and ET subjects had increased jerk ( $m^2/s^5$ ; smoothness of path sway) compared to PD subjects during the foam, feet apart, and eyes closed condition ( $p=0.01$  and  $0.04$ , respectively). On tremorography, FXTAS subjects showed reduced rapid alternating movement amplitude compared to PD subjects ( $p = 0.0045$ ), and PD subjects showed reduced rapid alternating movement amplitude and speed compared to ET subjects ( $p=0.0002$  and  $0.0115$ , respectively).

**Conclusion:** This pilot data demonstrates that FXTAS, PD, and ET subjects exhibit distinct deficits in gait, balance and tremor under normal, environmentally challenging and DT conditions. This suggests that these quantitative measures may be sensitive to distinguish FXTAS from PD and ET.

## Joint pain as premonitory urge in patient with Ehlers Danlos syndrome and Tourette's syndrome

**Primary Author:** Avram Frait, MD

**Contributors:** Gian Pal, MD, MD; Rush University Medical Center

**Introduction:** Ehlers Danlos syndrome (EDS) includes a group of heritable connective tissue disorders mainly characterized by joint hypermobility. There are many known neurologic complications of EDS including headache, muscle weakness, paresthesia, intracranial aneurysms and subarachnoid hemorrhage, spontaneous arterial dissection, cavernous sinus fistula, seizures, and neuropathy.

**Objective:** We report the case of a 21 year old male patient with EDS and Attention Deficit Hyperactivity disorder (ADHD) who presented with joint discomfort and was found to meet clinical diagnostic criteria for Tourette's syndrome (TS). We present this case to report an atypical pre-monitory urge which was attributed by the patient to an underlying mixed connective tissue disorder, but was in fact related to a co-morbid tic disorder.

**Methods:** A 21 year-old right handed male with past medical history of EDS and ADHD presented to the Movement Disorders Center at Rush University in Chicago with joint discomfort. He was not aware of any tics, but described a painful sensation in his hips, right shoulder, and neck which was followed by movement in these joints. He could briefly suppress the movements and described a sense of relief with their performance. He had a history of throat clearing when he was previously taking lisdexamphetamine for ADHD and his brother also has motor tics. His neurologic exam was notable for multiple tics including eye rolling, alternating eye blinking, mouth puckering, mouth twitching, right shoulder jerking, and right hip jerking.

**Results:** Basic lab-work including complete blood count, complete metabolic profile, electrolytes, thyroid, and parathyroid studies was normal. MRI was obtained of both hips and both shoulders. These tests were notable only for mild tendinosis of the supraspinatus and infraspinatus muscles in the left shoulder.

**Conclusion:** This patient showed evidence of motor tics on physical exam and provided a history of prior vocal tics when treated for ADHD. He thus met the diagnostic criteria for TS. Though the movements did not bother him, he was started on guanfacine given his increased risk for joint dislocation. This case describes an atypical pre-monitory urge of joint pain which preceded motor tics, and which was attributed a known diagnosis of EDS. We present this case to increase awareness of abnormal urges that can precede tics and which patients may attribute to a seemingly unrelated co-morbid disease.

## Defining gene expression changes in bone marrow of NDLD mice with a spontaneous mutation in the Ptpn6 gene.

**Primary Author:** Andrew Nesterovitch, MD

**Contributors:** Michael Tharp, MD (RMC); Tibor Glant, MD, PhD (RMC)

**Introduction:** Protein tyrosine phosphatase, non-receptor type-6 (Ptpn6) is a hematopoietic cell phosphatase that is expressed in all lineages of leukocytes. Ptpn6 is a negative regulator of signaling for multiple receptors of innate and adaptive immunities in both mice and humans. Mice with a spontaneous homozygous mutation in the Ptpn6 gene (Ptpn6 meb2/meb2) develop neutrophilic dermatosis-like disease (NDLD) with abnormal neutrophil infiltration into the skin, similarly to what is found in patients with neutrophilic dermatoses.

**Objective:** To further analyze differentially expressed genes in the bone marrow of mice with NDLD to gain insight into the role of Ptpn6 in myelopoietic bone marrow pathology.

**Methods:** An Affymetrix Mouse Genome 430 2.0 GeneChip Array was employed for the study. The hierarchical clustering and principal component analysis (PCA) were performed on Affymetrix TAC 3.1.

**Results:** We recently described gene expression profiles in bone marrow and skin from mice with NDLD. A total number of 1,511 probe sets in the bone marrow showed at least two-fold changes with  $FDR < 0.05$ , of which 256 probe sets had over four-fold changes. A group of 63 genes in the bone marrow of NDLD mice had more than a 4-fold change with  $FDR < 0.0001$ . The heterozygous mice (Ptpn6meb2/+) do not develop any skin inflammation. We further defined NDLD gene expression signature analyzing gene expression in bone marrow from homozygous and heterozygous mice. We identified a group of 25 genes which showed progressing changes (more than 3 folds) in expression between homozygous and heterozygous mice ( $FDR < 0.05$ ). The most of 25 genes were down-regulated in bone marrow of homozygous and heterozygous mice.

**Conclusion:** The most of the genes were related to development and regulation of B cells which is consistent with our previous finding of the elevated serum immunoglobulins and systemic autoimmunity, characterized by DNA antibodies and immune complex in NDLD mice.

## **Ovarian malignant transformation is associated with the decrease in DNA repair enzyme 8-oxo-guanine glycosylase**

**Primary Author:** Shenon Sethi, MBBS

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**Introduction:** Ovarian cancer (OVCA) in most cases is an age-associated malignancy and chronic oxidative stress is a risk factor for OVCA. Ovulatory injuries expose ovarian surface epithelial (OSE) cells to oxidative stress. Chronic oxidative stress damages the DNA by oxidizing deoxyguanosine to 8-oxo-7, 8-dihydro-2-deoxyguanosine (8-oxo-dG), a mutagen involved in ovarian carcinogenesis. The enzyme OGG1 (8-oxoguanine DNA glycosylase) excises 8-oxo-dG and repairs the damaged-DNA.

**Objective:** The goal of this study was to examine whether OGG1 expression, an indicator of DNA damage, increases during aging in postmenopausal women.

**Methods:** Expression levels of OGG1 were examined by immunohistochemistry and immunoblotting in premenopausal and postmenopausal ovaries and fimbrial tissues. BRCA1+ subjects and OVCA tissues were used as positive control specimen. The intensity of OGG1 staining intensities was examined under a light microscope and compared among different groups.

**Results:** Compared with the premenopausal women, expression of OGG1 was stronger in the OSE, inclusion cysts and fimbrial epithelium in aging subjects (postmenopausal ovaries) and BRCA+ subjects. OGG1 expression was strongest in ovarian tumors. Similar patterns were also observed in immunoblotting for OGG1 in pre-and postmenopausal ovaries as well as in BRCA1+ and OVCA specimen.

**Conclusion:** The results of this study suggest that OGG1 expression increases in association with ovarian aging in postmenopausal women. The intensity of expression increases remarkably with the development of ovarian carcinomas. Thus, OGG1 is a potential marker of age-associated DNA-damage leading to ovarian malignant transformation and may also offer a target for the prevention of OVCA development. Support: Swim Across America (to AB).

## Factors Predicting 30-Day Hospital Readmission After Kidney Transplant

**Primary Author:** Jamie Ostrem, PharmD

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**Introduction:** Hospital readmissions after kidney transplant have been associated with increased morbidity, mortality, decreased quality of life, and increased healthcare costs.

**Objective:** The objective of this study was to identify clinical factors associated with 30-day hospital readmission post kidney transplant at an academic medical center.

**Methods:** This study was a retrospective, single-center cohort study. A total of 224 patients were included who received a kidney transplant between July 1, 2014 and October 12, 2016. Patients were evaluated based on the 30-day hospital readmission post kidney transplant.

**Results:** A total of 59 (26.3%) transplant recipients were readmitted within 30 days of discharge. Readmission rates did not differ between age, race, or initial hospital length of stay. Diabetes as the cause of ESRD was associated with a readmission rate of 35.7% compared to 22.1% in those without diabetes ( $p=0.032$ ). Patients on dialysis prior to transplant had a readmission rate of 28.2% compared to those not on dialysis 5.6% ( $p=0.037$ ). There was a trend towards higher readmission rates for patients with history of CAD, cadaveric transplant, delayed graft function, subtherapeutic tacrolimus level at discharge, level of education less than a college degree, treatment for donor positive culture and treatment for urinary tract infection within 30 days post-transplant; however these were not found to be statistically significant factors. Interestingly, patients discharged on the weekend had a lower 30-day readmission rate compared to those discharged on weekdays (16.7% v. 30.9%  $p=0.024$ ).

**Conclusion:** In our population, diabetes as the cause of ESRD and dialysis prior to transplant had a statistically significant higher 30-day readmission rate. There was a trend towards higher readmission rates in patients with cadaveric transplant, history of CAD, delayed graft function, subtherapeutic tacrolimus level at discharge, level of education less than a college degree, treatment for donor positive culture and treatment for urinary tract infection.

**Significance:** Factors that are associated with increased 30-day hospital readmission may be areas of intervention to reduce readmission rates, improve patient outcomes, and reduce healthcare costs.

## Study of initiation of hypercholesterolemia in nephrotic syndrome

**Primary Author:** Lionel Clement, PhD

**Contributors:** Eduardo Molina-Jijon PhD (RUMC)

**Introduction:** Nephrotic syndrome comprises of proteinuria, hypoalbuminemia, hyperlipidemia (hypertriglyceridemia and hypercholesterolemia), edema, and lipiduria. We investigate the development of hypercholesterolemia in nephrotic syndrome. Proprotein convertase subtilisin/kexin type 9 (PCSK9) is predominantly expressed in liver, intestine, and to a lesser extent, in the kidney. Gain-of-function mutations in PCSK9 cause hypercholesterolemia in humans, whereas loss-of-function mutations lead to a reduction in low density lipoprotein (LDL) cholesterol and a marked decrease in the risk of coronary artery disease. Anti-PCSK9 antibodies are now being used for the treatment of statin resistant hypercholesterolemia.

**Objective:** We want to explore a potential link between hypercholesterolemia and proteinuria in nephrotic syndrome. This is based on the observation that PCSK9 is expressed in the CCD. We will explore mechanisms of hypercholesterolemia in nephrotic syndrome in an animal model of focal and segmental glomerulosclerosis (FSGS), and study the potential role of CCD PCSK9 in initiating hypercholesterolemia.

**Methods:** We followed Buffalo-Mna rats (IACUC 16-045) at 1, 4.5 and 6 months of age. We collected urine for 18 hours and measured proteinuria. We assessed plasma levels of cholesterol, and studied PCSK9 protein expression in plasma, glomeruli and liver.

**Results:** Buffalo-Mna rats develop proteinuria at 1 month of age that increases with time. They develop hypercholesterolemia by the age of 4-5 months. Western-blot showed that PCSK9 protein slightly increases in kidney cortex whereas expression in liver is not modified.

**Conclusion:** During proteinuria, renal cortical PCSK9 protein and plasma cholesterol increase at a stage when hepatic PCSK9 expression is unchanged. This led to the hypothesis that the initiation of hypercholesterolemia in nephrotic syndrome may be a result of increased tubular PCSK9 expression in response to proteinuria. We plan to measure PCSK9 protein levels in liver and plasma, and study its expression in kidney and liver by confocal microscopy.



## **Podocyte specific ZHX2 overexpression worsens Focal Segmental Glomerulosclerosis and improves Minimal Change Disease**

**Primary Author:** Maria Del Nogal Avila, PhD

**Contributors:** Hector Donoro Blazquez (RUSH); Caroline B. Marshall (UAB); Carmen Avila Casado (UToronto); Camille E. Mace (RUSH); Lionel C. Clement (RUSH); Sumant S. Chugh (RUSH)

**Introduction:** Zinc fingers and homeoboxes (ZHX) transcriptional factor family are major regulators of podocyte gene expression and are mostly expressed as heterodimers bound to transmembrane proteins. ZHX2-ZHX1 heterodimers are present mostly in the podocyte body and ZHX2-ZHX3 in the slit diaphragm. Loss of heterodimerization, is common in podocyte diseases and promotes nuclear entry of ZHX proteins

**Objective:** Demonstrate the importance of ZHX2 overexpression in the development of FSGS and MCD

**Methods:** Podocyte-specific ZHX2 transgenic rats were generated. Following baseline characterization, we induced Adriamycin nephrosis, a model of FSGS, and puromycin aminonucleoside, a model of MCD

**Results:** Three founder lines of ZHX2 podocyte-specific transgenic rats were characterized (TG14, TG142, TG144). Glomerular RNA expression of ZHX2 in heterozygous rats showed a fold-increase of  $1.13 \pm 0.10$  in TG14,  $1.50 \pm 0.09$  in TG142 and  $4.09 \pm 0.69$  in TG144. Confocal characterization of heterozygous TG144 rats revealed increase expression of ZHX2 in podocyte cell membrane distribution. Expression of ZHX3 and ZHX1 was unchanged. None of the ZHX2 transgenic rat lines had proteinuria at baseline. When compared with Sprague Dawley rat, NPHS2-promoter-ZHX2 TG rats had more proteinuria and more severe glomerular disease than controls after ADR treatment (TG144 and TG142>WT; proteinuria/18h:  $310.4 \pm 41.5$ mg,  $204.8 \pm 29.9$ mg and  $102.6 \pm 20.3$  mg, respectively) ( $p < 0.01$ ). Also, backcross of the ZHX2 transgene into the Buff/Mna rat background, a model of FSGS, for 8 generations was associated with more proteinuria ( $301.9 \pm 27.4$  mg in 18 h) than the Buff/Mna at age 8 month ( $193.8 \pm 23.7$ mg in 18 h) ( $p < 0.05$ ).

By contrast, proteinuria in PAN was less severe 10 days after treatment (TG144 and TG142<WT; proteinuria/18h  $178.9 \pm 13.4$ mg,  $169.1 \pm 37.8$ mg and  $351.7 \pm 38.9$ mg, respectively) ( $p < 0.05$ )

**Conclusion:** Overexpression of ZHX2 in podocytes had a protective effect in MCD but worsens the development of FSGS

**Significance:** ZHX2 has a major role in nephrotic syndrome

## Identification of molecular mechanisms of non-HIV collapsing glomerulopathy

**Primary Author:** Camille Mace, PhD

**Contributors:** Lionel C Clement, PhD (RUMC); Carmen Avila-Casado, MD, PhD (Toronto General hospital); Szymon Filip, PhD (RUMC); Sumant S Chugh, MD (RUMC)

**Introduction:** Collapsing glomerulopathy (CG) is an aggressive glomerular disease with rapid progression to end-stage renal disease. The etiology of CG has not yet been discovered. It has been related to the presence of circulating factors in the serum, infection or drugs... Presently, there is no specific treatment for non-HIV CG. Therefore, it is important to understand fully the mechanisms behind this disease, so that new forms of treatment may be developed.

**Objective:** We will use animal models of CG to identify the molecular mechanisms of non-HIV CG. The *Rrm2b* gene encodes p53R2, a catalytic subunit of ribonucleotide reductase that is induced by p53 in response to DNA damage and is required for DNA repair. A prior study shows severe proteinuria and glomerular capillary loop collapse in *Rrm2b*<sup>-/-</sup> mice. We re-characterized the *Rrm2b*<sup>-/-</sup> mouse model.

**Methods:** We followed *Rrm2b* male mice at the age of 6, 8, 10, 11 and 12 weeks (IACUC 16-059). We collected urine for 18h and measured urine albuminuria by ELISA. Mice were anesthetized and their kidney perfused with Dynabeads for glomerular isolation. mRNA isolated from glomeruli were used to generate cDNA and gene expression study was conducted by RealTime PCR. Kidney sections were obtained to study glomerular collapse by light microscopy.

**Results:** *Rrm2b*<sup>-/-</sup> mice develop mild albuminuria at age 6 weeks that increased progressively. No albuminuria was noted in the *Rrm2b*<sup>+/+</sup> and *Rrm2b*<sup>+/-</sup> males. After age 10 weeks, there was visible collapse and mice die around age 12 weeks. We studied longitudinal glomerular mRNA expression of podocyte and endothelial cell expressed genes in *Rrm2b*<sup>-/-</sup> and wild-type mice from 6 to 12 weeks of age. Interestingly, most of the genes that have altered expression at age 6 to 8 weeks have a reversal in expression pattern after age 10 weeks.

**Conclusion:** This study will provide better understanding of the pathogenesis of CG.

## **Innovative Educational Tool to Enhance Hysteroscopy Learning**

**Primary Author:** Karissa Hammer, MD

**Contributors:** Teresa Tam, MD, FACOG, FACS (Rush University Medical Center); Louis Fogg PhD (Rush University Medical Center)

**Introduction:** It has been established that hands-on training is known to improve resident learning. However, few have investigated lecture content and improvement of resident education on hysteroscopic instrumentation and assembly. This study evaluates a standardized educational curriculum in hysteroscopy for obstetrics and gynecology (OB/GYN) residents.

**Objective:** To evaluate a standardized educational curriculum in hysteroscopy for OBGYN residents.

**Methods:** A standardized hysteroscopic curriculum was developed in line with ACOG hysteroscopy training guidelines. The curriculum consists of a one-hour lecture followed by a hands-on hysteroscopic instrumentation session. Participants were given a pre-test prior to the lecture and a post-test after subsequent lectures. Residents from three different institutions in Chicago, Illinois from 2013 to 2016 were tested. Instrument assembly was graded by time spent for task completion.

**Results:** Repeated measures analysis of variance was used to assess data points, pre and post test scores compared by training year and overall improvement. There was a statistically significant score difference in each level of training from pre to post-test. This difference was linear, magnitude of effect the same on each training level (N=29, P value 0.035). On average, scores improved by 14%. Hysteroscopic assembly time decreased by 2.45 minutes (N=14, P value 0.03). Improvements did not change with level of training but were only related to exposure to lecture content.

**Conclusion:** An established curriculum made significant change in residents' knowledge of hysteroscopy and instrumentation as demonstrated by improved hysteroscopic assembly times and post-test scores. This tool demonstrated an impact in multiple residency programs and can be more widely applied to aid resident training in hysteroscopy.

**Significance:** The findings of this study could influence resident teaching in the future.

## Poster by Primary Author

Last Name:	First Name:	Poster #:
Abedin	Yasmin	91
Abello	Eric	171
Abello	Eric	183
Ahmed	Osman	28
Ahmed	Osman	43
Bernardoni	Eamon	147
Bernardoni	Eamon	149
Bery	Alexandra	190
Bhatt	Nidhi	1
Blodgett	Carly	81
Boley	Randy	138
Bradley	Lauren	106
Browning	Melissa	70
Caipa	Anuhya	98
Calma	Isadora Daphne	177
Casey	Paul	52
Casini	Gina	114
Cesarz	Alison	40
Chakradeo	Prachi	102
Chen	Lihua	173
Clement	Lionel	195
Cook	Andrew	10
Cotter	Eric	167
Cotter	Eric	168
Covington	Megan	24
Crowley	Stephanie	139
Crowley	Stephanie	141
Cutler	Vanessa	13
Davis	Mallory	90
Del Nopal Avila	Maria	196
DeSantiago	Jaime	31
Doan	Faith	60
Dobrilovic	Nikola	30
Dobrilovic	Nikola	33
Dobrilovic	Nikola	35
Drunasky	Michael	122

Last Name:	First Name:	Poster #:
Dunne	Therese	188
Dvorak	Stephen	125
Dyga	Nick	42
Eastman	Charmane	110
Eastman	Charmane	140
Ebert	Kerry	84
Emerson	Jacob	179
English	Kathleen	80
Esposito	Alessandra	148
Eugenio	Samantha	115
Ferrigno	Christopher	157
Ford	Haley	66
Ford	Haley	117
Forsberg	Ingrid	58
Forsythe	Brian	158
Forsythe	Brian	162
Fraint	Avram	184
Fraint	Avram	191
Friedrichs	Judy	136
Fughhi	Ibtihaj	32
Gallagher	Terry	92
Gamboa	Charlene	120
Garibay-Pulido	Diego	175
George	Anil	21
George	Anil	129
Glover	Crissy	143
Goldman	Jennifer	186
Gomez	Joanne Michelle	64
Grumish	Eve	123
Gupta	Kajal	11
Hall	Deborah	159
Halloway	Shannon	111
Halverson	Melissa	37
Hammer	Karissa	198
Hanak	Michael	48
Haut	Kristen	145
Heilingoetter	Ashley	56

Last Name:	First Name:	Poster #:
Hersh	Marc	101
Hoheisel	Stephanie	62
Hood	Adam	189
Hood	Megan	105
Hui	Jessica	23
Hulse	Eric	83
Inventor	Ben	63
Johanson	Hollis	166
Kahan	Alyssa	7
Karmali	Reem	15
Kase	Matthew	178
Kelly	Mackenzie	53
Kelmis	Caroline	6
Kennedy	Mary	135
Khan	Nicholas	19
Khodr	Christina	181
Kidwell	Adam	69
King	Carley	72
King	Kevin	12
Kloweit	Tyler	3
Kluga	Katie	47
Kolettis	Diana	49
Kosche	Cory	88
Kreinbrink	Paul	2
Kuhar	Hannah	59
Kundu	Madhuchhanda	20
LaBelle	Suzanne	26
LaBelle	Suzanne	79
Lange	Emily	36
Leanos	Lizette	9
Lerret	Nadine	121
Li	Michelle	74
Logan	Antonio	68
Losurdo	Holly	51
Mace	Camille	197
Manning	Blaine	152
March	Michelle	75

Last Name:	First Name:	Poster #:
Medernach	Rachel	126
Meksraityte	Edita	55
Melamed	Svetlana	100
Mell	Steven	165
Miller	Courtney	71
Minogue	Madeline	85
Mittal	Nupur	14
Mittal	Nupur	17
Mittal	Nupur	18
Moon	Chun 'Mark'	45
Moran	Meghan	150
Moran	Molly	50
Moreno	Cicely	77
Moseley	Alex	29
Moss	Angela	94
Nathan	Brent	57
Nesterovitch	Andrew	192
Nguyen	Brittany	146
Nguyen	David	128
Nikolaides	Jenna	78
Nipper	Allison	124
Nurko	Ilana	112
O'Brien	Michael	154
O'Brien	Michael	160
O'Hearn	Nicholas	61
Ohene-Nyako	Michael	187
O'Keefe	Joan	172
Ostrem	Jamie	194
Parulekar	Medha	176
Patel	Ishani	34
Perez	Ricardo	8
Peterson	Melissa	76
Peterson	Sarah	107
Petr	Jane	109
Rajapakse	Rohan	16
Richardson	Catherine	153
Rimar	Sarah	97

Last Name:	First Name:	Poster #:
Robertson	De'Andra	131
Robertson	Erin	180
Rooney	Kathryn	87
Rossi	Isolina	22
Sax	Megan	82
Saxena	Abhishek	116
Schoeneman	Samantha	133
Sethi	Shenon	193
Shinn	Leila	108
Siegel	Alan	170
Simon	Jacqueline C.	169
Skaff	Erick W.	86
Small	Elan	65
Steinbrecher	Kacie	155
Strong	Andrea	73
Sventy	Erin	38
Swartwout	Kathryn	89
Swift	Luke	142
Tamizuddin	Sara	132
Tharp	Emily	185
Tietjen	Kiira	54
Tobin	Grace	113
Torres	Veronica	182
Trevino	Robert	93
Usha	Lydia	4
Vaclavik	Elizabeth	144
Valdespino-Hayden	Zerbrina	137
Van Jacobs	Amanda	41
Vatinno	Amanda	118
Verson	Joshua	27
Visk	Chelsea	103
Vo	Nhi	25
Wagner	Linzy	130
Wallace	Jennillee	127
Wang	Kevin	96
Wang	Kevin	161
Wang	Kevin	163



Last Name:	First Name:	Poster #:
Wang	Lai	151
Washburn	Trevor	46
Weinstein	Rachel	174
Williams	James M.	104
Wilson	Adam	99
Wojtowicz	Aleksandra	67
Yellapa	Aparna	5
Yuh	Catherine	156
Zaferiou	Antonia	164
Zellner	Hillary	39
Zou	Denise	119

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Zaferiou	Antonia	164
Zellner	Hillary	39
Zou	Denise	119
Zuke	William	158

# JOIN US FOR THE 34TH ANNUAL RUSH UNIVERSITY FORUM FOR RESEARCH AND CLINICAL INVESTIGATION

## MARCH 1-2

See below for location details

## AGENDA

### Wednesday, March 1

#### Noon to 5 p.m.

Searle Conference  
Center

#### Sigma Xi Poster Session:

Open Viewing

#### 7 – 8:30 a.m.

Armour Academic  
Center, Room 539

#### 31st Annual Frederic A. de Peyster Memorial Lecture for the Rush Surgical Society

Surgical Services and Sciences Resident  
Research Competition  
Julie A. Freischlag, MD

*Vice Chancellor for Human Health Sciences and  
Dean of the School of Medicine at UC Davis*

#### 1– 2:40 p.m.

Cohn Research Building,  
Field Auditorium,  
Room 160

#### Research and Diversity

Research presentations  
Sponsored by Rush IMSD

#### 3 – 5 p.m.

Searle Conference  
Center

#### Judging of Posters

Announcement of winner will be made  
Thursday at 3:30 p.m.

#### 3 – 5 p.m.

Searle Conference  
Center

#### Social Event for Poster Session

**Engage** with students during poster and  
oral presentations.

**Discuss** big issues with faculty and find  
new collaborators.

**Join us** as we recognize outstanding work  
during the awards presentation.

**Visit [rsh.md/rush-forum](https://rsh.md/rush-forum) for more information**

### Thursday, March 2

#### 8 a.m. – 5 p.m.

Searle Conference  
Center

#### Sigma Xi Poster Session:

Open Viewing

#### 8:15 – 8:35 a.m.

Cohn Research Building,  
Field Auditorium,  
Room 160

#### Welcome & Research Update

Alejandro Espinoza Orías, PhD  
*Assistant Professor, Department of Orthopedic Surgery  
Chair, Research Forum*

Joshua J. Jacobs, MD

*Associate Provost for Research, Rush University*

#### 8:40 – 9:20 a.m.

Cohn Research Building,  
Field Auditorium,  
Room 160

#### Distinguished Keynote Speaker

Diana J. Wilkie, PhD, RN, FAAN

*Professor, Prairieview Trust – Earl and Margo Powers  
Endowed Professor*

*Director, Center of Excellence in Palliative Care Research  
Department of Biobehavioral Nursing Science  
College of Nursing, University of Florida*

#### 9:25 – 10:45 a.m.

Cohn Research Building,  
Field Auditorium,  
Room 160

#### Faculty Presentations

#### 10:50 – 11:35 a.m.

Cohn Research Building,  
Field Auditorium,  
Room 160

#### Denis A. Evans, MD, Lectureship The Scientific Leadership Council

David A. Bennett, MD

*Director, Rush Alzheimer's Disease Center  
Robert C. Borwell Professor of Neurological Sciences*

#### 12:30 – 1:50 p.m.

Cohn Research Building,  
Field Auditorium,  
Room 160

#### Student Presentations

#### 1:55 – 3:30 p.m.

Cohn Research Building,  
Field Auditorium,  
Room 160

#### Deans' Awards Presentations

#### 3:30 – 4 p.m.

Cohn Research Building,  
Field Auditorium,  
Room 160

#### Awards Ceremony

