TRANSFORMING CURIOSITY INTO INQUIRY

12TH ANNUAL
MEDICAL STUDENT RESEARCH FORUM

PROGRAM and ABSTRACTS

Tuesday, November 26, 2013
12:00 - 5:00 PM  •  TUESDAY, NOVEMBER 26, 2013
Health Sciences Learning Center

Noon - 1:00 PM
HSLC Atrium
Student Research Poster Session

1:00 PM
1306 HSLC
Opening Remarks
Presentation of the Dean’s Award for Excellence in Medical Student Research Mentorship
Robert Golden, MD
Dean and Vice Chancellor for Medical Affairs

1:15 - 2:00 PM
1306 HSLC
SHAPIRO GUEST LECTURE
Reflections on Medical Student Research
Pamela Kling, MD
Professor of Pediatrics, UW School of Medicine and Public Health

After graduating from the University of Iowa Carver College of Medicine, Dr. Kling completed her pediatrics residency at American Family Children’s Hospital, and joined the UW faculty in 2002, beginning an academic career specializing in neonatology and nutrition. Merging her clinical and research interests, Dr. Kling studies how red blood cells progress during infancy to either a state of iron deficiency or sufficiency, and how certain high-risk conditions may increase the risk of iron deficiency in later infancy. Her lab has been a supportive and productive research launching ground for undergraduates, medical students, residents and postdoctoral fellows. In recognition of her sustained dedication to student research, Dr. Kling was selected as the recipient of the 2012 Dean's Award for Excellence in Medical Student Research Mentorship.

2:15-3:00 PM
1306, 1335, 1345 HSLC
Student Research Podium Presentations (Concurrent Sessions)

3:15-4:00 PM
1306, 1335, 1345 HSLC
Poster Session and Reception for Students, Mentors and Guests

Support for the 12th Annual Medical Student Research Forum is provided by the Department of Academic Affairs, the Herman and Gwendolyn Shapiro Foundation, and the Wisconsin Medical Alumni Association
<table>
<thead>
<tr>
<th>SESSION A</th>
<th>Room 1306 HSLC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ben Traun</strong></td>
<td>A Qualitative Study of Pediatricians’ Approach to Treating Childhood Obesity in Wisconsin</td>
</tr>
<tr>
<td><strong>Liliana Palencia</strong></td>
<td>Epidermal Growth Factor Mediated Wound Repair in Human Embryonic Stem Cell-Derived Epithelial Cells</td>
</tr>
<tr>
<td><strong>Jimmy Xu</strong></td>
<td>Resolution of Thyroglobulin Antibodies after Total Thyroidectomy for Cancer</td>
</tr>
<tr>
<td><strong>Bryan Vonasek</strong></td>
<td>Maternal Attitudes and Coverage Rates of Childhood Immunizations in Rural Uganda</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SESSION B</th>
<th>Room 1335 HSLC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Hope Wilkinson</strong></td>
<td>Is Comprehensive Miscarriage Management Offered in Wisconsin?</td>
</tr>
<tr>
<td><strong>Joshua Bakke</strong></td>
<td>Colonic Distention Analysis According to Patient Position at CTC: Diagnostic Value of Right Lateral Decubitus Series</td>
</tr>
<tr>
<td><strong>Charles Penn</strong></td>
<td>Use of the Ankle Brachial Index (ABI) as a Possible Diagnostic Tool for Peripheral Artery Disease (PAD) in Diabetic Patients at Tikur Anbessa Specialized Hospital, Ethiopia</td>
</tr>
<tr>
<td><strong>Kevin Hanson</strong></td>
<td>Evaluating the Predictive Value of Findings on Routine Office-Based Audiometric Analysis for Identifying Cochlear Implant Candidates</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SESSION C</th>
<th>Room 1345 HSLC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Marielle Brenner</strong></td>
<td>Inhibition of Notch Signaling Reduces Healing of Splinted Cutaneous Excisional Wounds in Mice</td>
</tr>
<tr>
<td><strong>P. Chulhi Kang</strong></td>
<td>Optimization of an ELISA for Detection of Canine Anti-Human Tyrosinase Immunoglobulin</td>
</tr>
<tr>
<td><strong>Matthew Gevelinger</strong></td>
<td>Brain Activity Upon Awakening and Reports of Sleep Consciousness</td>
</tr>
<tr>
<td><strong>Anna Drewry</strong></td>
<td>Assessment of the Contemporary Role and Risks of Renal Mass Biopsy at a Single Institution</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SESSION D</th>
<th>Room 1306 HSLC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Daniel Tonellato</strong></td>
<td>Measuring Burden of Disease from Motorcycle Crashes Among Children in Vietnam: A Call to Action</td>
</tr>
<tr>
<td><strong>Conor O’Halloran</strong></td>
<td>Can Radiographs Predict Outcome in Patients with Idiopathic Clubfoot Treated with the Ponseti Method?</td>
</tr>
<tr>
<td><strong>Surbhi Singhal</strong></td>
<td>Distinguishing Classical Papillary Thyroid Microcancers from Follicular-Variant Microcancers</td>
</tr>
<tr>
<td><strong>Alexandra Erdmann</strong></td>
<td>Inflammation Contributes to Depression in Allogeneic Hematopoietic Stem Cell Transplant Recipients</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SESSION E</th>
<th>Room 1335 HSLC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Jacob Inda</strong></td>
<td>Tricuspid and Pulmonary Valve Replacement for Carcinoid Heart Disease</td>
</tr>
<tr>
<td><strong>Matthew Kutz</strong></td>
<td>Monitoring of 19F Labeled Human Natural Killer Cell Trafficking for Cancer Immunotherapy Using MRI</td>
</tr>
<tr>
<td><strong>Sarah Tweddell</strong></td>
<td>Rheumatoid Arthritis Patient Cardiovascular Disease Prevention Experiences: Qualitative Analysis and Implications</td>
</tr>
<tr>
<td><strong>Jennifer Wagner</strong></td>
<td>Increased Lysozomal B-galactosidase Expression is a Senescence Marker and Identifies Indolent Prostate Cancer</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SESSION F</th>
<th>Room 1345 HSLC</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Lucas Leonhard</strong></td>
<td>Patient Variables, Dosing Patterns, and Subsequent Outcomes during Warfarin Reinitiation</td>
</tr>
<tr>
<td><strong>Katherine Omernick</strong></td>
<td>Identifying High-Risk Patients for Hospital Readmission Following Radical Cystectomy and Urinary Diversion</td>
</tr>
<tr>
<td><strong>Greg Schleis</strong></td>
<td>What are the Key Elements of Patient-centered Self-management Programs for Type Two Diabetes?</td>
</tr>
<tr>
<td><strong>Kirollos Gendi</strong></td>
<td>Financial Burden of Prophylactic Nailing of the Femur on the Medicare System in the United States</td>
</tr>
</tbody>
</table>
1. Acher, Alexandra
   Readmission Reduction Tools: Examining the Etiology of Readmission Following Complex Cancer Resection

2. Ade, Lacmbouh
   Validating the Clinical Validity of Bladder Cancer Nomograms

3. Barker, Anna
   Patient Hand Hygiene at Home Predicts Their Hand Hygiene Practices in the Hospital

4. Bauer, Arielle
   Quantitative Cell-Based Cellular Fibronectin ELISA: Monitoring Anti-Fibrotic Compounds

5. Bergren, Ryan
   Does a Multidisciplinary Thyroid Clinic Improve Follow Up of Benign and Indeterminate Thyroid Nodules After Fine Needle Aspiration?

6. Bjerregaard, Robert
   A Straightforward Technique for Eliciting and Recording Compound Potentials in a Rat Spinal Cord

7. Bowen, DeMarco
   Estimation of HIV/HBV/HCV Seroprevalence in Ethiopia Using Rapid, Multiplex Antibody Detection

8. Brown, Sarah
   El Cáncer, Claro y Sencillo: Latino Cancer Education and Outreach in Madison, Wisconsin

9. Brunk, Andrew
   Predicting Urinary Tract Infection after Radical Cystectomy and Urinary Diversion

10. Chindhy, Shahzad
    Acuity Adaptable Patient Care Model Shortens Length of Stay and Improves Outcomes in Adult Cardiac Surgery

11. Christensen, William
    Identifying Prognostic Factors for Recurrence in Renal Cell Carcinoma Extending into the Venous System

12. Delaney, Amanda
    Barriers to Oral Health Awareness: Survey of the Health of Wisconsin (SHOW)

13. Dietze, Megan
    DNA Methyltransferase Silencing Effect on Spinal Axon Regeneration in Folic-Acid Treated Rat Progeny

14. Ebben, Benjamin
    Noninvasive Quantification of Tendon Biomechanics: Shear Wave Elastography Imaging in a Porcine Tendinopathy Model

15. Ehlenbach, Colin
    Preoperative Cognitive and/or Functional Impairment is Associated with the Need for Higher Level of Care After Hospital Discharge

16. Fling, Sean
    Patient Profile at Tikur Anbessa Specialized Hospital Vascular Surgery Clinic, Addis Ababa, Ethiopia

17. Gassner, Jennifer
    Retrospective 5-year Analysis of Frontal Bone Fractures and Resultant Symptoms

18. Gehrman, Max
    Biochemical Analysis of EPL Reroute in CP Surgery: A Cadaver Study

19. Gill, Paul
    The Effect of Exertion on Landing Asymmetry

20. Golbach, Brittney
    Evaluating Clinical Response to Electronic Health Record Surveillance of Childhood Obesity

21. Guenther, Chad
    Biopsy EVX1 Methylation and Gleason Score Upgrading at Radical Prostatectomy in Prostate Cancer

22. Hafez, Omeed
    Nox2 May Mediate Cyclosporine A-Induced Hypoxia

23. Hanzlik, Thomas
    Characterizing Readmission in Ulcerative Colitis Patients Undergoing Restorative Proctocolectomy

24. Johnson, Kimberly
    Filter Paper Screening for Iron Deficiency using Zinc Protoporphyrin/Heme

25. Kartheiser, Ryan
    Healthcare Payment Reform Models for Better Diabetes Care

Abstracts for student podium and poster presentations follow, listed alphabetically by student last name.
PoSTeR PReSenTATionS
Noon-1:00 pm and 4:00 - 5:00 pm      HSLC Atrium

26. Knopp, Samantha
   Environmental Pollutants Enhance TH17 Polarization in an Aryl Hydrocarbon Receptor-Dependent Manner

27. Kraemer, Mark
   Endoscopic Aqueductoplasty for Treatment of Obstructive Hydrocephalus

28. Lang, Andy
   Exercise-induced Hypoalgesia after Comparative Forms of Anaerobic Training in Healthy Adults

29. Lien, Jessica
   pRNA Nanoparticles as Tools to Improve Human Pluripotent Stem Cell-based Transplantation Strategies for Retinal Degenerative Disease

30. Mercier, Phillip
   Analyzing UW Health Care Workers’ Perspectives on Disaster Resource Allocation via Survey Tool

31. Mok, Valerie
   Identifying Predictors of a Difficult Thyroidectomy

32. Molnar, Mark
   The Age of Patients with Rib Fractures is Associated with Higher Complication Rates and Increased Length of Stay

33. Murray, Shannon
   Iron May Be the Critical Link Between Maternal Obesity and Asthma in Offspring

34. Muthuvel, Gajanthan
   The Surgical Apgar Score Correlates with an Increased Risk for Readmission in Emergency Surgery Patients

35. Nault, Ashley
   A Retrospective Review on the Number of Skin Biopsies Needed per Malignancy

36. Pham, Trinh
   Morphological Changes in Fibroblasts induced by PBMCs from Patients with Type II Diabetic Nephropathy

37. Raab, Lindsey
   Effect of Maturational Timing of Physical Activity Exposure on Post-Menarcheal Bone Outcomes

38. Regner, Caitlin
   Thematic Analysis of NIH Mentored K and Developmental Research (R21) Proposal Critiques

39. Renfrew, John
   Automated Evaluation of Radiology Reports for Performance Metrics

40. Riley, Sean
   Post-Dural Puncture Headaches Following Insertion of Cerebrospinal Fluid Drains for Thoracoabdominal Aortic Aneurysm Repair: Incidence and Risk Factors

41. Rivedal, David
   Benchmarking Quality for Endoscopic Ultrasound at UW Health

42. Robinson, Aaron
   Should Minimally Invasive Follicular Thyroid Cancer be Treated as a Benign or Malignant Lesion?

43. Roeder, Hannah
   Are Asymmetries in Force and Power Production Related to Knee Sprain Occurrence and Recovery in NCAA Athletes?

44. Ruzga, Anthony
   Tigecycline Elution From Polymethylmethacrylate Bone Cement

45. Shanahan, Matthew
   Is Chromogranin A Prognostic for Resected Pancreatic Neuroendocrine Tumors?

46. Shivaram, Meenakshi
   Pharmacotherapeutic Intervention to Improve Treatment Engagement Among Alcohol-Dependent Veterans After Hospital Discharge

47. Shlensky, David
   The Association of CARM1 Isoform mRNA Expression with Clinical and Molecular Characteristics in Breast Cancer Tumors, and the Differential Localization of CARM1 Protein Isoforms

48. Sookachoff, Michael
   Anesthetic Management of Patients Undergoing Interventional Pulmonology Procedures

49. Stabo, Nicholas
   Volumetric Assessment of Metastatic Colorectal Cancer: Should we RECIST?
50. **Sweetman, Sarah**  
Repeatability of Aortic Annulus Measurements on Pre-procedure CT Scans for Transcatheter Aortic Valve Implantation

51. **Taylor, Lindsey**  
Induction of the Nrf2-Antioxidant Response Element (ARE) Pathway in Cultured Hepatic Stellate Cells (HSCs) Leads to Increased Markers of HSC Activation

52. **Tesfazghi, Sara**  
A Novel HDAC Inhibitor AB3 Reduces Cell Proliferation and Induces the Notch Pathway in Medullary Thyroid Cancer Cells

53. **Vang, Xia**  
Involvement of a Surgical Service Improves Patient Satisfaction After a Small Bowel Obstruction Admission

54. **Vu, Vuong**  
Evaluating the Effects of an Interventional Resistance-Training Program on Strength and Lean Mass Acquisition in Adolescent Girls

55. **Walker, Alyssa**  
Effect of a Supervised Physical Therapy Program for Post-Concussion Syndrome

56. **Weinlander, Eric**  
The Novel Histone Deacetylase Inhibitor Thaiandespin-A Inhibits Anaplastic Thyroid Cancer Growth

57. **Weiss, Deena**  
Examining the Role of Cervical Ultrasound in Detecting Thyroid Pathology in Patients with Primary Hyperparathyroidism

58. **Wiederholt, Andrew; Erickson, Jonathan**  
Psychometric Properties of the Sport Concussion Assessment Tool (SCAT3)

59. **Yanny, Megan**  
Impact of Human Rhinovirus Species on Peripheral Blood Mononuclear Cell Immune Response

60. **Ziegele, Michael**  
Altered Mesenchymal Stem Cell Osteogenesis Contributes to Type I Diabetic Bone Loss

Abstracts for student podium and poster presentations follow, listed alphabetically by student last name.
Background: Morbidity, mortality, and length of stay following complex cancer resection have decreased in recent decades due to improved operative and perioperative care. However, 30 and 90-day readmission rates following pancreaticoduodenectomy remain at 15% and 19% respectively. While considerable research has been conducted regarding the medical risk factors for readmission following complex cancer resection, focusing on medical risk factors alone has not reduced readmission rates to desired levels. Applying a systems engineering methodology to assess the etiology of readmission following complex cancer surgery may show that patient outcome depends on the interaction of many variables and that patient behavior and relationship to his/her environment, support systems, tasks or instructions, the technologies required to fulfill those tasks, and the integration of these variables significantly influence patient outcome.

Methods: The Systems Engineering Initiative for Patient Safety (SEIPS) was the primary methodology used to generate the patient interview. SEIPS combines systems engineering, human factors engineering, and quality engineering in analysis of how systems design, quality management, job design, and technology implementations affect safety-related patient outcomes. The patient interview tool assesses the interaction of the patient with his/her environment, organization (familial, social support networks), post-operative tasks, and the technologies required to fulfill those tasks.

Results: The patient interview was completed in accordance with SEIPS methodology and theory, with emphasis on readmission as a dynamic interaction of many complex variables that influence patient readmission.

Conclusions: This patient interview tool will be used in future pilot studies to analyze contributing and mitigating factors for readmission from the patient’s perspective. An assessment of the interaction of these variables, rather than isolated factors, will be evaluated to assess how they contribute to persisting readmission rates.
Validating the Clinical Validity of Bladder Cancer Nomograms

Authors: Lacmbouh Ade, BS; Tracy Downs, MD, FACS

Department: Department of Urology, University of Wisconsin School of Medicine and Public Health

Mentor: Tracy Downs, MD, FACS

Support: Shapiro Summer Research Program, Department of Urology, University of Wisconsin School Of Medicine and Public Health

BACKGROUND: Early stage urothelial carcinoma of the bladder (UCB) is the fourth most common site of new human cancer diagnoses. It is estimated that in 2012, 14,880 bladder cancer deaths occurred in the United States. Seventy percent of most new bladder cancer cases are limited to the mucosal epithelium (Ta/Tis, Stage 0) and immediate connective tissue layer beneath the mucosa (T1, Stage I). Collectively these tumor stages (Ta, Tis, T1) are referred to as non-muscle invasive bladder cancer (NMIBC). NMIBC represents a heterogeneous group of tumors with completely different oncologic outcomes. Because of this heterogeneity, risk stratification is imperative for classifying patients with similar risks of recurrence and progression, which aids in determine the most appropriate management strategies. To date, the European Organization for Research and Treatment of Cancer (EORTC) risk tables are considered the most reliable tools for estimating progression and/or recurrence of NMIBC. The objective of our study was to analyze if the EORTC bladder cancer nomogram was accurate in predicting disease recurrence and progression in our dataset bladder cancer patients treated at the University of Wisconsin Hospital and Clinics.

METHODS: Surgical scheduling files were used to identify the charts of 208 patients who underwent a bladder biopsy or transurethral resection of bladder tumor(s) between 2010 -2012. To calculate the EORTC risk score for disease recurrence and disease progression, the following tumor characteristics were determined (tumor size, tumor grade, tumor stage, and number of tumors). Each patient was then risk stratified into low-, intermediate and high-risk for tumor recurrence and/or progression. Data was collected for each patient's primary tumor as well as any recurrent tumors (range: 0 -7 recurrent tumors).

RESULTS: The EORTC risk stratification scores were determined for 208 patients. In our UW study cohort, Over 70% of our patients had EORTC Intermediate risk score for disease recurrence and progression. 20% were high-risk and 10% low-risk for recurrence and progression using the EORTC risk stratification system.

CONCLUSIONS: NMIBC is a heterogenous disease requiring constant long-term surveillance studies, which contribute to increasing costs in health care expenditures. In fact, bladder cancer ranks the highest in lifetime per patient costs. Patients treated at UW Hospitals and Clinics received guideline based care compared to the national average. Future studies will allow us to analyze the role physician vs tumor variables play in disease recurrence and progression.
Colonic Distention Analysis According to Patient Position at CTC: Diagnostic Value of Right Lateral Decubitus Series

Authors: Joshua Bakke, BS; Jarret Kuo, MD; Jessica B. Robbins, MD; Meghan G. Lubner, MD; David H. Kim, MD; Perry J. Pickhardt, MD

Department: Department of Radiology, University of Wisconsin School of Medicine and Public Health

Mentor: Perry J. Pickhardt, MD

Support: Shapiro Summer Research Program; Department of Radiology

BACKGROUND: The purpose of this study was to compare total colonic gas volume and segmental luminal distention according to patient position at CT colonography (CTC), and determine which two patient positions should constitute the routine protocol.

METHODS: Volumetric analysis was performed on CTC examinations from 146 consecutive adults (mean age, 59.2 years; 81 males, 65 females; mean BMI, 30.9) where supine, prone, and right lateral decubitus series were sequentially obtained during continuous low-pressure CO2 insufflation. Total colonic gas volumes were assessed using a novel automated volumetric tool. In addition, two radiologists scored distention by segment using a 4-point scale (1=Optimal/2=Adequate/3=Inadequate/4=Collapsed).

RESULTS: Mean colonic gas volume (±SD) for supine, prone, and decubitus positioning was 1617 ± 567 ml, 1441 ± 505 ml, and 1901 ± 627 ml, respectively (p<0.001). The right lateral decubitus series was most voluminous in 73.3% (107/146) and lowest in 6.2% (9/146). The prone series showed lowest colonic volume in 73.3% (107/146) and highest in 0.7% (1/146). Cumulative segmental reader scores and percent inadequate or collapsed for supine, prone, and decubitus positions were 1.52, 1.67, and 1.29, and 10.3%, 12.0%, and 4.1%, respectively (p<0.001). The only mean segmental scores above 2.0 were the sigmoid on supine (2.32) and prone (2.42), compared with a mean score of 1.77 on decubitus (p<0.001).

CONCLUSIONS: The right lateral decubitus position consistently yields the best overall colonic distention at CTC, whereas the prone position is generally the worst. The decubitus view greatly improves sigmoid distention. Routine supine and decubitus positioning should be considered for standard CTC protocols. Automated volumetric analysis provides for an objective assessment of colonic distention.
Patient Hand Hygiene at Home Predicts Their Hand Hygiene Practices in the Hospital

Authors: Anna Barker, BA\textsuperscript{1}; Ajay Sethi, PhD\textsuperscript{1}; Emily Shulkin\textsuperscript{2}; Rachell Caniza\textsuperscript{2}; Sara Zerbel, MS\textsuperscript{3}; Nasia Safdar, MD, PhD\textsuperscript{2,3,4}

Department: \textsuperscript{1}Department of Population Health Sciences, \textsuperscript{2}Department of Medicine, University of Wisconsin School of Medicine and Public Health; \textsuperscript{3}Department of Infection Control, University of Wisconsin Hospital and Clinics; \textsuperscript{4}Division of Infectious Diseases, William S. Middleton Memorial Veterans Affairs Hospital

Mentors: Nasia Safdar, MD, PhD; Ajay Sethi, PhD, MHS

Support: University of Wisconsin School of Medicine and Public Health Integrated Training for Physician-Scientists NIH Training Grant, T32 GM 008692-16

BACKGROUND: Health care-associated infections (HAIs) rank among the top ten leading causes of death in the United States. The most recent data report an estimated 1.7 million HAIs in 2002, responsible for 98,000 deaths in the United States, and costs between $28 and $45 billion a year. Prevention of health care-associated infections is essential, and hand hygiene is the cornerstone of infection prevention. Many studies have focused on increasing compliance with hand hygiene among health care workers, including involvement and empowerment of patients. However, research focusing on hand hygiene practices of hospitalized patients themselves is scarce. This is important, because patients may be a common source of their own infections. Therefore, we sought to examine factors associated with patient hand hygiene practices. Improved hand hygiene by patients, much like hand hygiene by health care workers, may decrease health care associated infections.

METHODS: A convenience sample of 210 adult patients was selected from inpatient records at the University of Wisconsin Hospital, Madison, of which 207 patients participated in the study (98.6% response rate). In an interviewer-administered survey, patients self-reported their hand hygiene practices in the hospital and at home. Data were analyzed using univariate and multivariate logistic regression.

RESULTS: Overall, 48.3% of participants were female and the median age was 63 years (interquartile range 54-69). Patient hand hygiene was lower in the hospital compared to at home, both after restroom use (69.5% vs. 85.0%; P<0.001) and before eating (41.4% vs. 64.7%, P<0.001). Good hand hygiene practices at home were strongly associated with good hand hygiene practices in the hospital, both after restroom use (74.1% vs. 43.3%, P=0.001) and before eating (50.8% vs. 23.5%, P<0.001). Women reported being more comfortable than men asking health care workers to wash their hands (OR=2.52, 95% CI=1.15-5.54, P=0.004).

CONCLUSIONS: Understanding and leveraging the intrinsic value patients associate with hand hygiene, as determined by their hand hygiene practices at home and self-reported importance of hand hygiene for preventing infection, may be important for improving patients' hospital hand hygiene. Gender differences in comfort level for asking health care workers to wash their hands should be explored further.
Quantitative Cell-Based Cellular Fibronectin ELISA: Monitoring Anti-Fibrotic Compounds

Authors: Arielle Bauer, BS; Trinh Pham, MS; Debra Hullett, PhD; Bianca Tomasini-Johansson, PhD; Hans Sollinger, MD, PhD

Department: Department of Surgery, Division of Transplant Surgery, University of Wisconsin School of Medicine and Public Health

Mentor(s): Hans Sollinger, MD, PhD; Bianca Tomasini-Johansson, PhD; Debra Hullett, PhD

Support: Shapiro Summer Research Program; Discretionary funds (Hans Sollinger)

BACKGROUND: Fibronectin (FN) is an extracellular matrix glycoprotein present in blood and also expressed in tissues, including renal proximal tubule epithelial cells. Cellular FN is less soluble and more heterogeneous than plasma FN, consisting of multiple tissue-specific isoforms produced by alternative splicing of the EDA and EDB domains, two Type III FN repeats. An increase in cellular FN deposition into the extracellular matrix is one of the known hallmarks of fibrotic disease. In order to test and identify agents that may inhibit fibrosis, we developed a quantitative microplate assay to measure relative deposition of endogenously produced FN.

METHODS: Renal proximal tubular epithelial cells (HK-2) or foreskin fibroblasts (AH1F) were cultured and plated in 96-well microplates. Potential inhibitors were added to the cells in the microplate and allowed to incubate for 48h in KSFM or DMEM, 0.2% fatty-acid free BSA, respectively. Alamar blue was used to measure viability in the individual wells. Following washing and fixation, Alexa-488-Fn3 (monoclonal antibody to cellular FN) was added to plates and measured in a fluorescence microplate reader to quantitate FN fluorescence. Values for each well were corrected for individual cell viability.

RESULTS: The signal/noise ratio for the assay was >5. TGF-β (20ng/ml) increased endogenous FN 3-fold in AH1F cells. Dose-response curves were obtained for FUD (IC_{50} ~5nM), a known polypeptide inhibitor of FN, added to HK-2 and AH1F cells. Two small molecules (compounds 1 and 2) obtained through a diverse chemical screen, were tested for dose-response inhibition of fluorescence. After normalization, compounds 1 and 2 at a concentration of 1.3uM resulted in 30% inhibition of FN fluorescence in AH1F cells.

CONCLUSIONS: Because higher concentrations (>5uM) of compounds 1 and 2 display cytotoxicity, further tests using lower concentrations than 1.3uM should be performed on AH1Fs. Further research into structure-activity relationships with compounds 1 and 2 can be done to investigate ways in which to make them more effective inhibitors of FN deposition. The newly developed quantitative assay can be used to test changes in cellular FN fibrillogenesis elicited by possible modulators, with the long term goal of identifying potential anti-fibrotic therapeutics that work extracellularly.
Does a Multidisciplinary Thyroid Clinic Improve Follow up of Benign and Indeterminate Thyroid Nodules after Fine Needle Aspiration?

Authors: Ryan Bergren, BS; Jimmy Xu, BS; Juan Jaume, MD; David Schneider, MD, MS; Herbert Chen, MD, FACS; Rebecca S. Sippel, MD, FACS

Department: Department of Surgery, Division of Endocrinology, University of Wisconsin School of Medicine and Public Health

Mentor(s): Rebecca Sippel, MD, FACS; Herbert Chen, MD, FACS; David Schneider, MD, MS

Support: Shapiro Summer Research Program, Department of Surgery

BACKGROUND: Fine needle aspiration (FNA) is used to evaluate thyroid nodules for malignancy. Current guidelines recommend surgery for a follicular neoplasm, and a follow up ultrasound within 12 months after a benign FNA in order to evaluate for continued growth. However, compliance with these recommendations is variable. This study’s goal was to determine if there is a difference in follow up depending on the location in which the thyroid FNA is performed.

METHODS: A cohort of 456 patients that received an FNA in 2008-2009 from a primary care system at a single academic institution that had a benign or follicular neoplasm on FNA was identified. Patients were grouped based on where the FNA was performed: a multidisciplinary thyroid clinic (MDC) or radiology. Follow up data including referral for surgery, repeat imaging, and repeat FNA, were analyzed between the two groups.

RESULTS: During the study period, 310 (68%) FNAs were completed in the MDC and 146 (32%) in radiology. FNA results were benign in 429 (94%) patients and a follicular neoplasm in 27(6%). The mean age was 54 and 83% were female. Patients seen in each location had similar demographics and FNA results. 90% (N=29) of the follicular neoplasm FNAs underwent surgery and this was similar in both groups (95% vs. 80%, p=0.27). However, patients seen in the MDC clinic were more likely to be referred for surgery, even with a benign FNA (32% vs. 18%, p=0.0014). Of the 427 patients with a benign FNA, only 38% received the recommended imaging follow up. Patients seen in the MDC were significantly more likely to receive the recommended follow up imaging versus patients receiving their FNA in radiology (42 % vs. 29%, p=0.0047) and were more likely to get a repeat FNA ordered (18% vs. 6%, p=0.0002). Of those with follow up imaging, significant growth was seen in 44 (27%) patients. Repeat FNA was performed in 39% with significant growth and this was not statistically different between groups (42% (N=16) vs. 20% (N=1), p=0.38).

CONCLUSIONS: Overall compliance with recommendations after a follicular neoplasm FNA was excellent regardless of location. While compliance with follow up imaging after a benign FNA was overall suboptimal, utilizing a MDC did significantly increase compliance with recommended follow up imaging and may be a more effective mechanism to optimize the care of patients with thyroid nodules long-term.
A Straightforward Technique for Eliciting and Recording Compound Action Potentials in a Rat Spinal Cord

Authors: Robert Bjerregaard, BS; Casey Madura, MD; Kyle Fischer; Daniel Hellenbrand, MS; Amgad Hanna, MD

Department: Department of Neurological Surgery, University of Wisconsin School of Medicine and Public Health

Mentor: Amgad Hanna, MD

Support: Shapiro Summer Research Program; Department of Neurological Surgery

BACKGROUND: Electrophysiology experiments are commonly used to quantitatively assess neuronal function. Here we present a straightforward electrophysiological technique for stimulating and recording compound action potentials (CAPs) in a 15 mm section of exposed rat spinal cord. CAP amplitudes and velocities were measured in multiple rats; larger amplitudes indicated greater axonal recruitment, and faster conduction indicated increased axonal myelination and/or axon diameter. Previous studies have achieved limited success in recording CAPs across short distances due to stimulus artifacts interfering with the CAP signal at the recording electrode. The methods presented here substantially reduce the stimulus artifact amplitude while preserving the CAP signal, greatly increasing the signal to noise ratio in rat spinal cord electrophysiology experiments.

METHODS: A T8 to T12 laminectomy was performed on each rat prior to testing. Concentric bipolar microelectrodes were used to both elicit and record CAPs through a 15 mm spinal cord section. CAPs were elicited using 30 µs square-wave currents ranging from 250 µA to 1.5 mA. Evoked potentials were recorded with an identical concentric bipolar electrode. All signals were processed using a differential amplifier (gain of 20,000) and a 3 Hz to 3 kHz band-pass filter. 25 CAPs were recorded and averaged for each stimulating current to further reduce noise. Lidocaine was injected between the stimulating and recording sites and the electrophysiology experiments were repeated to eliminate CAPs, confirming the source of the electrical signals.

RESULTS: Compound action potentials were measured in multiple healthy rats and eliminated after lidocaine administration. Measurements of mean action potential velocity consistently ranged from 20 to 25 m/s, with some axons conducting as fast as 50 m/s and others as slow as 11.5 m/s. As stimulus currents were increased, CAP amplitude increased and variably plateaued.

CONCLUSIONS: The variation in action potential velocity is to be expected due to differences in myelination and diameter among axons in the spinal cord. The plateau of CAP amplitude with increasing currents is to be expected; a greater number of axons are depolarized with a larger stimulus current, with the entire spinal cord eventually being depolarized. These methods of measuring CAP conduction in spinal cord segments will be of great value in future studies assessing axon regeneration across various distances.
Estimation of HIV/HBV/HCV Seroprevalence in Ethiopia Using Rapid, Multiplex Antibody Detection

Authors: DeMarco Bowen, BS; Admasu Tenna, MD1; Aklilu Debela, MD1; Girma Tefera, MD2; Ryan Westergaard, MD, PhD, MPH2

Department: 1Department of Internal Medicine, Addis Ababa University School of Medicine; 2Department of Medicine, University of Wisconsin School of Medicine and Public Health

Mentor(s): Ryan Westergaard, MD, PhD, MPH

Support: Shapiro Summer Research Program; Global Health Institute, University of Wisconsin School of Medicine and Public Health; Department of Medicine, University of Wisconsin School of Medicine and Public Health

BACKGROUND: There are insufficient surveillance data available in Addis Ababa, Ethiopia to allow an accurate estimate of the prevalence of blood-borne pathogens among patients needing emergency medical and surgical treatment. We estimated the seroprevalence of HIV, HBV, and HCV among patients presenting to Emergency Department (ED) of Tikur Anbessa (Black Lion) Specialized Teaching Hospital, the national referral and teaching center of Ethiopia.

METHODS: During June and July of 2013, we collected remnant blood specimens from consecutive patients presenting to the ED at Black Lion Hospital. Basic demographic and clinical data were extracted from patients’ medical records and linked to specimens using an anonymous code, after which all patient identifiers were destroyed. Serum or plasma samples were tested with a multiplex HBV/HIV/HCV rapid antibody detection kit. Positive HIV and HBV samples were tested with a second HIV 1/2 rapid test kit and HBsAg test, respectively.

RESULTS: Of 336 patient samples, 44 (13%) were HIV seropositive, 101 (30%) were HBV seropositive, and 21 (6%) were HCV seropositive. Forty-five percent (20/44) of HIV positive samples were from patients known to have been previously diagnosed with HIV. Of 38 HIV positive samples tested with the HIV 1/2 rapid test, 33 (87%) were positive. Of 91 HBV seropositive samples tested with the HBsAg test, 21 (23%) were positive, indicating active infection. The age range of 20-35 showed the highest rate of positive samples, containing 24 (55%) of the HIV positive samples, 41, (41%) of the HBV positive samples, and 9 (43%) of the HCV positive samples.

CONCLUSIONS: We demonstrated a high seroprevalence of HIV and viral hepatitis among adult patients seeking care in the emergency department of an urban, academic hospital in Ethiopia. Combined serologic screening for HIV, HBV and HCV with rapid antibody detection kits is a feasible approach to collecting data about the risk of occupational exposure to these blood-borne pathogens. The majority of HIV and HBV positive samples were collected from patients not known to be HIV-infected based on the hospital chart, highlighting importance of universal contact precautions and hepatitis B immunization among health care workers in Sub-Saharan African settings.
Inhibition of Notch Signaling Reduces Healing of Splinted Cutaneous Excisional Wounds in Mice

Authors: Marielle A. Brenner, BS; Alex Thompson; Taylor J. Jaraczewski, BS; Priya R. Pathak; Madhuchhanda Roy, MD, PhD; Timothy W. King, MD, PhD, FACS, FAAP

Department: Department of Surgery, Division of Plastic Surgery, University of Wisconsin School of Medicine and Public Health

Mentor(s): Timothy W. King, MD, PhD, FACS, FAAP

Support: Shapiro Summer Research Program; AAPS/PSF Academic Scholarship Award

BACKGROUND: Complications due to impaired wound healing affect millions of people & management cost more than $20B/yr. In cutaneous wound healing keratinocytes proliferate, migrate across the wound bed, & then differentiate into a multilayered, waterproof barrier. We are interested in increasing the efficiency of the wound healing process by investigating the underlying mechanisms that regulate this process. Previously, we have shown that the Notch signaling pathway plays a role in keratinocyte proliferation & migration \textit{in vitro}. Here, we tested the effects of inhibition of Notch signaling on re-epithelialization of wounded epidermis in a murine stented wound model. Our hypothesis is that blocking the Notch pathway will decrease wound healing.

METHODS: 6 week old, male mice were anesthetized & full-thickness wounds were placed the ski of their backs (n=9). A 12 mm dia. silicone stent was secured around each wound with cyanoacrylate glue & interrupted 6-0 nylon sutures. Wounds were dressed with sterile N-terface & Tegaderm, then wrapped with Coban, & secured with Transpore tape. Dressings were changed every day after topical application onto the open wound bed of the Notch inhibitor, DAPT (30 uM) or vehicle (0.1% DMSO) for 10 days. Digital photographs were taken everyday. After 10 days, the wounds were harvested for histological analysis. Wounds were analyzed using ImageJ software & normalized to the inner circumference of the splint. Wound area was calculated as a percent area of the original wound size. Statistical significance was defined as p<0.05 using the students’ t-test.

RESULTS: Partial to complete re-epithelialization was seen in the wounded tissues over the experimental period in both the control & DAPT treated groups. Rates of wound closure were significantly reduced in DAPT treated wounds compared to control (p<0.02). No significant local side effects such as increased edema or allergic reaction were noted in the DAPT-treated mice.

CONCLUSIONS: DAPT decreases re-epithelialization of cutaneous wounds in the \textit{in vivo} murine stented wound healing model, indicating that Notch signaling plays a crucial role in wound healing in immunocompetent mice. Histological analysis including markers for keratinocyte migration, proliferation & angiogenesis/vascular density are underway. Based upon our findings, further study of Notch in wound healing should be conducted which may then lead to better therapeutics for the wound healing process in patients.
El Cáncer, Claro y Sencillo: Latino Cancer Education and Outreach in Madison, Wisconsin

Authors: Sarah Brown, BA; Rebecca Linskens, MA; Amy Williamson, MPP; Alexandra Adams, MD, PhD

Department: Cancer Health Disparities Initiative, University of Wisconsin Carbone Cancer Center

Mentor(s): Alexandra Adams, MD, PhD; Amy Williamson, MPP

Support: Shapiro Summer Research Program; Cancer Health Disparities Initiative, University of Wisconsin Carbone Cancer Center

BACKGROUND: There is a rapidly growing Latino population in Madison with specific health, health care and public health needs. While there are services offered to many underserved communities in Madison, health disparities persist for Latinos. The UW Carbone Cancer Center’s Cancer Health Disparities Initiative (CHDI) and Centro Hispano of Dane County are partnering on a pilot project to provide cancer health education to Madison’s Latino residents. The pilot project, El Cáncer, Claro y Sencillo, aims to increase community members’ knowledge about cancer prevention, promote informed patient decisions and empower residents to improve their health and the health of their families. CHDI drafted study design documents, a timeline, an evaluation grid and a logic model for the pilot. These were used to develop data collection instruments and to ensure that the adaptation process corresponded with pilot goals. CHDI then worked with community partners to adapt a cancer education intervention, and evaluated the materials.

METHODS: Upon initial adaptation of the materials, CHDI elicited feedback from community partners. After responding to the feedback, CHDI conducted focus groups with bilingual community members to evaluate the module. Additional qualitative and quantitative data will be collected to determine whether the intervention evokes changes in participants’ knowledge and behavioral intent. The partners will also conduct interviews with program participants to assess whether the program resulted in actual change in health behaviors.

RESULTS: Focus group participants reported overall satisfaction with the module content, literacy, graphics, layout, motivational quality and cultural relevance of the materials. The average participant rated the overall module 4.52 on a five point Likert scale. Participants also offered qualitative responses for module improvement.

CONCLUSIONS: Based on analysis of focus group data, CHDI finalized El Cáncer, Claro y Sencillo and determined that it reflected appropriate literacy, valuable health information and cultural relevance. This autumn, CHDI will train community-based bilingual trainers. The trainers will use El Cáncer, Claro y Sencillo to conduct cancer education workshops with community members. CHDI will collect data analyzing changes in participant knowledge, behavioral intent and health behaviors. Findings will be presented in academic and community reporting to add to the evidence base for this form of health programming.
Predicting Urinary Tract Infection after Radical Cystectomy and Urinary Diversion

Authors: Andrew Brunk, BS; Tracy M. Downs, MD, FACS; Fangfang Shi, MS

Department: Department of Urology, University of Wisconsin School of Medicine and Public Health

Mentor(s): Tracy M. Downs, MD, FACS

Support: Shapiro Summer Research Program; Department of Urology

BACKGROUND: Following radical cystectomy (RC) and urinary diversion, patients experience a high rate of complications, with estimates ranging from 20% to 50%. Urinary tract infection (UTI) is a common complication, though high rates of asymptomatic bacteriuria make diagnosis of clinically significant UTIs difficult. The objective of this study was to evaluate urinalysis and patient specific factors that could help clinicians accurately diagnose UTIs.

METHODS: We reviewed records of 238 patient encounters by 76 consecutive RC patients with bladder cancer from 2010 to 2012. Patients' presenting symptoms and bacterial culture data were used to identify cases of symptomatic UTI. We then calculated the sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of urinalysis and patient specific parameters for predicting UTIs. Non-UTI encounters within 30 days of surgery, cultures with three or more organisms with growth >100,000 cfu/mL and encounters with patients with indwelling stents of ureteral strictures were excluded.

RESULTS: A total of 38 UTIs occurred in 23 patients, with eight patients suffering multiple UTIs. The highest number of UTIs in a single patient was four. Calculated sensitivity, specificity, PPV and NPV were, respectively: fever (55.3%, 98.8%, 95.5%, 82.7%), urinalysis leukocyte esterase positive (92.1%, 43.9%, 43.2%, 92.3%), urinalysis nitrite positive (60.5%, 64.6%, 44.2%, 77.9%), urinalysis WBC >10 (100%, 11.0%, 34.2%, 100%) and blood WBC >12 (34.2%, 81.7%, 46.4%, 72.8%).

CONCLUSIONS: Urinalyses positive for leukocyte esterase, nitrites and white blood cells are frequently treated as urinary tract infections. However, substantial numbers of non-UTI RC patients present with leukocyte esterase and nitrite positive urine, and are asymptomatic. Misdiagnosing and treating these asymptomatic patients for UTIs could lead to antibiotic-resistant bacteria and unnecessary costs for patients. Presence of fever is limited as a diagnostic tool by the sizable percentage of UTI patients presenting without fever. The parameters reviewed in this project do not represent definitive measures for diagnosing UTI in patients following RC and urinary diversion.
Acuity Adaptable Patient Care Model Shortens Length of Stay and Improves Outcomes in Adult Cardiac Surgery

Authors: Shahzad A. Chindhy, BS¹; Niloo M. Edwards, MD²; Victoria Rajamanickam, MS³; Entela B. Lushaj, MD, PhD¹; Lucian Lozonschi, MD¹; Nilto C. De Oliveira, MD, FRCS¹; Takushi Kohmoto, MD, PhD¹; Satoru Osaki, MD, PhD¹

Department: ¹Department of Surgery, Division of Cardiothoracic Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI, United States; ²St. Peter's Hospital, NY, United States; ³Department of Biostatistics and Medical Informatics, Institute for Clinical and Translational Research, University of Wisconsin–Madison, WI, United States

Mentor(s): Entela Lushaj, MD, PhD; Satoru Osaki, MD, PhD

Support: Shapiro Summer Research Program; Department of Surgery Grant 233P970

BACKGROUND: The Acuity Adaptable Patient Care (AAC) unit system allows all beds within a nursing unit to negate the need for transfer with changes in patient status. The unit is specialty specific for all levels of patient care. This system was implemented in March 2006 for cardiothoracic surgery at our institution. The purpose of this study is to evaluate the impact of the AAC system on the outcomes after adult cardiac surgery.

METHODS: We retrospectively reviewed 2930 consecutive patients who underwent major adult cardiac procedures between January 2003 and December 2010. The cohorts were divided into the pre-AAC group (January 2003 to February 2006, n=1029) and the AAC group (March 2006 to December 2010, n=1901). Patient demographics and postoperative outcomes were assessed.

RESULTS: The proportion of coronary artery bypass grafting was significantly lower (pre-AAC vs. AAC: 43 vs. 35%, p<0.01), while those of aortic procedure (4 vs. 11%, p<0.01) and mechanical assist device insertion (3 vs. 5%, p=0.02) were higher in the AAC group. After the implementation of the AAC system, the incidence of all complications defined by the Society of Thoracic Surgeons (STS) database (49 vs. 34%, p<0.01), the median length of Intensive Care Unit (ICU) stay (49 [interquartile range, 27-99] vs. 26 [19-45] hours, p<0.01), that of hospital stay (6 [4-10] vs. 5 [4-7] days, p<0.01), and the readmission rate of ICU (5 vs. 2% p<0.01) were significantly decreased. Significant reductions in hospital mortality and the rate of hospital readmission <30-day were not observed.

CONCLUSIONS: The implementation of the AAC system has improved the outcomes after major cardiac procedures. The incidence of postoperative complications and length of stay have all decreased significantly without increasing readmission rate. AAC creates a system of fluid care with specialty trained nursing and other ancillary support that expedites discharge and improves overall patient outcomes.
DNA Methyltransferase Silencing Effect on Spinal Axon Regeneration in Folic-Acid Treated Rat Progeny

Authors: Megan Dietze, BS; Anaita Chindhy, BS; Nithya Hariharan, MD; Wil Gibbs; Joslyn Strebe; Sivan Vadakkadath Meethal, PhD; Bermans J. Iskandar, MD

Department: Department of Neurological Surgery, University of Wisconsin School of Medicine and Public Health

Mentor(s): Bermans J. Iskandar, MD

Support: Shapiro Summer Research Program; Department of Neurological Surgery

BACKGROUND: Dr. Iskandar’s laboratory has shown that treating adult rats with intraperitoneal folic acid leads to enhanced recovery from spinal cord injuries and increased sensory spinal axon regeneration into peripheral nerve grafts. This effect is mediated by DNA methylation, a potentially inheritable chemical modification in the DNA that is generated by the folate and methionine-methylation pathway. Accordingly, the progeny of these folic acid treated rats also showed improved axon regeneration after spinal injury. DNA methyltransferases (Dnmts) are responsible for transferring the methyl group from S-Adenosylmethionine in the methionine-methylation cycle, an extension of the folate pathway, to the CpG dinucleotides within DNA of the mammalian genome. The expression of two Dnmt types, Dnmt3a and Dnmt3b, is suppressed when a spinal cord injury occurs in rats, and an increase in Dnmt expression occurs with folic acid treatment. This study investigated whether Dnmt expression is also involved in axon regeneration in the progeny of folic acid treated rats by assessing axon regeneration in response to silencing the Dnmt genes.

METHODS: The F4 generation rats from folic-acid treated progenitors are given sharp C3 dorsal column transection. Three days later, the dorsal root ganglia at L4/L5 (which project axons to the injured segment) are harvested, the neuronal cell bodies extracted, and the cells cultured using standard cell culture protocols. Next, the cells are treated with siRNA transfection specific to Dnmt3a, Dnmt3b, or Dnmt1 to silence the corresponding gene. Cells are fixed and stained at 12, 24, and 48-hour timepoints. The slides are photographed and ImageJ is used to measure axonal regeneration.

RESULTS: We show decreased axonal regeneration from the 12-hour timepoints to the 48-hour timepoints for cells treated with siRNA specific for Dnmt3a, Dnmt3b, or Dnmt1, with variable effects in the controls.

CONCLUSIONS: The decrease in spinal axonal regeneration at longer time points in cells treated with Dnmt suggests that Dnmt plays an important role in axonal regeneration and that this is inherited in the progeny of folic-acid treated rats. Further studies are needed to establish more consistency in the results from controls.
Barriers to Oral Health Awareness: Survey of the Health of Wisconsin (SHOW)

Authors: Amanda Delaney, BA, MPH; Javier Nieto, MD, MPH, PhD

Department: Department of Population Health Sciences, University of Wisconsin School of Medicine and Public Health

Mentor(s): Javier Nieto, MD, MPH, PhD

Support: Shapiro Summer Research Program; Department of Population Health Sciences

BACKGROUND: Self-rated oral health represents an individual's view on health and access to healthcare. Oral health is becoming increasingly important to overall health. Oral hygiene such as tooth brushing and flossing are associated with reduced CVD risk. Preventive dental care reduces the risk of acute myocardial infarction and stroke. However, there is limited knowledge about awareness of oral health. The purpose of this study is to characterize the demographic factors that influence awareness of oral health.

METHODS: The SHOW core survey includes a questionnaire on self-reported oral health. In addition, during the 2009-2010 waves of SHOW, participants were offered an oral health examination. A total of 1,439 participants had both self-reported and objectively assessed oral health data.

RESULTS: Overall, 16.5% of this population needed urgent or early dental care. The need for dental care was higher among groups who were never married, non-white, depressed, a high school graduate or less, a current smoker, and lower income. In addition, dental need was higher among groups that had a lower self-rated health score and more time since last dental appointment. Among those who needed dental care, 58% reported their oral health status as poor or fair. Risk factors that influenced sensitivity were smoking, non-white race, depression, rural living, and lower education status. Among those who did not need care, 74% reported their oral health was good, very good, or excellent. Risk factors for sensitivity were being male, non-white, a smoker, and a high school graduate or less.

CONCLUSIONS: This study shows a substantial lack of awareness of oral health status among Wisconsin residents. In addition, there are certain subpopulations that have lower rates of awareness. These groups should be targeted for public health interventions. Further studies should be done to investigate effectiveness of awareness programs in these demographic groups.


DNA Methyltransferase Silencing Effect on Spinal Axon Regeneration in Folic-Acid Treated Rat Progeny

Authors: Megan Dietze, BS; Anaita Chindhy, BS; Nithya Hariharan, MD; Wil Gibbs; Joslyn Strebe; Sivan Vadakkadath Meethal, PhD; Bermans J. Iskandar, MD

Department: Department of Neurological Surgery, University of Wisconsin School of Medicine and Public Health

Mentor(s): Bermans J. Iskandar, MD

Support: Shapiro Summer Research Program; Department of Neurological Surgery

BACKGROUND: Dr. Iskandar’s laboratory has shown that treating adult rats with intraperitoneal folic acid leads to enhanced recovery from spinal cord injuries and increased sensory spinal axon regeneration into peripheral nerve grafts. This effect is mediated by DNA methylation, a potentially inheritable chemical modification in the DNA that is generated by the folate and methionine-methylation pathway. Accordingly, the progeny of these folic acid treated rats also showed improved axon regeneration after spinal injury. DNA methyltransferases (Dnmts) are responsible for transferring the methyl group from S-Adenosylmethionine in the methionine-methylation cycle, an extension of the folate pathway, to the CpG dinucleotides within DNA of the mammalian genome. The expression of two Dnmt types, Dnmt3a and Dnmt3b, is suppressed when a spinal cord injury occurs in rats, and an increase in Dnmt expression occurs with folic acid treatment. This study investigated whether Dnmt expression is also involved in axon regeneration in the progeny of folic acid treated rats by assessing axon regeneration in response to silencing the Dnmt genes.

METHODS: The F4 generation rats from folic-acid treated progenitors are given sharp C3 dorsal column transection. Three days later, the dorsal root ganglia at L4/L5 (which project axons to the injured segment) are harvested, the neuronal cell bodies extracted, and the cells cultured using standard cell culture protocols. Next, the cells are treated with siRNA transfection specific to Dnmt3a, Dnmt3b, or Dnmt1 to silence the corresponding gene. Cells are fixed and stained at 12, 24, and 48-hour timepoints. The slides are photographed and ImageJ is used to measure axonal regeneration.

RESULTS: We show decreased axonal regeneration from the 12-hour timepoints to the 48-hour timepoints for cells treated with siRNA specific for Dnmt3a, Dnmt3b, or Dnmt1, with variable effects in the controls.

CONCLUSIONS: The decrease in spinal axonal regeneration at longer time points in cells treated with Dnmt suggests that Dnmt plays an important role in axonal regeneration and that this is inherited in the progeny of folic-acid treated rats. Further studies are needed to establish more consistency in the results from controls.
Assessment of the Contemporary Role and Risks of Renal Mass Biopsy at a Single Institution

Authors: Anna Drewry, BS; Fangfang Shi, MS; William Christensen, BS; E. Jason Abel, MD

Department: Department of Urology, University of Wisconsin School of Medicine and Public Health

Mentor: E. Jason Abel, MD

Support: Shapiro Summer Research Program; Department of Urology

BACKGROUND: Renal mass biopsy (RMB) may be performed prior to definitive treatment of renal masses to allow a better assessment of an individual patient’s cancer risk. Traditionally, the reported accuracy of RMB to detect cancer was poor, and concerns over false negative results led to historically poor utilization. In addition, there remain concerns among patients and health care providers about the safety of percutaneous techniques for RMB and tumor spillage. This study aimed to assess the contemporary accuracy and risks of RMB.

METHODS: Clinical and pathologic data for 463 patients who underwent RMB at a single institution from 1/2000-6/2013 was reviewed.

RESULTS: Of the 510 biopsies performed, 84% yielded a definitive pathologic specimen. The use of the quadrant biopsy technique for masses $\geq 8$ cm improved definitive rates over standard biopsy technique ($n=42$ and $n=30$, definitive rates 100% vs. 86.6%, respectively). Definitive rates also varied by the physician performing the biopsy (mean 15.44%, range 6.98-26.19%, p-value 0.02), but this may represent a selection bias due to the retrospective nature of the study.

6 patients experienced a complication related to biopsy (1.17%), only 2 of which required intervention (0.39%); there were no cases of tumor spillage. Importantly, 33% of the patients who originally had a non-definitive biopsy were later diagnosed with cancer on subsequent biopsy or surgery. This implies that a non-definitive biopsy is not a substitute for a negative biopsy. Also of note, in the patients who underwent surgery following their biopsies, 40% had an increase in tumor grade and 15.5% had an increase in stage from cT1 to pT3/4 from biopsy to surgery.

CONCLUSIONS: RMB provides a cancer/no cancer diagnosis for 84% of patients with renal masses considering treatment. Limitations include inability to accurately predict tumor grade and stage which results in poor risk stratification. Less than 1% of RMB patients have major complications.
Noninvasive Quantification of Tendon Biomechanics: Shear Wave Elastography Imaging in a Porcine Tendinopathy Model

Authors: Benjamin Ebben, BS; Kenneth Lee, MD; Ryan DeWall, PhD

Department: Department of Radiology, Division of Musculoskeletal Radiology, University of Wisconsin School of Medicine and Public Health

Mentor(s): Kenneth Lee, MD; Ryan DeWall, PhD

Support: Shapiro Summer Research Program; Department of Radiology, Division of Musculoskeletal Radiology

BACKGROUND: Currently, tendinopathy management is guided by traditional ultrasonography, which can only provide morphological assessment of the injured tendon but does not quantify biomechanics. Biomechanic measures, such as tendon elasticity, would serve as a more direct biomarker in guiding the decision to undergo surgical intervention vs. conservative alternatives. Shear wave imaging (SWI) is an ultrasound-based elastography technique for the noninvasive quantification of tendon biomechanics. SWI tracks shear wave propagation through tendon tissue and calculates shear wave speed (SWS). SWS is proportional to the tissue elastic modulus and may predict tissue strength, an indicator of the likelihood of rupture, which is significant in guiding treatment approaches. We quantify the effect of structural damage in an animal tendinopathy model using SWI.

METHODS: 16 porcine flexor tendons were focally injected with a 0.05 mL bolus of 1.5% collagenase solution to induce focal structural damage. Collagenase has been used previously in other animal tendinopathy models. Control tendons were injected with saline (n=16). 8 tendons from each group were incubated at 37°C for 3.5 hours while the remaining 8 from each group were incubated for 7 hrs. Tendons were mechanically stretched to 0% and 1% strain using a Mark-10 Force Measurement System. Simultaneously, SWI was acquired proximal to (PROX), at (ROI), and distal to (DIST) the injection site using a Supersonic Imagine Aixplorer clinical ultrasound scanner. Unpaired t-tests were used to examine treatment effects on SWS with statistical significance set at < 0.05.

RESULTS: There were significant differences in SWS (saline > collagenase) at 1% strain and 7 hrs incubation for all three locations (PROX p=0.0031, ROI p=0.001, DIST p=0.0043). There were also significant differences at 0% strain and 7 hrs, but only at (p=0.0005), and distal to (p=0.0035), the injection site. No statistically significant differences were observed for 3.5 hrs incubation, at 0% or 1% strain.

CONCLUSIONS: Collagenase-mediated structural damage does appear to convey decreased tissue elasticity on SWI when ex vivo tendons are incubated for 7 hrs. These findings suggest that SWI may be a useful tool for predicting ultimate tissue strength in tendinopathic tissues. Pull-to-failure testing should be performed in the future and are expected to show that tendons with decreased SWS, and therefore, decreased elasticity, rupture at lower pulls forces.
Preoperative Cognitive and/or Functional Impairment is Associated with the Need for Higher Level of Care After Hospital Discharge

Authors: Colin C. Ehlenbach, BS; Sarah E. Tevis, MD; Gregory D. Kennedy, MD, PhD; Sarah C. Oltmann, MD

Department: Department of Surgery, University of Wisconsin School of Medicine and Public Health

Mentors: Gregory D. Kennedy, MD, PhD; Sarah C. Oltmann, MD

Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: Preoperative comprehensive geriatric assessment (CGA) has been found to predict morbidity and mortality in patients undergoing elective surgery. Preoperative risk factors have been shown to lead to post-discharge institutionalization. An association between preoperative risk factors, preoperative level of required care, and discharge to higher levels of care has not previously been demonstrated. This study aimed to identify validated cognitive and functional capacity measurements that correlate with discharge level of care in older adult patients undergoing general surgery.

METHODS: A retrospective review of general surgery patients from an academic, tertiary referral center ACS-NSQIP database was performed. Patients undergoing inpatient, non-emergent, general surgery procedures with complete electronic medical records were included in this study. Initial univariate analysis was performed between age groups of less than 65 years and 65 years and older. Univariate and multivariate analyses were then performed in patients 65 years and older to identify correlations between discharge level of care, 30-day readmission, and postoperative complications with cognitive, functional, and demographic risk factors.

RESULTS: Between 2006 and 2012, 3369 patients were included in the institutional ACS-NSQIP database, of which 2012 had complete electronic medical records and met inclusion criteria. Of patients less than 65 years old, 1.9% were discharged to a higher level of care, while 12.2% of patients 65 years and older were discharged to a higher level of care. Low Mini Mental State Examination score, low Lawton Instrumental Activities of Daily Living Scale score, advanced age, high American Society of Anesthesiologists physical status class, and long hospital length of stay were found to be associated with postoperative discharge to a higher level of care in patients 65 years and older. Long hospital length of stay was found to be associated with one or more postoperative complications and 30-day hospital readmission in patients 65 years and older.

CONCLUSIONS: Cognitive and functional capacity scoring can be used as simple ways to predict discharge to a higher level of care for older adults. Preoperative counseling in high-risk older adults needs to include the likelihood for discharge to a higher level of care, and if necessary, a timely referral to social work can be placed to facilitate postoperative discharge planning.
Inflammation Contributes to Depression in Allogeneic Hematopoietic Stem Cell Transplant Recipients

Authors: Alexandra A. Erdmann, BS¹; Mark B. Juckett, MD²,³; Christopher L. Coe, PhD⁴; Peiman Hematti, MD²,³; Ashley M. Nelson, BS¹; Paul J. Rathouz, PhD⁵; Erin S. Costanzo, PhD¹,³

Department: Departments of ¹Psychiatry; ²Medicine, Division of Hematology and Medical Oncology, ⁵Biostatistics & Medical Informatics, University of Wisconsin School of Medicine and Public Health; ⁴UW Department of Psychology; ³UW Carbone Cancer Center

Mentor(s): Erin S. Costanzo, PhD

Support: Shapiro Summer Research Program; Department of Psychiatry; National Cancer Institute (K07 CA136966, R21 CA133343); Forward Lymphoma Foundation

BACKGROUND: Allogeneic hematopoietic stem cell transplant (HSCT) is a potentially curative treatment for hematologic cancers. Depression is a prevalent concern for individuals undergoing this rigorous treatment. Recent studies suggest that proinflammatory cytokines can activate central nervous system pathways that evoke depressed mood. Given the high levels of inflammation seen in HSCT recipients, the major goal of this study was to investigate the association between inflammatory cytokines and depressive symptoms in this high-risk population. We also examined the extent to which inflammation was associated with neurovegetative versus cognitive and affective depression symptoms.

METHODS: Cancer patients undergoing allogeneic HSCT (N=54) completed the Inventory of Depression and Anxiety Symptoms at pre-transplant and 1, 3, and 6 months post-transplant. Circulating proinflammatory (IL-6, TNFα) and regulatory (IL-10) cytokines were assessed by ELISA in peripheral blood plasma at the same time points. Mixed-effects and subject-level fixed effects regression models were employed to examine relationships between cytokine levels and depressive symptoms.

RESULTS: Results indicated that participants with elevated IL-6 (z = 3.5, p < .01), and IL-10 (z = 2.0, p = .05) reported more severe depressive symptoms compared to participants with low/normal cytokine levels, and there was a trend for a similar effect of TNFα (z = 1.9, p = .058). Follow-up analyses clarified that relationships were seen for neurovegetative (z = 2.5-3.1, all ps <.05) but not for cognitive/affective symptoms of depression. All models adjusted for time since transplant, conditioning regimen, graft-versus-host-disease, and recipient's age. Within-subjects analyses revealed that among individual patients, changes in cytokine levels across the assessment points were associated with corresponding changes in depressed mood, with patients reporting greater overall and vegetative depression symptoms when IL-6 (z = 3.1, p <.01) and TNFα levels were elevated (z = 2.1, p = .04).

CONCLUSIONS: Results provide evidence for a novel biobehavioral pathway by which inflammation from conditioning therapy or transplant-related complications may contribute to depressive symptoms among HSCT patients, specifically neurovegetative symptoms. Findings suggest a potential treatment-related cause of depression that could be targeted to improve the quality of life of allogeneic HSCT recipients.
Patient Profile at Tikur Anbessa Specialized Hospital  
Vascular Surgery Clinic, Addis Ababa, Ethiopia

Authors: Sean Fling, BA; Girma Tefera, MD; Nebyou Seyoum, MD; Charles Penn, BS; Rakeb Tibebu

Department: 
1Department of Surgery, Division of Vascular Surgery, University of Wisconsin School of Medicine and Public Health; 2Addis Ababa University, Faculty of Medicine

Mentor(s): Girma Tefera, MD; Nebyou Seyoum, MD

Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: While the ravaging effects of infectious diseases are being curtailed internationally, chronic disease is becoming increasingly prevalent worldwide. Cardiovascular disease (CVD) is especially afflicting countries globally. Although there is bountiful information relating to the prevalence of chronic disease in more prosperous countries, there is little information that shows these trends in developing countries such as Ethiopia. Tikur Anbessa Specialized Hospital (TASH) is the largest hospital in Ethiopia and is located in the capital city, Addis Ababa. It has a relatively new vascular surgery clinic. The objective of this study was to develop a database for this new clinic and understand the significance of a patient profile. TASH was thought to serve as a good source for creating a patient profile on Ethiopian cardiovascular patients as the largest public hospital in Addis Ababa.

METHODS: An extensive data sheet was created using Microsoft Excel software. Paper copies were used to record patient's demographics including history, physical exam, vascular risk factors, and laboratory information. Ankle Brachial Index was also calculated using ratio of Ankle systolic pressure to best brachial systolic pressure (normal values range between .9 and 1.3). This test was used to identify patients with symptomatic and asymptomatic vascular disease. We initially assessed applicability of the database in the TASH setting.

RESULTS: Initially, an extensive data sheet was used to ensure that all pertinent data was collected. However, this method posed to be very difficult and time consuming. Over the course of the summer, a more comprehensive data sheet was developed working with the local experts. This current data sheet includes MR #, height, weight, calculated BMI, chief complaint, past medical history, lab values, imaging studies ordered, risk factors, previous vascular disease, final diagnosis, and disposition. This new data sheet is currently being used to collect information. As for future plans, the data sheet that has been modified will be put into an electronic format.

CONCLUSIONS: This project was very challenging given the constraints of time and the feasibility of data collection by physicians and nurses that are already severely overworked. The new data sheet is currently being tested for feasibility, and it is anticipated that the electronic version will result in the compilation of a patient profile representative of thousands of Ethiopian patients. This is presently the only vascular database in the country.
Retrospective 5-year Analysis of Frontal Bone Fractures and Resultant Symptoms

Authors: Jennifer Gassner, BS; Ahmed Afifi, MD; Ravi Garg, MD

Department: Department of Surgery, Division of Plastic Surgery, University of Wisconsin School of Medicine and Public Health

Mentor: Ahmed Afifi, MD

Support: Shapiro Summer Research Program; Department of Surgery, Division of Plastic Surgery

BACKGROUND: Facial fractures involving the frontal bone may cause significant injury to the central nervous system. Trauma to this area threatens the underlying structures within the skull, specifically the brain and eyes, and may cause severe and potentially fatal injuries, including cerebral hemorrhage, cerebral spinal fluid leakage, cranial nerve injury, prolonged loss of consciousness, seizures, and blindness. In this study, we sought to describe the incidence of frontal bone fractures at our institution and associated outcomes.

METHODS: A retrospective analysis of patients with craniofacial fractures seen at the University of Wisconsin between January of 2001 and December of 2005 was performed. The presence of a fracture involving the frontal bone was identified on review of CT imaging. Associated demographic information, Glasgow Coma Scale (GCS) score, and outcomes including death, paralysis, epilepsy, and optic neuropathy or blindness were determined by chart review.

RESULTS: We identified 149 patients with frontal bone fractures among 1,980 patients who sustained craniofacial trauma. The majority of patients were male (121 patients, 81.2%) and the most common mechanism of injury was motor vehicle accidents (97 patients, 65.1%). GCS scores on presentation were severe in 42 patients (28.0%), moderate in 8 patients (5.3%), and mild in 62 patients (41.3%). 18 patients (12%) died, 13 patients (8.7%) were paralyzed, 17 patients (11.4%) developed blindness or optic neuropathy, and 5 patients (3.4%) developed post traumatic epilepsy.

CONCLUSIONS: Frontal bone fractures are associated with severe outcomes involving injury to both the brain and eye. A further characterization of specific injury patterns of the frontal bone and associated ophthalmologic and neurologic complications will enhance our ability to predict patient outcomes and the likelihood and quality of recovery following surgical intervention.
Biomechanical Analysis of EPL Reroute in CP Surgery: A Cadaver Study

Authors: Max Gehrman, BS; Kenneth Noonan, MD; Jonathan Tueting, MD

Department: Department of Orthopedics and Rehabilitation, University of Wisconsin School of Medicine and Public Health

Mentor(s): Kenneth Noonan, MD; Jonathan Tueting, MD

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

BACKGROUND: Cerebral Palsy (CP) describes a group of disorders that cause activity limitation and loss of function. Our research will look at the particular symptom referred to as congenital clasped thumb, or thumb in hand deformity, where the thumb is “locked” in the palm of the patient’s hand, rendering the hand non-functional. In order to regain function of the thumb, surgical correction involving the transfer of the Extensor Pollicis Longus (EPL) is needed. There are different techniques involving the transfer of the EPL that allow improved function, but no research studies have been published describing which technique gives the optimal functional result. Our goal is to determine which EPL transfer gives the best biomechanical and functional result; create a standardized surgical procedure for the treatment of the thumb in hand deformity and other injuries that compromise thumb abduction.

METHODS: 5 fresh frozen, thawed cadaveric limbs were dissected to expose the superficial muscles on the posterior forearm of the wrist. The EPL was dissected out and attached to a calibrated spring. The force needed and the distance the EPL traveled was calculated for each thumb before any surgical intervention took place, calling these values the in situ force and in situ distance, respectively. We then performed 4 surgical techniques. In technique 1 the EPL was released by cutting the third dorsal compartment. Technique 2, the EPL was looped under the proximal portion of the Extensor Pollicis Brevis (EPB). Technique 3 the EPB was replaced with the EPL in the 1st dorsal compartment. Technique 4, a pulley was created from a flap from the first dorsal compartment. For each surgical technique we pulled the EPL tendon the in situ force and the in situ distance. We had attached motion sensors to each bone segment of the thumbs so the movements were recorded by a 3-D motion capture system.

RESULTS: We have insufficient data at this time. To date, we have run one specimen and are currently running the remaining five.

CONCLUSIONS: We will continue to run the cadaveric specimens and collect data using the motion capture system. Once data collection is complete we can move toward publishing a paper.
Financial Burden of Prophylactic Nailing of the Femur on the Medicare System in the United States

Authors: Kirollos Gendi, BA; John Heiner, MD

Department: Department of Orthopedics and Rehabilitation, University of Wisconsin School of Medicine and Public Health

Mentor(s): John Heiner, MD

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

BACKGROUND: Physicians in the United States treated over 142,000 patients in the Medicare system with metastatic disease to the skeleton in the year 2010 alone. This suggests that the amount of orthopedic oncology services and their associated costs could be a strain on Medicare. For those with secondary malignant neoplasms in the femur, prophylactic nailing is often used to reduce morbidities and enhance their quality of life. This study aims to assess the cost and financial burden of the procedure on the Medicare system.

METHODS: The Current Procedural Terminology (CPT) codes of Medicare patients undergoing prophylactic treatment of the femur (CPT code 27495) from 2005-2010 were searched using PearlDiver Technologies Inc. These patients were crossed with having International Classification of Disease-9 (ICD-9) codes for secondary malignant neoplasms of the bone. Facility charges, Medicare reimbursement and length of hospital stay were extracted from these patient files.

RESULTS: From 2005-2010, there was a mean of 1,280 inpatient Medicare cases of prophylactic treatment of the femur when the patient had metastatic disease. During this time, there was an increase in the patients with metastatic disease to the skeleton; however, there was no significant upward trend of increased prophylactic nailing. Likewise, there was no significant upward trend in estimated total hospital charges or total Medicare reimbursement after adjusting for inflation. However, there was a significant upward trend in average Medicare reimbursement per patient and average hospital charges per patient after adjusting for inflation. The mean length of hospital stay for each patient was 6.8 days.

CONCLUSIONS: Since the number of patients with secondary neoplasms to the skeleton has increased from 2005 to 2010, the number of patients with lesions in the femur must have also increased. Despite this, the lack of an increase in prophylactic nailing procedures most likely signifies an increase in other treatments that can prevent a pathologic fracture like bisphosphonates and radiation therapy.
Brain Activity Upon Awakening and Reports of Sleep Consciousness

Authors: Matthew Gevelinger, BS; Giulio Tononi, MD, PhD; Francesca Siclari, MD

Department: Department of Psychiatry, University of Wisconsin School of Medicine and Public Health.

Mentor(s): Giulio Tononi, MD, PhD; Francesca Siclari, MD

Support: Shapiro Summer Research Program; Department of Psychiatry

BACKGROUND: Dreaming is a distinct form of consciousness which occurs during sleep while one is disconnected from the external environment. It is a ubiquitous phenomenon across cultures, which provides a unique opportunity to study consciousness on a nightly basis. By definition, consciousness is a subjective phenomenon and not directly accessible to the investigator, who has to rely on retrospective reports that are obtained after awakening the subject. These reports, in turn, can be influenced by a variety of factors other than the conscious experience, including memory and sleepiness upon awakening. In this context, we set out to determine how brain activity upon awakening relates to reports of conscious experiences.

METHODS: We employed high-density EEG (hd-EEG), an ideal technique to study brain activity because of its inherent temporal and spatial resolution. Also, we implemented a serial awakening paradigm that allowed for the collection of a high number of sample awakenings per night without disrupting sleep patterns. Overall, five subjects were studied over 29 nights to give 505 awakenings. We focused on the 373 awakenings performed during Non-REM (NREM) sleep. 10-second segments were extracted from the hdEEG recording after the subjects were awakened, while they were lying quietly on their back. A time frequency transform of the EEG signal was performed to obtain power in the 1 to 50 Hz frequency band.

RESULTS: We find that EEG power in the low frequency range (1-7.5 Hz, in the theta and delta band) is greater in waking hdEEG recordings when subjects do not report a dream compared to when they do report a conscious experience in sleep. Spatially, this pattern of brain activity predominated over frontal regions. Additionally, we found that reports of white dreams, an experience where the subject has a dream but cannot report the content, show brain activity in a range between reports of reports of conscious experiences in sleep and those without.

CONCLUSIONS: These findings suggest that brain activity upon awakening, while a subject is awake, influences if a subject will report dreaming in sleep. Frontal theta activity is known to reflect local sleep and may affect attentiveness and memory recall, which may subsequently influence the reporting of dreams. In the future, we aim to determine whether brain activity during sleep states or upon awakening is a better predictor of sleep consciousness.
The Effect of Exertion on Landing Asymmetry

Authors: Paul Gill, BS, ATC; David Bell, PhD, ATC; Anthony Pennuto, MS, LAT

Department: Department of Orthopedics and Rehabilitation, University of Wisconsin School of Medicine and Public Health; Department of Kinesiology, University of Wisconsin

Mentor(s): David Bell, PhD, ATC

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

BACKGROUND: ACL injuries presently consume a significant portion of healthcare resources, with an estimated 100,000-250,000 injuries every year, each costing an average of $17,000- $20,000. Biomechanical irregularities and landing asymmetries are two neuromuscular factors that are thought to be largely responsible for non-contact ACL injury. Asymmetries of limb strength and jumping are believed to increase the risk of injury for those who have no prior injury history. Strength asymmetries greater than 15% have been associated with increased risk of lower extremity injury. One such factor that could further elucidate the relationship between asymmetry and ACL injury is exertion, as exertion is directly related to changes in frontal and sagittal plane kinetics and kinematics. The objective for this project was to determine how landing force asymmetry is altered in active individuals following exertion.

METHODS: 40 active subjects, 20 M and 20 F will be enrolled in the study and complete two days of testing. Test session 1 consists of a DXA body composition assessment and a Biodex strength assessment of the hamstrings and quadriceps. The second testing session consists of a movement assessment and the exertion protocol. Prior to exertion, the subjects perform 5 jump landings recorded by an Electromagnetic Motion Analysis Tracking System and force plates to measure joint motion and vertical ground reaction force (VGRF). A exertion protocol is then administered that included cone drills, jumping, wall sits, and planks. Finally, the subject performs 5 more jump landings, and VGRF is recorded to compare the force asymmetries between legs pre and post exertion. Asymmetry % = [(Right Limb – Left Limb) /.5(Right Limb + Left Limb)] x 100%, where zero indicates symmetry between limbs.

RESULTS: Currently 35 subjects have completed both days of testing, 17 M and 18 F. Preliminary data has shown a pre-exertion Asymmetry % of 20.97± 11.5 and a post-exertion Asymmetry % of 26.61±18.03, with a repeated measures ANOVA of P=0.076.

CONCLUSIONS: Although results thus far have not been statistically significant, the addition of 5 more subjects may change that. The results may also still be meaningful as there is a clear change in % force asymmetry in subjects post exertion. An alteration of the definition of asymmetry to include overall change in % asymmetry, instead of asymmetry in relation to zero or placing focus on outlier values within a single subject, instead of comparing average % between subjects may provide further information about the role of exertion on landing asymmetry.


Evaluating Clinical Response to Electronic Health Record Surveillance of Childhood Obesity

Authors: Brittney Golbach, BS; Brian Arndt, MD; Aaron Carrel, MD; Parvathy Pillai, MD, SciMetrika, LLC; Wisconsin Department of Health Sciences Division of Public Health; UW College of Agricultural and Life Sciences Department of Nutritional Sciences; Rural and Urban Scholars in Community Health (RUSCH) Program, University of Wisconsin School of Medicine and Public Health

Departments: 1Department of Family Medicine, 2Department of Pediatrics, 3Department of Population Health Sciences, University of Wisconsin School of Medicine and Public Health; 4SciMetrika, LLC; 5Wisconsin Department of Health Sciences Division of Public Health; 6UW College of Agricultural and Life Sciences Department of Nutritional Sciences, 7Rural and Urban Scholars in Community Health (RUSCH) Program, University of Wisconsin School of Medicine and Public Health

Mentor(s): Brian Arndt, MD; Larry Hanrahan, PhD

Support: Summer Student Research and Clinical Assistantship Program, Department of Family Medicine

BACKGROUND: The UW E-Health Public Health Information Exchange (PHINEX) project surveyed 25 UW Department of Family Medicine (UWDFM) clinics and found that 30% of children 2-17 were overweight (OV) or obese (OB). However, only 2% of those children were coded in the EHR as OB, and <1% as OV (Pillai, 2012). In 2011 the UW Health EHR began auto-coding visit BMI percentiles by weight category. As a follow-up to these efforts, the goals of this project were to determine the frequency at which UW Family Medicine providers adhere to best practice recommendations for OV/OB prevention and assessment in children.

METHODS: The study included 26 children ages 2-19 seen for well-child checks at the Northeast, Verona and Belleville UWDFM residency clinics. The Expert Committee Recommendations (ECR) by Barlow et al (2007) and OV/OB-related EHR well-child checklist items were used to develop an electronic appointment evaluation form, which was completed during observation of the appointments and with reference to EHR patient charts.

RESULTS: Data collected regarding counseling practices showed that less than half of appointments included discussion of all three of the counseling categories evaluated in this study (nutrition, physical activity and sedentary behavior). Physical activity was counseled on most consistently, while frequency of counseling in regards to sedentary behaviors was low across all weight categories. However, the frequency of counseling on all three categories was generally higher for obese children.

CONCLUSIONS: Although the auto-coding feature has offered consistency of BMI documentation, the lack of uniformity, clarity and completeness in the documentation of OV/OB diagnoses and family medical histories may be overshadowing any positive effects of the new system. Furthermore, while the Expert Committee Recommendations include more specific criteria, the results of this study would suggest that changing the EHR checklist to match the Expert Committee criteria would increase completion rates of the additional items, and thereby improve prevention and assessment of pediatric OV/OB.
Biopsy EVX1 Methylation and Gleason Score Upgrading at Radical Prostatectomy in Prostate Cancer

Authors: Chad Guenther, MA; David F. Jarrard, MD

Department: Department of Urology, University of Wisconsin School of Medicine and Public Health

Mentor(s): David F. Jarrard, MD

Support: Department of Surgery NIH T35 Training Grant DK062780

BACKGROUND: Of the men with prostate cancer (PCa) with Gleason score (GS) 6 that are managed with active surveillance, 30-50% undergo Gleason score upgrading (GSU) at the time of radical prostatectomy (RP). This upgrade is clinically significant, leading to increased risk of biochemical disease recurrence, need for adjuvant therapy, and cancer-specific mortality. Epigenetic information may provide a possible strategy to predict which tumors might be upgraded. Even-skipped homeobox 1 (EVX1) is a regulator gene that is significantly more methylated in high-grade tumors (GS≥8) than intermediate grade tumors (GS≤7) (BJC 2012). We hypothesized that patients with more EVX1 methylation at the time of diagnostic biopsy would be more likely to undergo GSU at the time of RP.

METHODS: Thirty formalin-fixed paraffin-embedded PCa core needle biopsies (GS 3+3) from our institution dating with matched clinical information were collected. At the time of RP, these samples either underwent GSU (N=15) or retained their Gleason score (RGS) (N=15). GSU samples were upgraded to either GS 3+4 or GS 4+3 at RP. Punch biopsy was used to extract tumor tissue from paraffin blocks. Samples were deparaffinized and had their DNA extracted. Sample DNA was then treated with sodium bisulfite to convert unmethylated cytosine to uracil. A MethyLight qPCR reaction using primers and probes designed to amplify and target a region in exon 1 was then performed.

RESULTS: Of the 30 biopsy specimens, 15 GSU specimens and 14 RGS specimens were amplified by qPCR. Mean ages of GSU and RGS cohorts were 59.5 years and 55.8 years respectively, and mean BMIs were 29.5 kg/m2 and 26.2 kg/m2 respectively. Mean PSA densities for GSU and RGS were .246 ng/mL2 and .156 ng/mL2 respectively, mean numbers of positive cores from biopsy were 2.73 and 2.79 respectively, and mean maximum core involvements were 30.67% and 27.86% respectively. Mean percent tumor cellularity of the sample cores removed for methylation analysis was 50% for GSU and 46.79% for RGS. The mean percent EVX1 methylation was 61.4% for GSU versus 65.7% for RGS (p=.736).

CONCLUSIONS: Results suggest EVX1 methylation status at biopsy cannot be used to predict GSU of low-risk PCa to intermediate-risk PCa at RP. Results may reflect the heterogeneity of separate tumor foci in PCa and the inability on biopsy to always sample the biologically significant region. Additionally, given that the GSU samples used were upgraded to GS 3+4 or GS 4+3 and not to GS 4+4 and greater, EVX1 methylation status may still predict GSU from low- to high-risk PCa.
Nox2 May Mediate Cyclosporine A-Induced Hypoxia

Authors: Omeed Hafez¹, BBA; Shannon Reese¹, MS; Aos Karim¹, BS; Nancy A. Wilson¹, PhD; Zaheer Akhtar², BS; Elizabeth Sadowski², MD; Arjang Djamali¹, MD, FASN

Department: Department of Medicine, ¹Division of Nephrology; ²Department of Radiology, University of Wisconsin School of Medicine and Public Health

Mentor: Arjang Djamali, MD, FASN

Support: Shapiro Summer Research Program; National Institutes of Health, NIDDK grant R01 DK092454

BACKGROUND: The use of Cyclosporine A (CsA), a calcineurin inhibitor, as maintenance immunosuppression in the management of solid organ transplantation is compromised by its chronic nephrotoxicity. This includes increased oxidative stress by an unknown mechanism. We hypothesized that the classical phagocytic Nox2 enzyme plays an important role in renal hypoxia mediated by CsA. We tested this hypothesis using the CsA-induced model of chronic nephrotoxicity in rats and mice.

METHODS: Fisher344 rats received CsA 15mg/kg/24h, no treatment, or CsA with a non-specific inhibitor of Nox activity for 4 weeks (n=6-8/group). Inhibition was achieved using Diphenyleneiodonium (DPI; 0.5mg or 1.0mg/kg/24h) or Apocynin (Apo; 16mg/kg/24h). Wild-type (WT) and Nox2 knockout (KO) mice received CsA 30mg/kg/24h or vehicle for 8 weeks (n=4-5/group). To characterize the effects of CsA on oxygenation, animals underwent blood oxygen level dependent MRI (BOLD-MRI), a non-invasive imaging method that uses hemoglobin as an endogenous contrast agent. Oxidative stress was further evaluated by measuring H₂O₂ levels in rat serum. CsA-induced fibrosis was evaluated with Western blots. Pimonidazole, a biomarker of tissue hypoxia, was injected in mice 60 minutes prior to tissue harvesting and detected via a horseradish peroxidase-labeled antibody. Pimonidazole detection was quantified using the Nuance multispectral imaging system.

RESULTS: Immunoblot analyses of kidney tissue lysates demonstrated that CsA therapy increased Nox2 and fibrogenesis (vimentin and p-smad3). Nox inhibition decreased fibrogenesis suggesting that Nox2 is a mediator of CsA-induced renal fibrosis. BOLD-MRI demonstrated that CsA decreased renal oxygenation (increased R2* levels) while the lack of Nox2 prevented these changes in rats and mice. These findings were supported by decreased H₂O₂ in serum from rats treated with Nox inhibitors. Pimonidazole staining was decreased in WT mice receiving CsA compared to Nox2 KO mice receiving CsA.

CONCLUSIONS: These studies indicate that Nox2 modulates intrarenal oxygenation and is involved in the pathogenesis of CsA-induced hypoxia. Specific Nox2 inhibition may play a role in preventing CsA nephrotoxicity.
Evaluating the Predictive Value of Findings on Routine Office-Based Audiometric Analysis for Identifying Cochlear Implant Candidates

Authors: Kevin D. Hanson, BS; Brian C. Gartrell, MD; Jennifer L. Ploch, MA, CCC-A; Samuel P. Gubbels, MD, FACS

Department: Department of Surgery, Division of Otolaryngology-Head & Neck Surgery, School of Medicine and Public Health

Mentor: Samuel P. Gubbels, MD, FACS

Support: Shapiro Summer Research Program; Department of Surgery, Division of Otolaryngology-Head & Neck Surgery

BACKGROUND: While the success of cochlear implantation in treating extensive sensorineural hearing loss has been well documented, patients who might receive benefit from the operation are not being considered for implantation due to a lack of consensus as to which patients are likely to meet the candidacy qualifications. The predictive value of findings on routine audiometric analysis for identifying cochlear implant (CI) candidates has not been evaluated. We sought to identify if findings on routine office-based audiometric analysis are predictive of CI candidacy status.

METHODS: The charts of all patients who were evaluated for CI candidacy at a tertiary care center cochlear implant program from June 2008 through June 2013 were included. Routine, unaided audiologic measures (pure-tone hearing thresholds and recorded monosyllabic word recognition test (MWRT) results) were then correlated with best-aided sentence-level word discrimination test (SWDT) results using either the Hearing in Noise Test (HINT) or AzBio sentences.

RESULTS: The degree of hearing loss at 250, 500, 1000, 2000, and 4000 Hz was significantly correlated with SWDT results. Additionally, 87% of patients who scored <30% in MWRT qualified for implantation using HINT sentences. Similarly, in patients whose MWRT scores were ≤35%, 81% and 93% met candidacy criteria for CI when using AzBio sentence testing in quiet and noise respectively.

CONCLUSIONS: Routine audiometry can be used to identify patients, who are struggling with their hearing aids that would likely meet cochlear implant candidacy. Specifically, the presence of a low-frequency or flat pattern of hearing loss, and MWRT scores of <35% when evaluating using AzBio sentences collectively identify a population of patients with hearing loss who are likely to meet candidacy criteria. Utilization of these predictive patterns on routine audiometry may assist hearing health professionals in deciding when to refer patients with hearing loss for a formal CI evaluation.
Characterizing Readmission in Ulcerative Colitis Patients Undergoing Restorative Proctocolectomy

Authors: Thomas Hanzlik, BS¹; Sarah E. Tevis, MD²; Pasithorn A. Suwanabol, MD²; Bruce A. Harms, MD²; Charles P. Heise, MD²; Eugene F. Foley, MD²; Gregory D. Kennedy, MD, PhD²

Department: ¹University of Wisconsin School of Medicine and Public Health; ²Department of Surgery, Section of Colorectal Surgery, University of Wisconsin School of Medicine and Public Health

Mentors: Gregory D. Kennedy, MD, PhD; Sarah E. Tevis, MD

Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: Postoperative readmissions increase costs and affect patient quality of life. Ulcerative colitis patients at our institution are at a high risk for postoperative readmission following restorative proctocolectomy. We aim to characterize patients undergoing restorative proctocolectomy with respect to 1) the timeframe of readmission, 2) the reason for readmission and 3) the risk factors associated with readmissions.

METHODS: Ulcerative colitis patients who underwent restorative proctocolectomy were identified from the prospectively maintained University of Wisconsin Colorectal Surgery database. We evaluated 533 patients who met our inclusion criteria. Restorative proctocolectomy at our institution is routinely performed as a 2-stage operation. The first stage involves a proctocolectomy with ileal pouch creation and diverting loop ileostomy. The second stage involves takedown of the loop ileostomy. Postoperative readmission rates and reasons for readmission were examined following both stages. Univariate and multivariate analyses were performed to evaluate for risk factors associated with 30 day readmission following stage I.

RESULTS: Following stage I of restorative proctocolectomy, 18.2% (n=97) of patients were readmitted within 30 days while 22.7% (n=121) were readmitted within 90 days. Younger patient age (OR 1.825, 95% CI 1.139-2.957), laparoscopic approach (OR 1.943, 95% CI 1.217-3.104) and increased length of initial stay (OR 1.155, 95% CI 1.090-1.225) were all associated with 30 day readmission. The most common reason for readmission was ileus/partial bowel obstruction, with 10% of patients readmitted for this reason within 30 days of stage I.

CONCLUSIONS: Patients undergoing restorative proctocolectomy are at high risk for readmission, particularly following the first stage of the operation. Novel treatment pathways to prevent ileus and subsequent dehydration as an outpatient may decrease the rates of readmission following restorative proctocolectomy.
Tricuspid and Pulmonary Valve Replacement for Carcinoid Heart Disease

Authors: Jacob J. Inda, BS; J. Wells Askew, MD; Heidi M. Connolly, MD; Zhuo Li, MS; Judy Lenoch, BA; Hartzell V. Schaff, MD

Department: Department of Cardiovascular Surgery, Mayo Clinic

Mentor: Hartzell V. Schaff, MD

Support: American Association for Thoracic Surgery Summer Intern Scholarship

BACKGROUND: Carcinoid tumors are a rare form of neuroendocrine cancer that typically originate in the gastrointestinal tract. Vasoactive substances secreted by hepatic metastases can cause a constellation of symptoms known as carcinoid syndrome, and these symptoms include cutaneous flushing, diarrhea, and more rarely a serious complication known as carcinoid heart disease. The cardiac complications of carcinoid tumors are due to valvular insufficiency resulting from fibrous tissue deposits on the tricuspid and pulmonary valves, and less commonly on left-sided heart valves. In patients displaying symptoms of right-sided carcinoid heart disease, the average survival is less than one year without valve replacement surgery. This study identifies preoperative variables that predict long-term survival and freedom from reoperation following valve replacement surgery for carcinoid heart disease.

METHODS: This retrospective outcomes study includes 195 carcinoid heart disease patients who were treated surgically at the Mayo Clinic between 1985 and 2012. All patients underwent tricuspid valve replacement, and many also had pulmonary (54%), aortic (8%), or mitral valve (8%) replacements.

RESULTS: Overall survival rates 5 and 10 years after operation were 35% and 25%. Variables that were predictive of mortality on univariate analysis included pre-operative plasma creatinine concentration (H.R.: 1.7, p=0.034), NYHA functional class III or IV (H.R.: 1.63, p=0.023), intravenous loop diuretics in the week preceding surgery (H.R.: 1.67, p=0.021), ascites (H.R.: 1.48, p=0.023), type II diabetes mellitus (H.R.: 1.88, p=0.033), mitral or aortic valve regurgitation (H.R.: 1.69, p=0.022), and right ventricular systolic dysfunction (H.R. 1.59, p=0.049). Treatment of hepatic metastases (ex. hepatic artery ligation) prior to surgery was predictive of freedom from reoperation (H.R.: 0.27, p=0.013). Multivariate Cox regression model analysis identified older patient age at the time of surgery (H.R.: 1.03, p=0.003), prior treatment with antineoplastic agents (H.R.: 1.47, p=0.051), and prior history of tobacco use (H.R.: 1.9, p=0.001) as predictors of mortality.

CONCLUSIONS: A number of preoperative variables are predictive of long-term survival and freedom from reoperation following valve replacement surgery for carcinoid heart disease. This information may assist physicians and patients in making informed, evidence-based decisions regarding potential benefit of valve replacement surgery for carcinoid heart disease.
Filter Paper Screening for Iron Deficiency using Zinc Protoporphyrin/Heme

Authors: Kimberly R. Johnson, BS; Steven L. Marmer, BS; Sharon E. Blohowiak, MS; Pamela J. Kling, MD

Department: Department of Pediatrics, University of Wisconsin School of Medicine and Public Health; Meriter Hospital

Mentor(s): Pamela Kling, MD

Support: Shapiro Summer Research Program; UW Cardiovascular Research Center

BACKGROUND: Iron depletion (ID) at birth, is common, but can impair brain and possibly kidney development. With earlier identification of at-risk children, long-term neurocognitive deficits could be prevented. Zinc protoporphyrin/heme (ZnPP/H) is an available, cost effective, and sensitive biomarker of iron status when measured in washed newborn whole blood. ZnPP/H is a candidate for newborn screening. Bilirubin interferes with ZnPP/H readings, but interference is reduced with the enzyme, bilirubin oxidase (BO). Hypothesis: To examine whether ZnPP/H from filter paper spots holds promise as a simple and inexpensive screening test.

METHODS: De-identified cord blood was collected and washed ZnPP/H ratios were measured by hematofluorometry as the comparison value. Unwashed blood was spotted onto Whatman 903 filter paper newborn screening cards, simulating heelstick collection. Specimens were dried and eluted from the paper using PBS (control), BO, or a DNA buffer from the Newborn Screening Lab. Treatments were repeated at 1, 2, and 5 days to measure stability of the ratio over time and assess for correction factors.

RESULTS: Filter paper ZnPP/H ratios were higher when eluted, compared to rinsed blood. With ≤24 hrs on filter paper, elution with PBS and BO were highly correlated with rinsed blood (R²=0.85, p<0.01), and performance of the DNA buffer was lower (R²=0.7, p<0.01). With increased time on filter paper, ZnPP/H readings rise. Unexpectedly, combining serial trials of the same experiment caused the coefficient of determination to fall, making designation of a correction factor not possible. However, the highest ¼ (most abnormal) are generally identifiable.

CONCLUSIONS: With increased time on filter paper, ZnPP/H readings obtained by hematofluorometry increased and identity lines shifted for all elution treatments. Nevertheless, the line of identity still depicted a relationship of washed ZnPP/H to the eluted values, thereby showing predictability power. The inability to reproduce equivalent lines of identity for serial trials of the same experiment indicates day-to-day variability and possible low precision of the hematofluorometer. Creation of a more precise and specific machine would greatly reduce this variability, and steps towards its development have begun. Furthermore, the Newborn Screening Lab, would need a machine to be automated and determination of an appropriate second tier (more definitive) test, such as HPLC, needs to be established. Therefore, using dried blood spots on filter paper to measure ZnPP/H still holds promise.
Optimization of an ELISA for Detection of Canine Anti-Human Tyrosinase Immunoglobulin

Authors: P. Chulhi Kang, MS; Cindy Zuleger, PhD; Michael Macklin, MS; Mark Albertini, MD

Department: Department of Medicine, University of Wisconsin School of Medicine and Public Health

Mentor(s): Mark Albertini, MD

Support: Shapiro Summer Research Program; Mark Albertini BH32 Melanoma Gift Account

BACKGROUND: Malignant melanoma (MM) causes much morbidity and mortality, and new treatments are needed. Dogs spontaneously develop melanoma and provide an excellent model for human MM. DNA vaccines with cDNA for human tyrosinase (huTYR) can activate canine immune cells and prolong the survival of some dogs with melanoma. We plan to study DNA microseeding (i.e., delivery of DNA into the skin with a modified tattoo device) as a novel vaccine for dogs with MM. To measure canine humoral responses to huTYR, we developed and optimized an Enzyme-Linked Immunosorbent Assay (ELISA).

METHODS: We evaluated serum from normal dogs and from a dog with melanoma vaccinated with huTYR. Suitable primary and secondary antibodies were identified and optimal concentrations determined. Two non-overlapping positive controls were required for this ELISA: (1) A control to verify huTYR binding to the 96-well plates; and (2) A control to verify recognition of primary antibody (i.e., IgG in dog serum) by the secondary detection antibody. A mouse monoclonal anti-huTYR IgG and a goat anti-mouse IgG-HRP were used as primary and secondary antibodies, respectively, to verify huTYR binding to 96-well plates. The anti-mouse secondary detection reagent used does not recognize canine IgG. Therefore, a second detection reagent (i.e., goat anti-canine IgG-HRP) was used for recognition of IgG in dog serum.

RESULTS: The optimal concentration of recombinant huTYR plated on 96-well ELISA plates was determined to be 1 µg/ml. Normal dog serum (pooled serum from healthy dogs) demonstrated low levels of binding to huTYR at higher concentrations and was used to verify binding between canine IgG and goat anti-canine IgG-HRP in the experimental case. Further, normal dog serum provided a negative control for evaluation of anti-huTYR antibodies in the vaccinated versus unvaccinated dog. This ELISA was successfully optimized in normal dogs to detect humoral responses to huTYR, and it was then used to study a dog previously vaccinated with huTYR DNA by microseeding. That dog did not develop a detectable antibody response to huTYR.

CONCLUSIONS: A canine anti-huTYR ELISA was optimized to use as part of a larger effort to evaluate the immunogenicity of DNA microseeding in comparison with other vaccination delivery systems in dogs with spontaneous melanoma. This canine model will be used to identify potentially effective treatments for subsequent testing in humans with melanoma.
Healthcare Payment Reform Models for Better Diabetes Care

Authors: Ryan Kartheiser, BS; Karen Timberlake, JD

Department: UW Population Health Institute, Department of Population Health Sciences, University of Wisconsin School of Medicine and Public Health

Mentor: Karen Timberlake, JD

Support: Shapiro Summer Research Program; Wisconsin Health Information Organization

BACKGROUND: In 2012, 23% of all health care dollars in America were spent on diabetic patients, with prices for diabetic medical services rising 5-17% above inflation since 2007. Upward trends in medical costs, combined with an increasing prevalence of diabetes, make it more important than ever to find cost-effective ways to improve the quality of medical care for diabetes and associated co-morbidities. Traditional fee-for-service (FFS) payment structures provide reimbursement for the quantity of care delivered, giving providers financial incentive to provide more services at higher prices, rather than prevent illness. Payers and providers have been implementing new payment approaches that move away from FFS and bend the cost curve by aligning incentives among all parties to provide the most efficient care possible. Interest in these new models is increasing as more organizations form Accountable Care Organizations (ACOs) that will be responsible for keeping healthcare costs low for an entire population, while maintaining quality.

METHODS: A literature review was conducted to understand what type of evidence-based medical care is poorly reimbursed under the current FFS payment system, and to identify examples of payment reform projects in the private sector that successfully reduced costs while maintaining quality for patients with a chronic illness.

RESULTS: Many aspects of care that are proven to be effective in the management of diabetes and associated comorbidities are poorly reimbursed under the current FFS payment model, such as care coordination, telemedicine, and diabetes self management education. Different payment systems have been used to realign payment so that these types of services are better incentivized, including care coordination fees, nurse care manager support, pay for performance programs, shared savings programs, and global budget programs.

CONCLUSIONS: Although interest is growing in finding alternative payment models for chronic disease, movement away from FFS is proceeding slowly. Models that move towards a global payment system have been shown to be effective at reducing costs while maintaining quality, but there are many barriers to implementation. Commonly cited barriers include: the considerable time needed before reforms produce cost savings, lack of trust between payers and providers, and provider concerns about taking on additional financial risk without adequate data and reporting tools to manage populations of patients.
Environmental Pollutants Enhance TH17 Polarization in an Aryl Hydrocarbon Receptor-Dependent Manner

Authors: Samantha Knopp, MA; John Fechner, MS; Joshua Mezrich, MD

Department: Department of Surgery, Division of Transplantation, University of Wisconsin School of Medicine and Public Health

Mentor(s): Joshua Mezrich, MD

Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: The aryl hydrocarbon receptor (AHR) is a cytosolic receptor with the ability to influence T cell polarization to a T regulatory or T helper 17 (Th17) phenotype. Air pollution is a risk factor for asthma and other airway diseases, and IL-17 expression can exacerbate airway disease. Polycyclic aromatic hydrocarbons (PAHs), which are ligands of the AHR and present in air pollution in varying composition and concentration, are a possible exacerbating factor of airway disease. This study examines the effects of various sources of PAHs on T cell differentiation to a Th17 effector response. We hypothesize that air pollution samples will increase Th17 polarization in vitro via the AHR.

METHODS: Naïve CD4⁺CD62L⁺ T cells were isolated from the spleens of wild type C57BL/6 (B6) and AHR⁻/⁻ mice and placed in culture for four days under Th17 conditions (anti-CD3/anti-CD28 antibodies + IL-6 + transforming growth factor-β; antibodies to interferon-γ and IL-4 were included in some experiments). At the start of culture concentrations of urban dust particles (UDP) or environmental air samples obtained from the Wisconsin State Laboratory of Hygiene were added. At the end of culture, intracellular cytokine staining (ICC) was used to determine the degree of Th17 differentiation. Cytokine levels in culture supernatant were assessed using ELISA.

RESULTS: B6 naïve T cells cultured in the presence of UDP under Th17 conditions resulted in enhanced Th17 differentiation, shown by ELISA and ICC. AHR⁻ naïve T cell cultures showed no significant increase in IL-17 at any concentration of UDP. Flow cytometric analysis of B6 naïve T cells cultured under Th17 conditions also showed that there was increased expression of the AHR in IL-17 positive cells compared to IL-17 negative cells. ICC and ELISA showed increased IL-17 expression with addition of diesel environmental air sample to murine B6 naïve T cells cultured under Th17 conditions. AHR⁻ naïve T cells cultured under the same conditions failed to demonstrate a similar increase in either ICC or ELISA.

CONCLUSIONS: These preliminary results show that Th17 polarization in vitro is enhanced with addition of UDP or diesel extract to culture conditions. These effects were found to be AHR dependent. Preliminary findings suggest high doses of environmental samples may be more toxic to T cells with lower AHR expression, allowing preferential survival of IL-17-producing T cells. These early findings suggest a possible mechanism of immune-modulation by air pollutants with potential clinical implications for airway disease.
Endoscopic Aqueductoplasty for Treatment of Obstructive Hydrocephalus

Authors: Mark Kraemer, BS; Carolina Sandoval-Garcia, MD; Bermans J. Iskandar, MD

Department: Department of Neurological Surgery, University of Wisconsin School of Medicine and Public Health

Mentor(s): Bermans J. Iskandar, MD; Carolina Sandoval-Garcia, MD

Support: Shapiro Summer Research Program; Department of Neurological Surgery

BACKGROUND: Obstruction of the Sylvian aqueduct is a common cause of non-communicating hydrocephalus. Advances in endoscopic technology have led to better treatment options for aqueductal obstructions, eliminating the need for problematic chronic shunting. Cerebral aqueductoplasty is an emerging treatment for membranous and short-segment stenoses of the Sylvian aqueduct. Traditionally, this procedure has been performed via a coronal approach, passing through the lateral ventricle, foramen of Monro, and third ventricle into the aqueduct. Here we present our 15-year experience treating aqueductal obstructions using a suboccipital foramen magnum trans-fourth ventricle approach.

METHODS: A retrospective chart review was performed to document the success of cerebral aqueductoplasty procedures via the foramen magnum trans-fourth ventricle approach between 1998 and 2011. Pathologies included primary membranous and/or focal aqueductal obstruction proven or presumed to be infectious/inflammatory in origin; fourth ventricular entrapment; and cystic obstructions of the cerebral aqueduct.

RESULTS: Twenty-eight patients underwent 32 cerebral aqueductoplasty procedures. Symptoms of sensorimotor and bulbar dysfunction were associated with ventricular dilation in the majority of cases. At a mean of 7 years of postoperative follow up, clinical and/or radiologic goals were achieved in >80% of patients. A stent was successfully placed in four patients to maintain aqueduct patency. Five patients required placement of a shunt to manage their hydrocephalus. Four patients required two or more operations to reach clinical goals. Surgical complications included transient vertical diplopia and upgaze weakness, CSF leak, and rarely injury to the brainstem. There was no endoscopy related mortality.

CONCLUSIONS: Cerebral aqueductoplasty via the foramen magnum trans-fourth ventricle approach is effective and safe. When performed by an experienced neuroendoscopist, aqueductoplasty is the preferred treatment for management of membranous and/or short-segment stenosis of the cerebral aqueduct, select cases of entrapped fourth ventricle, and cystic lesions of the aqueduct. Long-term success is likely to be maintained when CSF flow is re-established in the absence of a CSF shunt, thus improving on the typically disappointing natural history of these disorders.
Monitoring of $^{19}$F Labeled Human Natural Killer Cell Trafficking for Cancer Immunotherapy Using MRI

Authors: Matthew Kutz, BS$^1$; Myriam Bouchlaka, PhD$^1$; Jeremy W. Gordon, MS$^2$; Sean Fain, PhD$^2$; Christian M. Capitini, MD$^1$

Department: $^1$Department of Pediatrics, Division of Hematology, Oncology and Bone Marrow Transplant, University of Wisconsin School of Medicine and Public Health; $^2$Department of Medical Physics, University of Wisconsin School Of Medicine and Public Health

Mentor(s): Christian M. Capitini, MD

Support: Shapiro Summer Research Program; UW Carbone Cancer Center; St. Baldrick’s Summer Fellowship

BACKGROUND: Natural killer (NK) cells are a promising immunotherapy treatment for pediatric refractory metastatic solid tumors that may improve survival and diminish toxicity over traditional chemoradiotherapy. NK cells are lymphoid cells of our innate immune system that kill virally infected and tumor cells and produce inflammatory cytokines that can cause direct anti-tumor activity and activate other tumor effectors in the tumor-microenvironment. Previous research showed that NK cells can prevent leukemia relapse following haploidentical stem cell transplant, target solid tumors common in adults, and that pediatric solid tumors are also sensitive to NK cell-mediated cytotoxicity. One challenge of translating NK therapy to clinical application is the inability to effectively and noninvasively track NK cells after infusion. It is not known if NK cells traffic directly to tumors and mediate cytotoxicity, or if they traffic to other tissues and stimulate other effector cells, thus indirectly eliminating the tumor. Because there is negligible endogenous fluorine signal in tissues, our lab is optimizing the non-radioactive isotope fluorine-$^{19}$F as a safe and effective means of labeling NK cells and tracking them in vivo using dual $^1$H/$^{19}$F MRI.

METHODS: We developed protocols for labeling NK cells with $^{19}$F and assessed their effects in vitro. NK cells were labeled with varying doses of $^{19}$F. $^{19}$F uptake was verified by NMR. Viability was assessed using trypan blue stain exclusion under microscope. Killing capacity was assessed using a $^{51}$Cr release killing assay with K562 leukemia cells. NK cell activating receptor expression, cytokine and granule production were assessed via flow cytometry. For in vivo trafficking immune-deficient mice were injected with ex vivo $^{19}$F labeled NK cells and imaged at multiple time points using a 4.7 Tesla volumetric dual $^1$H/$^{19}$F MRI coil.

RESULTS: No effects on NK cell viability, proliferation, killing capacity, activating receptor expression, cytokine production or cytotoxic granule production were seen with $^{19}$F labeling compared to controls. $^{19}$F MRI signals were detected.

CONCLUSIONS: $^{19}$F labeling does not affect the ability of human NK cells to kill human tumor cells in vitro. Further testing of the $^1$H/$^{19}$F MRI coil to optimize sensitivity and imaging protocols may result in a novel imaging technique to monitor NK cell for therapeutic treatments.
Exercise-induced Hypoalgesia after Comparative Forms of Anaerobic Training in Healthy Adults

Authors: Andy Lang, BS; Ben Rawson, DO; Kelli Koltyn, PhD; Nalini Sehgal, MD

Department: Department of Orthopedics and Rehabilitation, University of Wisconsin School of Medicine and Public Health

Mentor(s): Ben Rawson, DO

Support: Midwest Pain Society-Addison/Blonsky Grant

BACKGROUND: Exercise, in various forms, has been shown to attenuate pain intensity ratings and increase pain thresholds. This poorly understood phenomenon is known as exercise-induced hypoalgesia (EIH). Studies have shown EIH with high intensity aerobic exercise and with low intensity anaerobic training. No study has compared the EIH effects of isometric and concentric exercises. This study aims to examine EIH following low intensity anaerobic isometric and concentric exercise, with a secondary objective of examining potential differences in male and female EIH response.

METHODS: 32 healthy males and females participated in 3 randomized sessions. Each session included two periods Forgioni-Barber pain stimulation for a maximum of 120 seconds. Between stimulation, participants performed isometric or concentric exercise, or rested. Pain rating from 0-100 was recorded every 20 seconds, and participants pressed a button upon first perception of pain to record threshold.

RESULTS: Pain ratings decreased from pre to post-intervention across groups (p<0.001). However, there were no significant differences between groups. The rating in concentric group had the largest drop of 13 units (p=0.058), isometric group decreased 11.9 (p=0.174), and control decreased 9.0. Men reported less pain than women at baseline (p=0.018), but females had a greater after intervention (p=0.010). Pain Thresholds increased by an average of 12.6 sec for each sex and intervention (p=0.001), however men had higher pain thresholds at baseline and post-intervention (p=0.027). Subjects with higher catastrophizing scores (SCS>9) were found to have higher pain ratings by 15.28 points from pre- to post-intervention across all variables.

CONCLUSIONS: Though pain ratings and thresholds decreased post-intervention in all groups, no significant difference was found between exercise groups and control. Men were found to have significantly higher pain thresholds at baseline and post-intervention. The high placebo effect found in our study contrasts previous research that showed significant differences in EIH compared to controls. This may be due to exercise intensity/duration, faulty assumptions on statistical analysis, or fundamental differences in nociceptive mechanisms between healthy subjects and those suffering from painful conditions, especially chronic. Further studies may examine larger pools of subjects, different exercise protocols, plasma biomarkers as well as subjects with painful conditions.
Patient Variables, Dosing Patterns, and Subsequent Outcomes During Warfarin Reinitiation

Authors: Lucas G. Leonhard, BS; Richard L. Berg, MS; James K. Burmester, PhD; Joseph J. Mazza, MD; John R. Schmelzer, PhD; Steven H. Yale, MD

Department: Marshfield Clinic Research Foundation, Clinical Research Center, Marshfield, Wisconsin

Mentors: Steven Yale, MD; James Burmester, PhD; Joseph Mazza, MD; Richard Berg, MS; John Schmelzer, PhD

Support: Shapiro Summer Research Program; Marshfield Clinic Research Foundation, Clinical Research Center

BACKGROUND: Warfarin is an oral anticoagulant used in the long-term treatment and prevention of venothromboembolic disease. Patients undergoing elective surgical and non-surgical procedures who are deemed at risk may require temporary warfarin discontinuation followed by warfarin reinitiation after their procedure. Because there is little information available regarding the best methods for warfarin reinitiation, we investigated current practices as a way to inform future management decisions.

METHODS: In this retrospective study, 205 cases from a cohort of Marshfield Clinic patients on a stable therapeutic warfarin dose prior to discontinuation (defined as three consecutive INRs in the 2.0-3.5 range 10 days or more before warfarin was discontinued) were subjected to analysis. Warfarin dose and dates of discontinuation and reinitiation were collected from patient medical records. Patients were divided into three groups based on whether they received the same, a higher, or a lower dose at reinitiation. The three patient groups were compared based on the time to INR of at least 2.0 and greater than 3.5, and the percent of INRs in therapeutic range (2.0 – 3.5). Patient variables including demographic data, current medical status, warfarin information, adverse events, and medications were abstracted from clinic and hospital electronic records. These variables were individually analyzed to detect differences among the three dosing groups.

RESULTS: Of the 205 valid cases, 74 were reinitiated at a higher dose, 99 at the same dose, and 32 at a lower dose. Cases in the higher dose group reached a therapeutic INR of at least 2.0 more quickly than the other two groups (p = 0.001). Cases in the higher group obtained an INR greater than 3.5 faster compared to the two other groups. This difference was not statistically significant. There was no significant difference in the percentage of INRs in therapeutic range between the three groups. While patient characteristics varied among the dose groups, the only variable found to reach statistical significance (p ≤ 0.05) was the length of hospitalization.

CONCLUSIONS: We observed varied dosing strategies for reinitiating patients on warfarin, and could not identify a single, best strategy. While reinitiating at a higher dose may achieve a therapeutic INR more quickly, it also may lead to increased risk for supra-therapeutic INRs and associated bleeding events. Many factors may influence whether a physician reinitiates a patient at a different dose than his/her prior therapeutic dose. We found that patients with longer lengths of hospitalization were more likely to receive lower warfarin doses. However, in the absence of clinical indications for modification, we believe patients with a previously established effective dose should be reinitiated at that same dose.
pRNA Nanoparticles as Tools to Improve Human Pluripotent Stem Cell-based Transplantation Strategies for Retinal Degenerative Disease

Authors: Jessica Lien, BS; Lynda Wright, MS; David Gamm, MD, PhD

Department: Department of Ophthalmology and Visual Sciences, University of Wisconsin School of Medicine and Public Health

Mentor(s): David Gamm, MD, PhD

Support: Shapiro Summer Research Program; Arnold and Mable Beckman Initiative for Macular Research

BACKGROUND: Age-related macular degeneration is a degenerative eye disease that damages the center of the retina called the macula resulting in a loss of vision in the center of the visual field. It is the leading cause of worldwide blindness in the elderly and there is currently no effective treatment. Studies are being done using stem cell technology to generate retinal cells to repopulate the retina.

In previous work, the Gamm Lab observed that stem cell derived retinal cells integrate into the host retina with varying efficiencies and the transplanted retinal cells have poor survival. Thus, being able to select for specific subpopulations of cells would allow for enhanced promotion of cell survival after transplantation. The Gamm Lab is trying to find a clinically viable method to accomplish this using RNA nanotechnology.

RNA’s unique folding and thermodynamic stability make it a great candidate for delivery of medical therapies to cells. RNA nanoparticles (pRNA) may be the right tool to track and sort cells and may be used as a potential pro-survival mechanism to isolate the desired subpopulation of stem cell derived retinal cells.

METHODS: Initial experiments to test the efficacy of pRNA in a prenatal human progenitor line found that pRNA treatment decreased proliferation and may have an apoptotic effect on progenitor cells without affecting the differentiated neurons. This work was extended to retinal cultures using improved pRNA constructs containing cy3 fluorophore and EGFR aptamer to negatively select against proliferating cells, thereby generating the enriched source of retinal cells.

Neuroretinal cultures derived from differentiating human pluripotent stem cells were treated with the pRNA. The cells were fixed and immunocytochemistry performed to provide biomarkers for visualization with epifluorescence and confocal microscopy analysis. In addition, RT-PCR was performed to determine EGFR expression and western analysis for any change in EGFR activation and signaling.

RESULTS: EGFR aptamer-Cy3-pRNA targeted proliferating progenitors and glial cells in differentiating human neural progenitors. The pRNA demonstrated both anti-proliferative and pro-apoptotic effects.

CONCLUSIONS: EGFR aptamer pRNA has the ability to target proliferating cells in retinal cultures derived from human pluripotent stem cells with the potential to enrich for specific retinal cell types. Thus, pRNA show considerable promise as a tool to track, sort, and manipulate donor cell populations for retinal transplantation.
Analyzing UW Health Care Workers’ Perspectives on Disaster Resource Allocation via Survey Tool

Authors: Phillip J. Mercier, BS; Ann P. O’Rourke, MD, MPH

Department: Department of Surgery, University of Wisconsin School of Medicine and Public Health

Mentor(s): Ann P. O’Rourke, MD, MPH; Suresh K. Agarwal Jr., MD, FACS, FCCM, FCCP

Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: Disaster planning is a critical element of prompt response during relief efforts. In large scale disasters, many care elements become limited, including oxygen supply, ICU beds, and ambulation to care centers. Optimal care for a given disaster victim may not align with the goal of maximizing overall public health outcomes. Distribution of these finite resources is a large source of controversy, even amongst health care workers. To ensure an effective and efficient recovery, it is imperative that relief efforts are conducted in a coordinated manner. In order to collect and interpret the prevailing opinions surrounding disaster resource allocation, our group developed a survey tool. Information collected via this survey will enable disaster preparedness planning committees to better focus discussion when designing protocols for disaster relief efforts.

METHODS: We reviewed current literature concerning the ethics involved in resource allocation. Considerable time was dedicated to development of an effective survey tool. This included utilization of the expertise of the University of Wisconsin Survey Center. Survey techniques, including using parallel question wording, transition statements, matrices, and optimal placement of demographic questions were used. Following survey development an IRB exemption application was completed and submitted.

RESULTS: IRB exemption was approved and the project is currently in pre-deployment stage. The survey will be distributed to UW health care workers and students via email lists once further permission is obtained.

CONCLUSIONS: After survey deployment and data collection, analysis will be performed. Results will be important in aiding discussions amongst the many players involved in disaster response planning. The conclusions drawn from this survey will provide a snapshot of the perspectives of UW Health Care workers concerning resource allocation in disaster situations. Further plans include deploying a reworked survey to the public to assess and integrate their viewpoints surrounding resource allocation during disasters.
Identifying Predictors of a Difficult Thyroidectomy

Authors: Valerie M. Mok, BS; Sarah C. Oltmann, MD; Herbert Chen, MD, FACS; Rebecca S. Sippel, MD, FACS; David F. Schneider, MD, MS

Department: Department of Surgery, Division of Endocrine Surgery, University of Wisconsin School of Medicine and Public Health

Mentor(s): David F. Schneider, MD, MS

Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: Predicting the difficulty of a thyroid operation can improve OR scheduling and patient safety. We have previously shown that a novel Thyroidectomy Difficulty Scale (TDS) had high inter-rater agreement; TDS scores correlated with operative times and complication rates. The purpose of this study is to identify predictors of a more difficult thyroidectomy.

METHODS: A four item (vascularity, friability, mobility/fibrosis, gland size), 20-point TDS, with each item graded on a scale of 1-5, was used to score the difficulty of thyroid operations for a variety of diagnoses. Preoperative labs, medications, comorbidities, and postoperative complications were recorded for each patient. Operative times were standardized to each surgeon’s average time. The difficult thyroidectomy (DT) and non-difficult thyroidectomy (NDT) patients were compared using t-test, Fisher’s exact test, Chi-squared test, and Wilcoxon Rank-Sum test, where appropriate. A final multivariate logistic regression model was then constructed with significant (p<0.05) variables from a univariate analysis.

RESULTS: 189 patients were scored using TDS. 146 patients were female (77.25%) and the median age was 49 years +/- 15.0 SD. In this cohort, 69 (36.5%) suffered from hyperthyroidism, 42 (22.2%) from Hashimoto’s, 34 (18.0%) from thyroid cancer and 36 (19.0%) from multinodular goiter. A threshold TDS score of greater than 10 was selected to define DT. Cases meeting this definition of DT took an average of 19.1% longer and experienced nearly three times the complication rate compared to the NDT group (p<0.01). Among hyperthyroid patients, the DT group had a higher frequency of patients treated with Lugol’s potassium iodide drops (81.6% DT vs. 58.1% NDT, p=0.032), experiencing ophthalmopathy (31.6% DT vs. 9.7% NDT, p=0.028) and the presence of (>4 IU/mL) anti-thyroglobulin antibodies (34.2% DT vs. 12.9% NDT, p=0.05). For patients with thyroid cancer, the DT patients had a higher mean thyroglobulin compared to the NDT patients (897 ng/mL vs. 55 ng/mL, p=0.027). Using multivariate analysis, hyperthyroidism, high (>150 ng/mL) thyroglobulin and the presence of anti-thyroglobulin antibody was independently associated with DT.

CONCLUSIONS: Using TDS, we demonstrated that hyperthyroidism is associated with more difficult thyroidectomy. Preoperative thyroglobulin levels and anti-thyroglobulin antibodies are markers of a more difficult operation. This can assist surgeons in counseling patients about operative risk and improve OR scheduling.
The Age of Patients with Rib Fractures is Associated with Higher Complication Rates and Increased Length of Stay

Authors: Mark Molnar, MS, MPharm; Hee Soo Jung, MD; Anuoluwapo Elegbede, MD; Ann O'Rourke, MD, MPH; Suresh Agarwal, MD, FACS, FCCM, FCCP

Department: Department of Surgery, University Of Wisconsin School of Medicine and Public Health

Mentor(s): Suresh Agarwal, MD, FACS, FCCM, FCCP

Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: Age in patients with rib fractures have been associated with increased mortality; however, the impact of age and rib fractures upon other post-operative factors, such as complications and length of stay has not been studied.

METHODS: A retrospective review of a prospectively collected and validated database at a large, university, Level I trauma center was reviewed from 2008 to 2012. 5 common complications; atelectasis, pleural effusion, pneumonia, respiratory failure, and pulmonary edema, were examined in three groups: Ages 18-29, Ages 30-59, and Ages 60 and above. Furthermore, hospital length of stay was examined for each of these cohorts.

RESULTS: Over the 5 year period, a total of 1,500 rib fracture patients were found. Although trends towards increasing atelectasis and pneumonia, were found, particularly in the oldest group, these did not reach statistical significance. However, older patients (Ages 60 and above) were found to have a statistically significant increase in pleural effusion (p=0.02), respiratory failure (p<0.01), and pulmonary edema (p<0.01). Furthermore, older patients (60 and above) were found to have longer hospital stays than both the younger (18-29) and middle aged (30-59) patients with rib fractures.

CONCLUSIONS: Rib fractures contribute greatly to morbidity and complication in elderly patients. Furthermore, elderly patients utilize greater acute hospital care than their younger counterparts. Future efforts should emphasize preventions of rib fractures in all patients, but particularly the elderly. Aggressive management of older patients with rib fractures should be implemented in order to attempt to decrease the rate of complications.
Iron May Be the Critical Link Between Maternal Obesity and Asthma in Offspring

Authors: Shannon E. Murray; Natalie C. Dosch; Rachel M. Weigert; Elyssa F. Guslits; Theresa W. Guilbert; Christopher L. Coe; Pamela J. Kling

Department: Department of Pediatrics, University of Wisconsin School of Medicine and Public Health; Harlow Center for Biological Psychology, Madison, WI

Mentor(s): Pamela J. Kling, MD

Support: Shapiro Summer Research Program; UW Cardiovascular Research Center; Meriter Foundation

BACKGROUND: Maternal pre-pregnancy obesity is associated with asthma diagnosis in offspring, however, no clear mechanism for this association has been found. Our lab previously showed that obesity was linked to poorer iron status in offspring. Other studies suggest iron status plays a key role in this unknown mechanism. We analyzed newborn iron status and lymphocyte Th1/Th2 cytokine expression in obese vs. control pregnancies. Our hypothesis was that depleted newborn iron in obese pregnancy alters developmental inflammatory processes, predisposing to asthma.

METHODS: The University of Wisconsin and Meriter Hospital IRBs approved this study. Eligible subjects included mothers delivering healthy term newborns from routine scheduled caesarean sections. Umbilical cord blood samples from control and obese pregnancies were analyzed for iron status, including measures of hemoglobin (Hb), zinc protoporphyrin/heme ratio (ZnPP/H), and ferritin. Lymphocytes were isolated for cell culture, stimulated with phytohyemagglutinin, and incubated for 24 hours in normal media or low iron media with deferoxamine (DFX). Cytokine expression profiles were examined using a multiple cytokine array. Statistical analysis included t-test and ANOVA.

RESULTS: Cord blood from 11 control and 12 obese pregnancies showed similar HB and ZnPP/H measures of erythrocyte iron, but a trend for lower ferritin in obese pregnancy. White blood cell counts did not differ between obese and controls; however, obese had higher cord Th2-associated eosinophil counts than control (p<0.05). Production of the Th1 cytokine, IFN-gamma, trended lower in obesity and was completely inhibited by low iron DFX media (p<0.05). The anti-inflammatory cytokine IL-10 was also inhibited by DFX (p<0.03). By contrast, the pro-inflammatory cytokine IL-8 was similar between groups and unaffected by low iron conditions.

CONCLUSIONS: The combination of higher Th2-associated eosinophil counts and lower Th1-stimulated cytokine expression are consistent with a relative dysregulation of the balance between Th1 and Th2 cytokines in offspring of obese pregnancy. A predominance of Th2 cytokines can create an atopic phenotype that predisposes to asthma and allergies. Iron may be the critical link between obese pregnancy and future asthma development in offspring.
The Surgical Apgar Score Correlates with an Increased Risk for Readmission in Emergency Surgery Patients

Authors: Gajanthan Muthuvel, BS; Sarah E. Tevis, MD; Suresh K. Agarwal, MD, FACS; Gregory D. Kennedy MD, PhD, FACS

Department: Department of Surgery, University of Wisconsin School of Medicine and Public Health

Mentor(s): Gregory D. Kennedy, MD, PhD, FACS

Support: Department of Surgery NIH T35 Training Grant DK062780

BACKGROUND: Preventable readmission has become a national focus. It is clear that surgical patients present specific challenges to those interested in preventing readmission. Patients undergoing emergency surgical procedures are at particularly high risk for readmission and little is known about this complex outcome in this patient population. We are interested in determining if there are readily available data variables to predict risk of readmission. The surgical Apgar score (SAS) is calculated from intraoperative variables and has been shown to be predictive of postoperative mortality in the non-emergent setting. The objectives of this study were to characterize 30-day readmissions in emergent general surgery and to determine whether certain variables were associated with readmissions. We hypothesized that the SAS correlates with risk for readmission in emergency general surgery patients.

METHODS: Variables of interest were obtained from retrospective analysis of the University of Wisconsin NSQIP database in addition to the electronic medical record. We identified adult general surgery patients who underwent an emergency procedure from 2006-2012. Univariate analysis identified factors associated with 30-day readmission. Factors with p<0.1 were included in multivariate analysis to reveal potential risk factors for readmission.

RESULTS: As compared with non-emergency surgery patients, patients with emergent procedures had a higher rate of readmission (11.1% vs. 15.2%, p = 0.004). The SAS (OR 3.297, CI 1.074-10.121, p=0.037), and the combined variable of the American Society of Anesthesiologists Physical Status Classification (ASA class) and hospital length of stay (OR 4.370, CI 2.251-8.486, p<0.001), were highly associated with 30-day readmissions in adult emergency general surgery patients.

CONCLUSIONS: Given the significance of readmission after emergency surgery, it is important to establish measures that identify patients at high risk for readmission before they are discharged. We have identified objective measures that allow for the stratification of patients into low- and high-risk groups. Patients found to be high risk could be given modified postoperative care that may include additional education, discharge to a destination with a higher standard of care, or closer follow-up. Furthermore, the stratification of patients will enable the study of prospective interventions designed to decrease unplanned readmissions in emergency surgery patients.
A Retrospective Review on the Number of Skin Biopsies Needed per Malignancy

Authors: Ashley Nault, BS; Joshua Tarpley, BA; Chong Zhang, MS; KyungMann Kim, PhD; Justin Endo, MD; Joanna McGetrick, MD; Daniel Bennett, MD; Yaohui Gloria Xu, MD, PhD

Department: Department of Dermatology, University of Wisconsin School of Medicine and Public Health

Mentor(s): Yaohui Gloria Xu, MD, PhD; Daniel Bennett, MD

Support: Shapiro Summer Research Program; Department of Dermatology

BACKGROUND: Histopathologic evaluation is the gold standard for the diagnosis of skin cancer. Yet, excessive skin biopsies can impact efficiency and cost and cause associated morbidities. There is no established benchmark to which providers may quantitatively compare their biopsy effectiveness. A prior study determined a number needed to treat (NNT) for all cancer, non-melanoma skin cancer (NMSC) and melanoma of 2.22, 1.6, and 15, respectively. A different, but similar study, reported a NNT of 30 for melanoma. These studies suggest significant variability amongst practice settings and providers. To the best of our knowledge, our study is the first to compare the number needed to biopsy (NNB) between dermatology physicians and dermatology advanced practice providers (APPs).

METHODS: This is a retrospective study of all skin biopsies read by UW dermatopathologists from January 1, 2010, to February 15, 2010. Biopsies with the intention of diagnosing a skin cancer were included; inflammatory conditions, cosmetic and functional removals, re-excisions, and biopsies with insufficient documentation were excluded. The NNB for one NMSC was calculated by dividing the total number of non-pigmented lesions by those diagnosed as NMSC. The same calculation was used for melanoma NNB.

RESULTS: Of 1,074 biopsies included, 55% were clinically non-pigmented lesions. One-fourth of biopsies were diagnosed as NMSC and 2% were diagnosed as melanoma. Most melanomas were biopsied from the trunk while most NMSCs were biopsied from the face. Skin type was collected from over 70% of subjects and more than half had a Fitzpatrick skin type I or II. The NNB for any skin cancer was 3.59. The NNB for NMSC was 2.21 while the NNB for melanoma was 21.95. The NNB of any skin cancer for advanced practice providers was 6.35—more than double the NNB for physicians (NNB = 2.97; P<0.0001). The NNB for NMSC by provider type was 3.22 for APPs; for physicians it was 1.99 (P<.0001). The difference in NNB for melanoma between provider types was not statistically significant (NNB APP = 38.2, NNB physician = 17.18; P=0.0987). The NNB was lower for older patients and males. Compared to NNB for biopsies with no history of skin cancer, there was a significantly greater NNB with a history of melanoma and a smaller NNB with a history of NMSC.

CONCLUSIONS: The NNB for any cancer, melanoma and NMSC was higher than the respective NNB reported by Wilson et al. NNB for melanoma was lower than that reported by Hansen et al. NNB varied by provider type, subject age and gender, and history of skin cancer. This is the first preliminary study demonstrating the difference between physicians and APPs. Ongoing studies with more sample recruitment and representation from various dermatology practices will provide a more objective assessment.
Can Radiographs Predict Outcome in Patients with Idiopathic Clubfoot Treated with the Ponseti Method?

Authors: Conor P. O'Halloran, BS; Blaise A. Nemeth, MD; Matthew A. Halanski, MD; Catherine Carlyle Zimmermann, MD; Kenneth J. Noonan, MD

Department: Department of Orthopedics & Rehabilitation, University of Wisconsin School of Medicine and Public Health

Mentor(s): Kenneth J. Noonan, MD; Blaise A. Nemeth, MD; Matthew A. Halanski, MD

Support: Shapiro Summer Research Program; Department of Orthopedics & Rehabilitation

BACKGROUND: The Ponseti Method of serial casting has become the standard of care for clubfoot. There is currently no classification scheme for the severity of clubfoot that has prognostic value. The aim of this study is to determine if radiographic measurements, taken prior to tenotomy, can predict recurrence in children with idiopathic clubfoot treated in the manner of Ponseti.

METHODS: A retrospective chart and radiographic review was performed on children with idiopathic clubfoot treated in the manner of Ponseti over a ten-year period with follow-up to at least 2 years of age. Other inclusion criteria included having a forced dorsiflexion lateral foot radiograph prior to tenotomy. The following angles were measured in duplicate on the pre-tenotomy radiographs: foot dorsiflexion (defined as the angle between the tibial shaft and the plastic plate used to dorsiflex the foot), tibio-calcaneal, talo-calcaneal, and talo-first metatarsal angles. Clinical review of patient records identified patients who had a recurrence, defined as requiring additional tenotomy or other operative procedure.

RESULTS: 45 patients (71 feet) were included in the study. The median follow up was until 4.6 years of age. The Intra-reader reliability (ICC) was acceptable for all measures. 13 of the 71 feet required additional surgery, occurring at a median age of 3.6 years. Of the four radiographic measures, only foot dorsiflexion had a statistically significant Hazard Ratio (HR). (HR=1.04, p=.03). Youden's method identified 16.6 degrees of dorsiflexion as the optimal cut-off. Feet with at least that amount of dorsiflexion (n=21) experienced no recurrences, feet with less than that amount of dorsiflexion (n=50) experienced 13 recurrences (p=0.007).

CONCLUSIONS: Reduced foot dorsiflexion on lateral forced dorsiflexion pre-tenotomy radiograph was associated with an increased risk of recurrence. This information may guide treatment by identifying patients in whom casting has not produced sufficient correction to proceed to tenotomy. In the opinion of the authors, radiographic measurements of dorsiflexion are more objective and reproducible than clinical measurements of equinus, and therefore more clinically relevant. Dorsiflexion to 15 degrees past neutral appears to predict successful treatment via the Ponseti method.
Identifying High-Risk Patients for Hospital Readmission Following Radical Cystectomy and Urinary Diversion

Authors: Katherine Omernick, BS; Tracy Downs, MD; Sarah Tevis MD; Glen Levenson, PhD; Gregory Kennedy MD, PhD; David Jarrard, MD; E. Jason Abel, MD

Department: Department of Urology, University of Wisconsin School of Medicine and Public Health

Mentor: Tracy Downs, MD

Support: Shapiro Summer Research Program, Department of Urology, University of Wisconsin School of Medicine and Public Health

BACKGROUND: Thirty-day readmission rates following radical cystectomy are as high as 20%. Recent legislation penalizing hospitals for higher than predicted thirty-day readmissions has increased focus on preventing readmissions in surgical patients.

METHODS: We performed a retrospective analysis of national ACS-NSQIP data from 2011. Evaluated patients included adults who underwent radical cystectomy and urinary diversion. We excluded patients who died within thirty days of operation or had a time from operation to discharge ≥30 days. Our primary outcome of interest was readmission within thirty days of radical cystectomy. Pearson’s X² test was used to analyze categorical variables while independent T-test was used for continuous variables. Variables with a p ≤0.1 in the univariate analysis were used as independent variables in a multivariate logistic regression analysis. All tests were two-tailed and statistical significance was defined as p≤0.05. Analyses were performed using IBM SPSS Statistics 21.

RESULTS: We identified 610 patients who underwent radical cystectomy in 2011. The overall readmission rate was 22.8% (N=139). The average age was 67.5 years old, 80% were male and 31.6% were obese. The average time from operation to discharge was 8.91 days. On multivariate analysis age <60 years (OR=1.781, 95% CI 1.083-2.931) and an increased number of postoperative complications were found to independently predict readmission. Compared with patients with no complications, those with one complication were more frequently readmitted (OR = 2.5, 95% CI 1.425-4.269). Readmission increased further with two or more complications (OR= 11.1, 95% CI 6.315-19.670). To determine whether patients <60 years were readmitted more frequently due to a greater prevalence of continent urinary diversions, the age groups were stratified by urinary diversion type: continent or incontinent. Compared to the <60 years incontinent diversion group, ≥60 years incontinent diversion and the ≥60 years continent diversion groups did not have a significantly different incidence of readmission. However, the <60 years continent diversion group had a considerably higher readmission rate (OR=2.7, 95% CI 1.191-6.125).

CONCLUSIONS: We found that patients <60 years with continent urinary diversions and patients who suffered postoperative complications are at a high risk for readmission after radical cystectomy. These high-risk patients may benefit from increased perioperative teaching and close postoperative follow-up to increase the efficiency and effectiveness of their care.
Epidermal Growth Factor Mediated Wound Repair in Human Embryonic Stem Cell-Derived Epithelial Cells

Authors: Liliana Palencia, BS; Amritava Das, MEng; Sean Palecek, PhD; Susan Thibeault, PhD; Ciara Leydon, PhD

Department: Department of Surgery, Division of Otolaryngology, University of Wisconsin School of Medicine and Public Health

Mentors: Susan Thibeault, PhD; Ciara Leydon, PhD

Support: Department of Surgery NIH T32 Training Grant DC009401-04

BACKGROUND: Vocal fold injury due to blunt trauma, iatrogenic injuries, surgical intubation, or laryngeal infections and inflammation can result in the loss of the vibratory function of vocal folds, leading to dysphonia. Following injury, the fundamental goal of wound healing is the reconstitution of functional vocal fold tissue, including the epithelium. The mechanisms underlying reepithelialization, an early and necessary part of vocal fold wound repair, are not known. Physical inaccessibility and ethical constraints preclude study of human vocal folds in vivo. The aim of this study was to explore how epidermal growth factor (EGF) and its receptor, the epidermal growth factor receptor (EGFR), mediate reepithelialization by cell proliferation in an in vitro model.

METHODS: To assess the wound repair response to injury, we created a scratch wound in a three-dimensional model of vocal fold mucosa of human origin developed in our laboratory. The model consists of human embryonic stem cell-derived simple epithelial cells co-cultured with primary vocal fold fibroblasts. Rate and extent of wound healing, EGFR activation, and cell proliferation post-injury were analyzed with and without application of both exogenous EGF and an EGFR inhibitor, Gefitinib. Extent of wound repair was calculated as a percentage of the original wound. EGFR activation was visualized via immunocytochemistry using an anti-tyrosine 1068 antibody, while cell proliferation was visualized using an anti-ki67 antibody.

RESULTS: Results indicate that in vivo vocal fold epithelial wound healing can be successfully replicated in our three-dimensional model of vocal fold mucosa. Increased density and heterogeneous distribution of Ki67 in the epithelium was observed post-injury in the area surrounding the scratch wound, indicative of proliferation and reepithelialization in the vocal fold mucosa model. Wound repair after injury was stimulated by EGF but depressed with concurrent addition of Gefitinib.

CONCLUSIONS: These results indicate that EGF stimulates wound healing in an EGFR dependent manner. These findings provide insight into how EGF and EGFR may regulate the wound repair response of stem cell-derived epithelial cells in a three-dimensional model of vocal fold mucosa. This study demonstrates that our novel model of wound healing in vocal fold mucosa can be used successfully to gain insight into the mechanisms that enable and regulate epithelial repair following injury.
Use of the Ankle Brachial Index (ABI) as a Possible Diagnostic Tool for Peripheral Artery Diseases (PAD) in Diabetic Patients at Tikur Anbessa Specialized Hospital, Ethiopia

Authors: Charles Penn, BS; Sean Fling, BA

Department: ¹Department of Surgery, Division of Vascular Surgery, University of Wisconsin School of Medicine and Public Health; ²Addis Ababa University, Faculty of Medicine

Mentor(s): ¹Girma Tefera, MD; ²Nebyou Siyoum, MD

Support: Department of Surgery NIH T35 Training Grant DK062780

Background: In low and middle-income countries, much focus has been on infectious diseases however non-communicable diseases such as cardiovascular disease are getting to epidemic proportions. The objective of this study was to use Ankle-Brachial Index (ABI) test to estimate the prevalence of PAD in Diabetic patients at Tikur Anbessa Specialized Hospital (TASH) in Addis Ababa, Ethiopia.

Method: This study was conducted at the TASH diabetic clinic. We collected information pertaining to patient demographic, physical examination, measured and calculated their ABI. The ABI value was used to define the presence or absence of peripheral vascular disease amongst all patients. Normal value was 0.9 to 1.3. ABI values of less than 0.9 were considered abnormally low and those >1.3 suggested severe vascular calcification and none compressibility. Other vascular risk factors such as smoking, lipid profile, and other evidence of concomitant vascular disease were also documented.

Results: During the months of May and June 2013, a total of 140 patients were evaluated. This included 73 females, and 67 males with a mean age of 51 (range 17-85). 9.5% of the patients had ABI less than 0.9 while 10.1% had ABI > 1.3. Most patients suffered from type 2 diabetes (65%). 2.6% had a previous amputation, 4.5% had foot ulcers, 3.6% had history of previous myocardial infarction. Only 1.4% of the patients were current smokers, however, 16% of the patients admitted to having smoked in the past. We did observe a statistically significant correlation between the presence of previous amputations and the presence of PAD.

Conclusion: This is the first attempt to screen for vascular patients at TASH diabetic clinic. Our results suggested about 20% prevalence of PAD amongst these diabetes patients. This cross-sectional study is probably an underestimation of the actual prevalence due to the small sample size and selection bias of patients who can can afford to be seen at this specialized hospital.
Morphological Changes in Fibroblasts Induced by PBMCs from Patients with Type II Diabetic Nephropathy

Authors: Trinh T. Pham, MS; Arielle Bauer, BS; Debra Hullett, PhD; Bianca Tomasini-Johansson, PhD; Hans Sollinger, MD, PhD, FACS.

Department: Department of Surgery, Division of Transplantation, University of Wisconsin School of Medicine and Public Health

Mentor(s): Bianca Tomasini-Johansson, PhD; Debra Hullett, PhD; Hans Sollinger, MD, PhD, FACS

Support: Department of Surgery NIH T35 Training Grant DK062780

BACKGROUND: Diabetic nephropathy (DN) is defined as renal failure associated with Type II diabetes; it is the most common cause of end-stage renal disease, and has been termed “a medical catastrophe of worldwide dimensions”. The increasing prevalence of DN makes it imperative to search for mechanisms leading to fibrotic kidney disease. Findings from the lab have shown that peripheral blood mononuclear cells (PBMCs) from patients with nephropathy can alter morphology in renal epithelial cells in-vitro. Because “activated” fibroblasts are the likely generators of extracellular matrix proteins (fibrosis, when in excess), we investigated whether there are pro-fibrotic changes associated with fibroblasts when co-cultured with PBMCs from Type II DN patients.

METHODS: We used cryopreserved PBMCs extracted from blood of healthy volunteers or patients with DN. Fibroblasts from an immortal line (AH1F) were cultured in DMEM, 10%FBS, then plated in a 24-well plate, on gelatin-coated coverslips for 24h in 0.2% fatty acid BSA in DMEM prior to addition of 1 X10^6 PBMCs per coverslip in RPMI, 1% FBS and or the addition of fibronectin (FN) assembly inhibitor FUD (500nM), or with TGF-β (20ng/ml) in RPMI. Mixed cultures were incubated for 48h, washed with PBS, fixed and permeabilized, blocked with BSA and incubated with antibodies to matrix proteins or with phalloidin for actin. Analyses included phase contrast imaging and immunofluorescence (IF).

RESULTS: Phase contrast revealed fibroblasts undergo morphology changes in the presence of PBMCs from patients with DN. Fibroblasts were hypertrophic and erratic in directionality relative to those treated with normal PBMCs. Fibroblast density seemed markedly reduced in presence of diseased PBMCs, however, AH1F cell counts (DAPI) suggest otherwise. IF findings for actin stress fibers paralleled morphological findings as seen by phase contrast. Both FN and α-smooth muscle actin staining were inconclusive. Fewer PBMCs (stained with anti-CD45 antibodies) adhered to coverslips when cells were treated with FUD, suggesting FN may be critical for PBMCs to adhere to fibroblast monolayer.

CONCLUSIONS: The directionality of fibroblasts was altered in the presence of PBMCs from patients with DN compared to those of normal subjects, suggestive of a migratory phenotype. This suggests a mechanism via which “diseased” PBMCs may promote the initial stages of fibrosis. Further experiments need to be carried out to identify a quantifiable marker of the observed changes induced by diseased PBMCs to confirm these findings.
Effect of Maturational Timing of Physical Activity Exposure on Post-Menarcheal Bone Outcomes

Authors: Lindsay Raab, BS²; Brittney Bernardoni, BS²; Jodi N. Dowthwaite, PhD³; Paula F. Rosenbaum PhD⁴; Tamara A Scerpella, MD¹

Department: ¹Department of Orthopedics and Rehabilitation, University of Wisconsin School of Medicine and Public Health; ²UW School of Medicine and Public Health; ³Department of Orthopedic Surgery, SUNY Upstate Medical University; ⁴Department of Public Health and Preventive Medicine, SUNY Upstate Medical University

Mentor(s): Tamara A. Scerpella, MD

Support: Shapiro Summer Research Program; SMPH Department of Orthopedics and Rehabilitation; Orthopedic Research and Education Foundation; SUNY Upstate Medical University; the National Institute of Arthritis, Musculoskeletal and Skin Diseases (R03AR047613; R01AR054145)

BACKGROUND: Adolescent bone accrual is closely tied to pubertal development. For females, approximately half of adult bone mass is acquired in four circum-menarcheal years. Modifiable factors, especially physical activity and diet, are responsible for ~40% of variation in peak bone mass. Increased physical activity during growth is associated with increased bone acquisition, yet the most opportune window for activity exposure remains unclear. Thus the primary aim of the present study was to determine the maturational window during which physical activity exposure (PA) maximally contributes to ‘adult’ bone parameters.

METHODS: Subjects in the current analysis are a subset from an ongoing longitudinal study (1997-present) including female gymnasts (GYM) and non-gymnasts (NON). Subjects underwent annual whole body and regional (forearm, hip, lumbar spine) DXA scans, as well as semi-annual anthropometry, maturation and physical activity (PA) tracking (h/wk of organized PA, including gymnastics and all other non-aquatic PA). Subjects were included if they had DXA scans at ~1yr pre-menarche (PRE) and ~5yrs post-menarche (POST), with complete PA data between scans. ANCOVA assessed PRE to POST change in characteristics and outcomes. Regression analyses were performed to evaluate the explanatory value of PA for bone outcomes, independently testing several maturity periods: the entire adolescent inter-scan interval; ~1 year pre-menarche to 1 year post-menarche; 1 to 3 years post-menarche; 3 to 5 years post-menarche. Analyses accounted statistically for baseline gynecological age, baseline bone trait, adult body size and change in body size between scans.

RESULTS: Baseline bone measures explained ~20% to ~60% of variance for most adult bone outcomes, indicating significant tracking from pre-menarche to adulthood. Evaluated in separate models, physical activity averaged across the entire inter-DXA adolescent period and activity 1-3 years post-menarche were significant factors in adult 1/3 radius and Sub-head bone mineral content (BMC). Activity 3-5 years post-menarche was a significant factor in Femoral Narrow Neck Width, Endosteal Diameter and Buckling Ratio. Gymnasts and non-gymnasts did not differ for subject characteristics other than fat mass and activity exposure, but most unadjusted bone outcomes differed between gymnasts and non-gymnasts.

CONCLUSIONS: Although the majority of early adult bone status is explained by factors that precede menarche, organized activity participation in late adolescence appears to yield significant advantages in whole body and radius bone mass, and in indices of femoral neck structure and strength. These preliminary findings suggest that for females, high quality physical education programming should be continued throughout middle school and high school to reduce lifetime fracture risk in women via weight-bearing activity.
Thematic Analysis of NIH Mentored K and Developmental Research (R21) Proposal Critiques

Authors: Caitlin Regner, BS; Anna Katz, PhD; Molly Carnes, MS, MD

Department: Department of Medicine, Center for Women’s Health Research, University of Wisconsin School of Medicine and Public Health

Mentor: Molly Carnes, MS, MD

Support: Shapiro Summer Research Program; Department of Medicine

BACKGROUND: Men are more likely than women to succeed in the transition to independent research careers. NIH’s mentored K and R21 awards are important precursors for R01 grants—the traditional benchmark of an independent research career. Research shows that feedback from reviewers can influence career persistence; but the extent to which peer reviewers of scientific grants provide men and women with different feedback remains largely unknown.

METHODS: We performed a qualitative thematic analysis of 158 proposal critiques from 65 unfunded and 31 funded applications for mentored K (17 PIs) and R21 (13 PIs) awards. Applicants submitted their proposals to NIH between 2005-2008 and were from a single large public research university.

RESULTS: Comparison of thematic trends in the unfunded and funded proposal critiques of male and female investigators showed many broad similarities: critiques of unfunded K and R21 proposals contained greater criticism and negative remarks than critiques of funded proposals, which contained more positive remarks about applicants and their research. Subtle sex-differences in thematic trends were also identified: criticism more often took the form of advice in critiques of male investigators’ unfunded proposals, while it questioned female investigators’ competence and ability; praise and positive remarks in funded proposal critiques assured the success and competence of male investigators, but highlighted the expertise of mentors or collaborators and the hard work of female investigators.

CONCLUSIONS: Results suggest that gender stereotypes about competence may operate in NIH peer review. Future studies are needed to verify results and test the influence of reviewers’ feedback on persistence in academic medicine.
Automated Evaluation of Radiology Reports for Performance Metrics

Authors: John Renfrew, BS; Jason Stephenon, MD; Alejandro Munoz, PhD

Department: Department of Radiology, University of Wisconsin School of Medicine and Public Health

Mentor(s): Jason Stephenson, MD

Support: Shapiro Summer Research Program; Department of Radiology

BACKGROUND: Medical staff credentialing committees and accountable care organizations (ACOs) are requiring more and more radiologist performance measurements (metrics). Using human graders to evaluate large numbers of radiology reports to create performance metrics is costly. We devised an automated process for generating performance metrics and evaluated the automated process using human grading as the reference standard. Previous studies have reported favorable performance (accuracy, sensitivity and specificity, positive and negative predictive value) when compared to human report grading for detection of clinical conditions, recommendations for further imaging (RAI), and documentation of clinician contact (DCC). This project builds on previous methodology to increase algorithm accuracy, and to integrate the algorithm into the quality assurance apparatus of an active radiology practice.

METHODS: We used the Java programming language (Sun Microsystems, Redwood City, CA) to construct a computer algorithm which automatically processed radiology reports. We used an iterative process of comparing the results of the computer algorithm to human grading in batches of 250 reports, using a total of 5,500 reports. We refined the algorithm to improve performance over previous studies via four methods: Stratification of DCC keywords to improve accuracy, development of qualifying lists, limiting the search to the impression field, and instituting sentence-level analysis.

RESULTS: The accuracy of the RAI algorithm was 99.1%, the sensitivity (recall) 90.3%, the specificity 99.6%, the positive predictive value (precision) 93.8% and the negative predictive value 99.4%. The F1 score was 0.921. The accuracy of the DCC algorithm was 99.8%, the sensitivity (recall) 98.5%, the specificity 99.9%, the positive predictive value (precision) 99.0% and the negative predictive value 99.8%. The F1 score was 0.988.

CONCLUSIONS: We developed an automated process for the detection of recommended additional imaging (RAI) and direct clinician contact (DCC) in a large general practice radiology group that was accurate when compared to human grading. Such an automated process allows for calculation of radiology performance measures in a cost-effective manner, which will be in greater and greater demand by medical staff credentialing processes and accountable care organizations over the next several years.
Post-Dural Puncture Headaches Following Insertion of Cerebrospinal Fluid Drains for Thoracoabdominal Aortic Aneurysm Repair: Incidence and Risk Factors

Authors: Sean P. Riley, BS; Diana Khatib, MD; Melanie J. Donnelly, MD; Kristopher M. Schroeder, MD

Department: Department of Anesthesiology, University of Wisconsin School of Medicine and Public Health

Mentor(s): Kristopher Schroeder, MD

Support: Shapiro Summer Research Program; Department of Anesthesiology Research and Development Fund; John D. Arndt and the Anna K. Arndt Professorship

BACKGROUND: Cerebrospinal fluid (CSF) drains during thoracoabdominal aortic aneurysm (TAA) repair have become a well-established method of reducing the incidence of post-operative paraplegia. Unfortunately, however, dural puncture for spinal drain placement also increases patient risk for post-dural puncture headaches (PDPH). While previous studies have aimed to identify incidence and risk factors for PDPH in patients receiving spinal anesthesia, there is limited data about the incidence and risk factors for PDPH in patients receiving dural puncture with large-bore needles such as those used for CSF drainage during TAA repair.

METHODS: Following Institutional Review Board approval, a retrospective chart review was conducted of 235 patients who received preoperative spinal drain placement and survived to discharge following TAA repair at the University of Wisconsin Hospitals and Clinics between January 18, 2005 and July 21, 2012. Inpatient and outpatient records were analyzed and data on demographics (age, gender, BMI), pre-existing medical conditions (diabetes, smoking history, preoperative headaches), baseline pain score, American Society of Anesthesiologists (ASA) Score, preoperative opioid use, spinal drain details (needle size and kit used, number of dural puncture holes, first recorded CSF pressure, volume of CSF drained), duration of hospitalization and development of PDPH were all recorded.

RESULTS: Of the 235 patients reviewed in this study, 43 patients developed PDPH (18.3%). Data analysis revealed that both younger age (59.0 ± 17.4 vs. 69.4± 11.5; p< 0.001) and a history of preoperative headaches (27.9% vs. 8.3%; p≤ 0.001) were risk factors for developing PDPH following insertion of a spinal drain during TAA repair. All other factors were not found to be significant (p > 0.05).

CONCLUSIONS: PDPH have only recently become recognized as potential complications of dural puncture for placement of CSF drains during TAA repair. Of the 235 patients reviewed in our study, 43 patients (18.3%) developed PDPH. This demonstrates that PDPH are a fairly common complication secondary to CSF drain placement. Younger age and a preoperative history of chronic headaches appear to place patients at greatest risk for developing PDPH. Our results suggest that patients who are younger and/or have a history of chronic headaches should be well educated about the risk of developing PDPH and should be carefully monitored following spinal drain placement for symptoms of PDPH.
Benchmarking Quality for Endoscopic Ultrasound at UW Health

Authors: David Rivedal, BS; Mark Benson, MD; Deepak V. Gopal, MD, FRCP(C), FACP, AGAF, FACG, FASGE

Department: Department of Medicine, Division of Gastroenterology and Hepatology, University of Wisconsin School of Medicine and Public Health

Mentor(s): Mark Benson, MD; Deepak V. Gopal, MD, FRCP(C), FACP, AGAF, FACG, FASGE

Support: Shapiro Summer Research Program; Department of Medicine, Division of Gastroenterology and Hepatology

BACKGROUND: Pancreatic cancer is the fourth leading cause of cancer deaths in America and prognosis is usually poor. However, with early diagnosis provided by endoscopic ultrasound (EUS) prognosis is improved. One of the issues with diagnostic endoscopic procedures is the variation in quality between endoscopists. This variation has led to the establishment of procedural quality measures, in which colonoscopy is the gold standard. EUS has recommended quality measures, however none have been assessed. The goal of this study was to retrospectively analyze quality measures with the hopes of creating an easy and reproducible quality assurance checklist that will decrease endoscopist variability and improve overall quality of EUS at UW Health.

METHODS: Chart review was performed on all patients who underwent EUS at UW Health between January 1st and May 21st of this year. Variables of interest were recorded in a spreadsheet and analysis was performed. We chose to focus on fine needle aspiration (FNA) diagnostics of pancreatic masses. Recorded FNA variables relating to diagnosis and cytology included total pass number, adequate pass number, cytology technician, and cytologist. Adequate passes were determined by comparing the dictation note to the cytology report. If there was a discrepancy, the cytology report was used as the default.

RESULTS: A total of 288 EUSs were performed at UW Health over the time period including 49 pancreatic mass lesions. FNA diagnosis rates of pancreatic mass lesions (excluding cysts) was 70% overall and ranged from 68-75% between endoscopists. FNA diagnosis rates for cytology technicians and cytologists ranged from 50-91% and 20-86% respectively.

CONCLUSIONS: This study has shown that there is wide variation between endoscopists and the cytology team at UW Health. The overall FNA diagnosis rate for pancreatic mass lesions is lower than the national average of 88-90%. Further inquiry into the causes of this variation is the next step in this process. We hope to implement a concise quality assurance checklist that can help to decrease this variation in the near future.
Should Minimally Invasive Follicular Thyroid Cancer Be Treated as a Benign or Malignant Lesion?

Authors: Aaron Robinson, BS; David Schneider, MD, MS; Rebecca Sippel, MD, FACS; Herbert Chen, MD, FACS

Department: Department of Surgery, Division of Endocrine Surgery, University of Wisconsin School of Medicine and Public Health

Mentor(s): Herbert Chen, MD, FACS

Support: Department of Surgery NIH T32 CA090217-11

BACKGROUND: Follicular thyroid carcinoma (FTC) is the second most common type of thyroid cancer, comprising about 15% of all thyroid cancer incidences. Hurthle cell carcinomas are considered a subtype of FTC and therefore are included as part of the study. FTCs are classified into two subtypes: classic (C), which exhibit both vascular and capsular invasion and minimally invasive (MI), which only has limited capsular invasion. Both types, like all well-differentiated thyroid cancers, are traditionally treated the same: a completion thyroidectomy usually followed by radioiodine ablation. However, the two entities may behave in distinctly different manners. We hypothesize that MI-FTC may behave more like a benign follicular adenoma rather than C-FTC, and therefore may not require total thyroidectomy and radioactive iodine. This would preserve normal thyroid function and minimize risk to the parathyroid glands.

METHODS: A prospective thyroid database was reviewed to include patients with Follicular and Hurthle Cell tumors. Data on recurrence rates, disease-free survival, and requirement for follow-up surgery and/or radioiodine were compared amongst the groups. Disease-free survival was determined by the Kaplan-Meier method with log rank analysis. ANOVA and Chi-Square analysis were used to evaluate age (at time of surgery) and gender, respectively.

Kaplan-Meier
Disease-free survival was calculated based on date of operation to date of latest follow up. Patients with persistent disease (10) were removed from the analysis; all of the persistently diseased patients had C-FTC. Patients that presented with another primary tumor simultaneously were eliminated as it couldn’t be determined the source of the recurrence. Any patients with metastatic cancer to the thyroid (thyroid wasn’t the initial source of cancer) were also removed.

RESULTS: 481 patients met criteria for inclusion: 349 were classified as Follicular and 132 as Hurthle Cell tumors. In total, there were 419 (87%) benign adenomas, 21 (4.5%) MI-FTCs, and 41 (8.5%) C-FTCs. Patients with adenomas were younger (adenoma= 50.8±0.71, MI-FTC=53.8±3.13, C-FTC=56.8±2.71 years, p=0.035) and were more likely to be female (adenoma=79.5%, MI-FTC=66.7%, vs. C-FTC=54.7%, p=0.001). The rates of total thyroidectomy were 19.8% for adenomas, 38.1% for MI-FTC, and 61.9% for C-FTC (p=0.000). There were 5 recurrences noted, all of C-FTC classification. Importantly, the 16 year disease-free survival was 100% in the adenoma group, 100% in the MI-FTC group, and 36.6% in the C-FTC group (p=0.000).

CONCLUSIONS: MI-FTCs behave similar to adenomas with 100% disease-free survival with up to 16 years of follow-up. These data suggest that MI-FTCs could be potentially treated by thyroid lobectomy alone like follicular adenomas, rather than total thyroidectomy, and perhaps should be classified as a distinct clinical entity.
Are Asymmetries in Force and Power Production Related to Knee Sprain Occurrence and Recovery in NCAA Athletes?

Authors: Hannah Roeder, MPH; M. Alison Brooks, MD, MPH; Jen Sanfilippo, MS, LAT; Bryan Heiderscheit, PhD, PT

Department: ¹Department of Orthopedics and Rehabilitation, University of Wisconsin School of Medicine and Public Health; ²Department of Athletics, University of Wisconsin-Madison

Mentor: M. Alison Brooks, MD, MPH

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

BACKGROUND: Elevated asymmetry in lower limb force and power production may place athletes at greater risk of injury. The purpose of the research is two-fold: (1) Current evidence is mixed on whether lower extremity asymmetry is elevated prior to an initial injury. We investigated whether asymmetry was greater among athletes who subsequently sustained a knee sprain requiring surgery versus matched controls who did not. (2) Force and power production is a product of lean mass and neuromuscular control. We investigated whether asymmetries in force, power, lean mass, and balance changed from baseline to post-surgery measurements and over time following reconstructive knee ligament surgery.

METHODS: Badger Athletic Performance (BAP) conducts performance testing with its NCAA athletes. We used the maximal vertical jump to assess muscular force and power, iDXA body composition scans to measure lower extremity lean mass, and Y-balance reach distance to determine balance. The athletic department tracks injuries via the Sports Injury Management System (SIMS). We paired the performance and injury databases. To investigate if asymmetry can predict an initial knee sprain injury requiring surgery, we used a case-control design with matching for sport, gender, and performance testing date. To explore whether lean mass or neuromuscular factors contributed to force and power asymmetry, we assessed change in each variable from baseline to post-surgery and the correlation between asymmetry in each variable and time since surgery.

RESULTS: Neither power nor force asymmetry was greater in athletes who subsequently sustained a knee sprain requiring surgery (n=5, 4M, 1F) versus controls (n=15, 12M, 3F) who did not. Asymmetry in force (p=0.0085), power (p=0.0090), and lower extremity lean mass (p=0.011) significantly increased from baseline to initial post-surgery measurements; balance asymmetry, however, did not change significantly from baseline. Force and power asymmetry and lower extremity lean mass asymmetry tended to decrease with time after surgery; however reach asymmetry showed no appreciable pattern based on time after surgery.

CONCLUSIONS: Our findings (1) support that force and power asymmetry did not predict which athletes developed an initial knee sprain injury requiring surgery and (2) suggest that lean mass asymmetry may contribute to asymmetries in muscular force and power following knee sprain surgery without evidence for balance asymmetry as a contributing factor. Our results may help inform rehabilitation programs following reconstructive knee surgery.
Tigecycline Elution From Polymethylmethacrylate Bone Cement

Authors: Anthony Ruzga, BS1; Matthew Squire, MD, MS1; Paul Hutson, PharmD, MS2; Josh Slane, MS3

Department: 1Department of Orthopedics and Rehabilitation, University of Wisconsin School of Medicine and Public Health; 2University of Wisconsin-Madison School of Pharmacy; 3Department of Materials Science and Engineering, University of Wisconsin-Madison

Mentor(s): Matthew Squire, MD, MS

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

BACKGROUND: Prosthetic joint infection (PJI) of hip and knee replacements (THA and TKA, respectively) remains a significant impediment to long-term THA and TKA survival. Polymethylmethacrylate bone cement (PMMA) has been historically used as a drug carrier biomaterial at the time of TKA surgery or during surgical eradication of TKA or THA PJI. These antibiotic impregnated bone cements have been shown to significantly decrease the occurrence of surgical site infections as well as the need for surgical revision. The increased incidence of surgical site infections with resistant bacterial strains necessitates the investigation of PMMA elution of new antibiotic compounds. The purpose of this study was to determine the elution characteristics of tigecycline from PMMA in order to demonstrate the viability of tigecycline as a candidate for use in antibiotic impregnated bone cements.

METHODS: Three groups of pellets were constructed with Palacos PMMA bone cement containing either no tigecycline, 0.4 g, or 1.0 g / 40 g pack of PMMA. All PMMA samples were subjected to a seven day elution in normal saline at 36.5°C on a rotary shaker. Saline samples were collected at 4, 8, 12, 24, 48, 72, 96, 120, 144, and 168 hours, with the pellets being transferred to a new saline bath at each sampling point. Tigecycline content of the eluent was analyzed using HPLC, and tigecycline concentration vs. time curves were generated. The percentage of bacterial strains of importance in PJI susceptible to the concentration of eluted tigecycline will be determined for each time point of the elution study, as this process is still ongoing.

RESULTS: Tigecycline concentrations above the FDA susceptibility breakpoints of 0.25 and 0.5 µg/mL for streptococci and staphylococci respectively were detected only within the first 24 hours of sampling. Tigecycline concentrations in the eluent greater than 0.25 µg/mL were not detected beyond the 4 hour elution point for the 0.4 g pellets or beyond the 24 hour elution point for the 1.0 g / 40 g pack of PMMA pellets. The majority of the total eluted tigecycline was detected at the 4 hour elution point with a concentration of 2.4 and 9.6 µg/mL for the 0.4 and 1.0 g pellets respectively.

CONCLUSIONS: Due to the undesirable elution characteristics of tigecycline from PMMA, with concentrations beyond 24 hours being below the minimal inhibitory dose of several important bacterial strains, we cannot recommend its use in bone cements.
What are the Key Elements of Patient-centered Self-management Programs for Type Two Diabetes?

Authors: Gregory Schleis, BS; Sally Kraft MD, MPH

Department: Department of Quality, Safety, and Innovation, University of Wisconsin Medical Foundation

Mentor(s): Sally Kraft MD, MPH

Support: Shapiro Summer Research Program; Department of Quality, Safety, and Innovation; University of Wisconsin Medical Foundation

BACKGROUND: To continue the work of the UW Health Diabetes Initiative, this study was done to focus on patient-level interventions while the previous work had focused on delivery system redesign. The need for redesign is imminent as the cost of medical services is rising while implementation of chronic care self-management tools is an area that can bring down the cost of health care. It is thought that self-management programs are effective in controlling type two Diabetes and that physicians want a standard set of self-management tools.

METHODS: To identify the effective components of a self-management program, a literature review was done. The search engine was Pubmed and the parameters were “Diabetes self-management tools.” After the results returned, 8 articles were chosen based on relevancy in the titles. Interviews were also done with healthcare providers and surveys at the Odana and Wingra clinics. A1C control rates were compared. Following the interviews, an assessment of current self-management applications and uwhealth.org was done.

RESULTS: The results of the study show that self-management tools are beneficial in helping with reduction in A1C but the programs needed more intensive support in order to support long term outcomes. Internet self-management tools seemed to improve biological and psychosocial outcomes moderately for all but the numbers were not maintained. We found that there was less variance of A1c control rates in the Odana clinic (which has a standardized set of self-management tools for patients) than in the Wingra clinic (which doesn’t have a standard set of tools). The p value was 0.003012. When asked about self-management tools, 10 out 11 surveyed physicians believed that a standardized set of self-management tools would be helpful. Self-management application and uwhealth.org reviews results were given to the Certified Diabetic Educators (CDE) at both UW Health and UWMF.

CONCLUSIONS: Self-management tools are currently being integrated into Diabetes management. Clinics that have a standardized set of self-management tools tend to perform better at A1c control than clinics without a standard set of self-management tools. Physicians are on board to have a standard set of self-management tools. UW Health should consider a self-management plan involving the Wisconsin Institute for Healthy Living’s (WIHA) program “Healthy Living with Diabetes” in order to help patients manage their diabetes.
Is Chromogranin A Prognostic for Resected Pancreatic Neuroendocrine Tumors?

Authors: Matthew A. Shanahan, BS; Clifford S. Cho, MD; Philip A. Rudnitzky; Glen LeVerson, PhD; Emily R. Winslow, MD; Sharon M. Weber, MD

Department: Department of Surgery, University of Wisconsin School of Medicine and Public Health

Mentor(s): Sharon M. Weber, MD

Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: Previous studies have suggested prognostic potential for the tumor marker chromogranin A (CgA) for pancreatic neuroendocrine tumors (pNETs), but results to date have been controversial. Our purpose was to explore the clinical usefulness of preoperative CgA in predicting survival and recurrence in patients with resected pNETs.

METHODS: Patients who underwent resection of a pNET between 2002 and 2013 and had a CgA level tested within 3 months before surgery were identified from a prospective database. An elevated preoperative CgA was defined as a CgA lab value above the normal limit of the assay.

RESULTS: 38 patients met inclusion criteria, of which, 16 patients (42%) had elevated preoperative CgA. Operations included: 13 pancreaticoduodenectomies, 22 distal pancreatectomies, 1 central pancreatectomy and 2 enucleations. There were no differences in tumor size, node positivity, margin status, or tumor grade between the two groups on univariate analysis. Disease-free survival (p=0.008) and overall survival (p=0.05) were negatively impacted by an elevated preoperative CgA level (median FU 2.1 years). The only independent predictor of DFS on multivariate analysis was elevated preoperative CgA (HR 9.36, 90% CI 1.60-54.7, p=0.037). There were no independent predictors of OS.

CONCLUSIONS: In patients with resected pNETs, an elevated preoperative CgA level was associated with decreased disease-free and overall survival, and was the only independent predictor of DFS. Preoperative CgA appears to be a clinically useful prognostic marker following resection of pNET.
Pharmacotherapeutic Intervention to Improve Treatment Engagement Among Alcohol-Dependent Veterans After Hospital Discharge

Authors: Meenakshi Shivaram, BS; Randy Brown, MD, PhD, FASAM; Dean Krahn, MD; Michele Gassman, MA

Department: Departments of Psychiatry and Family Medicine, University of Wisconsin School of Medicine and Public Health

Mentor(s): Randy Brown, MD, PhD, FASAM; Dean Krahn, MD

Support: Shapiro Summer Research Program; UW Institute for Clinical and Translational Research, Type 2 Pilot Award

BACKGROUND: In 2010, 18.5 million people met criteria for having an alcohol use problem, but only 8% of this group received the treatment necessary. Even when problem drinkers become hospitalized as a result of their alcohol use, they seldom receive recommended behavioral treatment. We hypothesize that alcoholics treated with hospital-administered, long-acting injectable naltrexone, when compared to daily oral naltrexone, will consume lower levels of alcohol immediately following hospitalization. This lower level of consumption, we hypothesize, will lead to greater engagement in substance abuse behavioral treatment. For a secondary study aim, we hypothesize that long-term injectable naltrexone, when compared to daily oral naltrexone, will reduce consumption of highly rewarding foods and reduce pleasure experienced from behaviors other than drinking that can become compulsions, such as gambling, shopping, eating, and sex.

METHODS: This study is a pilot study that will show whether or not the proposed recruitment methods and study design are feasible. We will recruit 50 inpatients with alcohol use disorders at the William S. Middleton Memorial VA Hospital. Participants will be randomized to one of two parallel study conditions: (1) an initial 50 mg oral dose of naltrexone prior to hospital discharge plus a 30-day prescription for oral naltrexone, or (2) a single 380 mg intramuscular injection of naltrexone (duration of action = 30 days) administered prior to discharge.

The study will involve three points of assessment. In addition to scales assessing alcohol use, we will administer the Yale Food Addiction Scale (YFAS), as well as a 13-item Hedonic Response Survey to assess pleasure gained from a variety of behaviors. Finally, we will administer a brief questionnaire to qualitatively assess frequency of dessert consumption. Analyses will include calculating effect sizes for the relationship between treatment engagement (any treatment and number of sessions) and each of the measures. The YFAS results will be analyzed using an ANOVA test and a t-test, and the 13-item Hedonic Response Survey results will be analyzed using repeated measures ANOVA. The qualitative questionnaire will be used to generate potential questions for a follow-up study.

RESULTS: Recruitment is ongoing. We have 4 active subjects.
The Association of CARM1 Isoform mRNA Expression with Clinical and Molecular Characteristics in Breast Cancer Tumors, and the Differential Localization of CARM1 Protein Isoforms

Authors: David Shlensky, BS; Wei Xu, PhD; Lee Wilke, MD

Department: Department of Surgery, McArdle Laboratories, University of Wisconsin School of Medicine and Public Health

Mentor(s): Lee Wilke, MD; Wei Xu, PhD

Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: Breast cancers are classified by differences in several receptors, including the estrogen (ER) receptor. Coactivator-associated arginine methyltransferase 1 (CARM1) is an ERα coactivator that can methylate diverse cellular targets. Full-length CARM1 (CARM1FL) is automethylated at R551 in Exon 15, but the alternatively spliced CARM1ΔE15 lacks this site. These isoforms function differently in transcription regulation and protein methylation in cell models. CARM1ΔE15 is dominant in ER- breast cancer cell lines, and may be oncogenic. Molecular changes that arise in malignancy, including alterations in mRNA splicing, are potential targets for cancer therapy. We hypothesized that the level of the short isoform would be higher in ER- tumors compared to ER+ and benign tumors. We also hypothesized that each isoform might localize differently.

METHODS: Twelve human breast cancer and 3 benign fibroadenoma tumors were processed to quantify mRNA transcripts by qRT-PCR. Immunofluorescence studies to localize CARM1 isoforms were performed on MB-MDA-231 ER- breast cancer cells with E15 antibody, which binds CARM1FL, and E16, which binds both isoforms. DAPI and phalloidin were used to stain the nucleus and cytoplasm. Data were analyzed by ANOVA and relationships were determined between continuous variables via bivariate correlations.

RESULTS: Human breast cancers did not have higher expression of CARM1FL or CARM1ΔE15 (p=0.21 & 0.31) compared to fibroadenomas. Triple-negative tumors, ER+/PR+ tumors, and fibroadenomas did not differ in CARM1FL or CARM1ΔE15 expression (p=0.39 & 0.30). Tumors from patients with lymph node involvement did not express more CARM1FL or CARM1ΔE15 (p=0.94 & 0.67). In MDA-MB-231, E15 localized chiefly to the nucleus versus the cytoplasm, with a significantly higher pixel intensity of 11.7 and 0.44, respectively (p = 0.001). E16 also localized to nucleus and cytoplasm, with a higher intensity of 28.16 and 5.92, respectively (p<0.005). The percentage of cytoplasmic to total fluorescence was higher for total CARM1 (15.75 %) than CARM1FL (3.39%; p < 0.005).

CONCLUSIONS: CARM1 isoform mRNA levels are not associated with patient characteristics or molecular subtypes in breast tumors. Recent studies, however, have shown that high CARM1 protein expression correlates with poor prognosis. Our results imply that CARM1FL is likely nuclear, whereas CARM1ΔE15 is cytoplasmic and nuclear. Studies are needed to validate this localization in human samples.
Distinguishing Classical Papillary Thyroid Microcancers
From Follicular-Variant Microcancers

Authors: Surbhi Singhal, BS; Rebecca S. Sippel, MD, FACS, Herbert Chen, MD, FACS; David F. Schneider, MD, MS

Department: Department of Surgery, Division of Endocrine Surgery, University of Wisconsin School of Medicine and Public Health

Mentor(s): David Schneider, MD, MS

Support: Department of Surgery; Department of Surgery NIH T35 Training Grant DK062709-8

BACKGROUND: Papillary thyroid microcarcinomas, defined as tumors less than or equal to 1 cm, account for much of the rising incidence of thyroid cancer. Management of these microcarcinomas remains controversial. Follicular-variant is the most common subtype of papillary thyroid cancer. Typically, both classical papillary microcarcinomas (mPTC) and micro follicular-variant papillary thyroid cancers (mFVPTC) are considered together for clinical and research purposes. The purpose of this study was to use population-level data to characterize differences between mFVPTC and mPTC.

METHODS: We searched the Surveillance, Epidemiology, and End Results (SEER) database to identify adult patients who were diagnosed with mFVPTC or mPTC between 1998 and 2010. Cases without histologic confirmation, or those diagnosed at autopsy were excluded. Binary comparisons were made with the student’s t-test, chi-squared test, or Wilcoxon rank-sum test where appropriate. Clinically significant lymph node metastases were defined as at least two positive regional lymph nodes. Multivariate logistic regression was used to analyze the relative importance of histologic type in the development of lymph node metastases.

RESULTS: Of the 30,926 cases that met our search criteria, 8,697 (28.1%) were mFVPTC. The mean age of patients with mFVPTC was slightly older than those with mPTC (51.4 ± 13.7 vs. 49.7 ± 13.8, p<0.01) and a greater percentage of patients with mFVPTC were older than 45 (68.0% vs. 63.4%, p<0.01). Interestingly, multifocal tumors occurred with greater frequency in the mFVPTC group compared to the mPTC group (35.4% vs. 31.7%, p<0.01). In contrast, lymph node metastases were nearly twice as common in the mPTC group compared to the mFVPTC group (6.8% vs. 3.6%, p<0.01). Multivariate logistic regression confirmed that patients with mPTC had a 77% increased risk of lymph node metastases compared to patients with mFVPTC (OR 1.77, 95% CI 1.5 – 2.1, p<0.01). The two groups did not differ in terms of tumor size, distant metastases, extrathyroidal extension, ethnicity, treatment received (extent of resection and radioactive iodine), or disease-specific survival.

CONCLUSIONS: Multifocality is not unique to classical mPTC and occurs more often in mFVPTC. The risk of lymph node metastases is greater for mPTC than mFVPTC. The surgeon should be aware of these features as they may influence the extent of resection or the performance of lymph node dissection for these microcarcinomas.
Anesthetic Management of Patients Undergoing Interventional Pulmonology Procedures

Authors: Michael F. Sookchoff, BA; Richard E. Galgon, MD, MS

Department: Department of Anesthesiology, University of Wisconsin School of Medicine and Public Health

Mentor: Richard E. Galgon, MD, MS

Support: Shapiro Summer Research Program; Department of Anesthesiology

BACKGROUND: The field of interventional pulmonology is expanding and allowing complex thoracic procedures to be done less invasively, often under mild sedation. When complex patients are treated, however, the growing consensus is that an anesthesia provider should be involved. Yet, literature on the best anesthetic management for these patients is lacking. Thus, the aim of this study was to characterize anesthetic management patterns and techniques used in interventional pulmonology procedures at our institution.

METHODS: Charts of patients who underwent an interventional pulmonology procedure with anesthesia between 2008 and 2013 at UW Hospital were identified using departmental billing records. Patients who underwent other thoracic surgeries or rigid bronchoscopies, those already intubated, and those managed via sedation were excluded. Patient characteristics, procedure, proceduralist, and anesthesia type, use of paralytic drugs, and airway management characteristics were extracted. For intergroup comparisons, a p-value < 0.05 was considered statistically significant.

RESULTS: From 2864 identified encounters, 783 records were analyzed after exclusions. Patients were more often male (56%), averaged (SD) 62 (13) years old, had a BMI (SD) of 28 (6) kg/m², most commonly assigned an ASA physical status of 3 (59%), and most often underwent endobronchial ultrasound (57%). Diabetes, GERD, and OSA were present in 15%, 31%, and 8% of patients, respectively. Two percent were known to be difficult to intubate; however, most patients had reassuring airway features. General anesthesia was maintained with inhaled versus intravenous agents in 86% versus 14% of patients, while endotracheal tubes (ETTs) were used more commonly over supraglottic airways (SGAs) for airway maintenance (66% vs. 34%). However, when SGAs were used, they were highly successful (SGA-to-ETT conversion rate = 0.4%) and paralytic drugs (PDs) were more often avoided (91% vs. 22% PD-free for SGAs vs. ETTs, respectively; p<0.0001).

CONCLUSIONS: Patients receiving general anesthesia for interventional pulmonology procedures are often older males with significant co-morbidities. General inhalational anesthesia with an ETT for airway maintenance is most common; however, SGA use is also highly successful and more often allows avoidance of paralytic drug use, which may lead to reductions in pulmonary complications in this high risk population. Further evaluation regarding this point is warranted.

1) Sarkiss M. Curr Opin Pulm Med 2011; 17: 274-8
2) Abdelmalak B, Gildea T, Doyle DJ. Curr Pharm Design 2013; 18, 6314-24
Volumetric Assessment of Metastatic Colorectal Cancer: Should We RECIST?

Authors: Nicholas Stabo, BS; Meghan Lubner¹, MD; Sam Lubner², MD; Alejandro Munoz del Rio¹, PhD; Perry Pickhardt¹, MD

Department: ¹Department of Radiology, University of Wisconsin School of Medicine and Public Health; ²Department of Medicine, Division of Medical Oncology, University of Wisconsin School of Medicine and Public Health

Mentor(s): Perry J. Pickhardt, MD; Meghan G. Lubner, MD

Support: Shapiro Summer Research Program; Department of Radiology

BACKGROUND: It has been well established that tumor burden is useful in determining disease progression, course of treatment, and overall survival. It is thus important that the size of tumors be measured accurately to convey this tumor burden. Traditionally, uni-dimensional (1D) linear measurements following Response Evaluation Criteria in Solid Tumors (RECIST) have been the standard practice for measuring tumors. The purpose here is to compare uni-dimensional and volumetric assessment of metastatic colorectal cancer burden in predicting response to treatment and survival.

METHODS: Analysis of CT images in 107 patients (mean age 58.7, 47 F, 60 M) who received chemotherapeutic treatment for metastatic colorectal cancer was performed. Both uni-dimensional and volumetric (3D) measures were retrospectively obtained on index lesions at three time points (beginning, midpoint and endpoint; mean interval 4.1 mos, median 3.7 mos). Measurements were summed and compared to obtain best overall response. Patient response was categorized based on RECIST 1.1 (CR, complete response; PR, partial response; SD, stable disease; PD, progressive disease). Survival data was correlated (mean follow up 19.9 mos ±17.1 mos, median 14.7 mos). Concordance of RECIST classification between 1D and 3D measures was assessed and Cox survival models for the measurements as continuous variables were constructed. Kaplan-Meier models with categorical tumor response were also constructed and compared.

RESULTS: There was a 19% discordance in response classification between 1D and 3D measures, and 70% of these involved a move between PR and SD. Mean overall survival was 20.2 ± 17.3 months, median survival 14.9 months. Kaplan-Meier curves for 1D vs. 3D were very similar in appearance. Both 1D and 3D measurements separated PD from the SD/PR group, but neither separated SD and PR well. Cox HR and p values were similar for both groups when viewed as continuous variables (1D HR for best response 1.008 95% CI 1.002, 1.015 p=0.013, 3D HR for best response 1.002, 1-1.003, p=0.02).

CONCLUSIONS: Although there is some discordance in RECIST classification between 1D and 3D measurements, overall the two measures show similar ability to stratify progressive disease from other disease response categories and create similar survival models when taken either as categorical or continuous variables.
Repeatability of Aortic Annulus Measurements on Pre-Procedure CT Scans for Transcatheter Aortic Valve Implantation

Authors: Sarah Sweetman, BS; Carrie Bartels, BS; Scott Nagle, MD, PhD

Department: Department of Radiology, University of Wisconsin School of Medicine and Public Health

Mentor(s): Scott Nagle, MD, PhD

Support: Shapiro Summer Research Program; Department of Radiology

BACKGROUND: The transcatheter aortic valve implantation (TAVI) procedure is offered to patients suffering from critical aortic stenosis who are at high risk for surgical valve replacement. Prior to the procedure, a CT scan is necessary to measure the size of the aortic valve annulus for the purpose of choosing the correct device size. There are several alternative annular measurements that have been proposed. The purpose of this study was to determine the intra-observer variability of each of these measurements.

METHODS: In this IRB-approved retrospective study, CTA images from 45 patients evaluated during TAVI workup at UW were analyzed. The following measurements of the aortic annulus were performed in a randomized, blinded fashion by a medical student reader (SS): mean diameter, best-fit elliptical area, and area based on a free-form contour. Each measurement was repeated at least 2 weeks later to avoid recall bias. Student's paired t-test was used to assess for any systemic differences between the repeated measurements. The mean differences between the repeated measures were determined along with 95% confidence intervals.

RESULTS: There were no statistically significant differences between the 2 measurements of mean diameter (p=0.34), best fit ellipse area (p=0.25), and free-form area (p=0.31). Mean differences between mean diameter measurements were 25.2 ± 2.5 mm (1st measurement) and 25.0 ± 2.5 mm (2nd measurement). 95% CI (absolute difference) was -0.2 mm [-0.5 mm – 0.2 mm]. Mean differences between best fit ellipse area measurements were 467 ± 94 mm² and 475 ± 89 mm². 95% CI was 8 mm² [-6 mm² – 13 mm²]. Mean differences between free-form area measurements were 471 ± 95 mm² and 478 ± 94 mm². 95% CI was 7 mm² [-7 mm² – 13 mm²]. There was no significant difference between best fit ellipse area and free-form area (mean area: p=0.09; absolute difference: p=0.80; or percent difference: p=0.58).

CONCLUSIONS: The intra-reader repeatability of all 3 measures of the aortic annulus was quite good, especially considering the relative inexperience of the reader. Mean diameter precision was within approximately ±0.5 mm or ±2%. Best fit ellipse and free-form annular area measurement precision was approximately ±10 mm or ±4%. There was no significant difference between best fit ellipse and free-form annular area measurements. These limits of precision should be included in the TAVI screening CTA report. Future work will evaluate inter-reader variability by comparing measurements made by readers with differing levels of experience.
**Induction of the Nrf2-Antioxidant Response Element (ARE) Pathway in Cultured Hepatic Stellate Cells (HSCs) Leads to Increased Markers of HSC Activation**

**Authors:** Lindsay Taylor, BS¹; Lung-Yi Lee, MD¹; Li Zhang, PhD¹; Jeffrey A. Johnson, PhD²; David Foley, MD¹

**Department:** ¹Department of Surgery, University of Wisconsin School of Medicine and Public Health ²Division of Pharmaceutical Sciences, University of Wisconsin-Madison School of Pharmacy

**Mentor(s):** David Foley, MD

**Support:** Shapiro Summer Research Program; Department of Surgery

**BACKGROUND:** Oxidative stress is a major stimulus of hepatic stellate cell (HSC) activation and hepatic fibrosis. The Nrf2-ARE pathway protects cells from oxidative damage. The relationship between the Nrf2-ARE pathway and HSC activation remains poorly understood. The purpose of this *in vitro* study was to determine whether induction of the Nrf2-ARE pathway in HSCs decreases HSC activation and the expression of fibrogenic genes.

**METHODS:** Primary murine HSCs were isolated from Nrf2 wild-type (WT) and Nrf2 knockout (KO) mice. Transforming growth factor beta 1 (TGF-β1) was used to activate HSCs. Nrf2 WT and KO HSCs were grown to confluence in 6-well plates and then treated with or without TGF-β1 (3.0ng/mL). After 24h, RNA was isolated from cultured cells. Quantitative RT-PCR was used to quantify mRNA abundance of Nrf2-dependent genes and fibrogenic genes that are markers of HSC activation (*SMA*, *COL1A1*, *TIMP1*, *MMP2*, and *MMP9*). To evaluate the effect of pharmacologic induction of Nrf2, WT HSCs were treated with vehicle or tert-Butylhydroquinone (tBHQ), a known inducer of the Nrf2-ARE pathway, for 24h prior to TGF-β1 treatment. RNA and protein were isolated, and the same endpoints were evaluated. Statistical analysis was performed with one way-ANOVA followed by Fisher’s LSD *post hoc* test, or Student’s *t*-test as appropriate. *P*<0.05 indicates statistical significance.

**RESULTS:** Treatment of Nrf2 WT and KO HSCs with TGF-β1 resulted in significant increases in gene expression of *SMA*, *TIMP1*, *MMP2*, and *MMP9*. When compared to WT HSCs, Nrf2 KO cells demonstrated significantly lower mRNA abundance of *SMA*, *COL1A1*, and *TIMP1*, but increased *MMP2* and *MMP9* both at baseline and with TGF-β1 treatment. Western blot demonstrated decreased SMA protein in Nrf2 KO HSCs as compared to WT. Treatment of WT HSCs with tBHQ resulted in significant increases in Nrf2-dependent gene expression. Treatment of HSCs with tBHQ followed by TGF-β1 resulted in significantly higher expression of *SMA*, *MMP2*, and *MMP9* as compared to HSCs treated with TGF-β1 in the absence of tBHQ.

**CONCLUSIONS:** Treatment of HSCs *in vitro* with TGF-β1 led to increased HSC activation and increased expression of fibrogenic genes: *SMA*, *TIMP1*, *MMP2* and *MMP9*. Contrary to our hypothesis, the absence of Nrf2 in HSCs led to decreases in markers of HSC activation, and pharmacologic induction of Nrf2 in HSCs led to increases in markers of HSC activation. Further studies are needed to clarify the role of the Nrf2 in HSC activation.
A Novel HDAC Inhibitor AB3 Reduces Cell Proliferation and Induces the Notch Pathway in Medullary Thyroid Cancer Cells

Authors: Sara Tesfazghi1, BS; April Harrison1, BS; Ajitha Dammalapati1, MS; Colin Korlesky1; Casi M. Schienebeck2, PhD; Weiping Tang2, PhD; Renata Jaskula-Sztul1, PhD; Herbert Chen1, MD FACS

Department: 1Department of Surgery, Division of Endocrine Surgery, University of Wisconsin School of Medicine and Public Health; 2Pharmaceutical Sciences, University of Wisconsin-Madison School of Pharmacy

Mentor(s): Herbert Chen1, MD FACS; Renata Jaskula-Sztul1, PhD

Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: Medullary thyroid cancer (MTC) is a rare and aggressive neuroendocrine (NE) tumor with limited treatment options. Surgery is not curative, with patients having recurrent and/or incurable disease. AB3 is a novel HDAC inhibitor which shows promise as a potential therapeutic. Its effects of decreasing cell proliferation, NE tumor markers, and activation of the Notch pathway in MTC cell lines (TT and MZ) were investigated for the first time.

METHODS: The cytotoxicity of AB3 on TT and MZ cells was measured by determining the IC50 values. The MTT assay (3-(4, 5-Dimethylthiazole-2-yl)-2, 5-diphenyltetrazolium bromide) was used to measure cell proliferation. Treatments up to 2 µM were administered at 2, 4, 6, and 8 days. To validate these results, a live cell count with trypan blue was performed. The effects of AB3 on cell death were investigated by three independent assessments: 1) PI stain-based sub-G1 cell fraction analysis, 2) Annexin V staining in conjunction with PE DNA staining of nonviable cells, and 3) detection of protein expression of apoptotic markers via Western Blot. Protein expression of NE tumor markers ASCL1 and CgA were also detected by Western Blot. The mRNA expression of Notch isoforms was performed via quantitative RT-PCR analysis. The luciferase assay for CBF1 binding (Notch pathway mediator) was used to measure the functional activity of Notch.

RESULTS: We demonstrated that the IC50 value for AB3 treatment in TT and MZ cells was 1.5 µM. AB3 decreased cell proliferation in a dose and time dependent manner. The mechanism of growth inhibition was found to be apoptosis, evident by increased sub-G1 cell fraction (G0 DNA content). Annexin V/PE staining confirmed a dose dependent AB3 induced apoptosis. Protein expression of anti-apoptotic markers was decreased. Western blot analysis revealed ASCL1 and CgA reduction in both cell lines. AB3 activated the Notch pathway as evident by an induction of Notch 2 isoform in the MZ cell line and induction of Notch 3 in the TT cell line. CBF1 binding analysis revealed that the Notch pathway is activated.

CONCLUSIONS: We demonstrated that AB3 behaves as a potent inhibitor of MTC cell proliferation at low µM concentrations. By altering the malignant phenotype, this therapeutic provides exciting evidence for its use in the treatment of intractable MTC.
Measuring Burden of Disease from Motorcycle Crashes among Children in Vietnam: A Call to Action

Authors: Daniel Tonellato, BA\(^1\); Bui Van Truong, MD, MPH\(^2\); Lotte Brondum, BSN, MA\(^2\); Tiffany Frazer, MPH\(^3\); Peter Layde, MD, MSc\(^3\); Scott Hagen, MD\(^1\)

Departments: \(^1\)Department of Pediatrics, University of Wisconsin School of Medicine and Public Health; \(^2\)Asia Injury Prevention Foundation; \(^3\)Department of Global and Public Health, Medical College of Wisconsin

Mentor: Scott Hagen, MD

Support: Shapiro Summer Research Program; Department of Pediatrics, University of Wisconsin School of Medicine and Public Health

BACKGROUND: Motorcycles are the primary mode of transportation for Vietnamese families. In developed countries, motorcycle use is associated with a higher rate of disability than automobile use. The comprehensive motorcycle helmet law in Vietnam, passed in 2007, has had a significant effect in preventing adult motorcycle crash injury. This law was broadened in 2010 to include enforcement of helmet use in children, but its effect on childhood injury is unclear. We aim to identify ways to measure motorcycle related injury burden in children and identify opportunities to decrease these injuries.

METHODS: A comprehensive review of the literature and data related to the burden of motorcycle crash disability in children was conducted in an effort to 1) describe what is currently known in Vietnam, 2) determine the effect of recent policies, and 3) propose future research. Medline was used to search for literature on the burden of disease from motorcycle crash injury among children in Vietnam, and citations in these articles were reviewed to ensure completeness. Additionally, unpublished work from Vietnamese and international researchers was reviewed.

RESULTS: Childhood injury incidence and outcome data related to disability from motorcycle use is unavailable in Vietnam due to a lack of a registry, and relevant literature is diverse and varied in methodology. There is a significant burden of disease secondary to road traffic injuries (RTIs) among children in Vietnam, estimated at 30,959 Disability-Adjusted Life Years (DALYs) for children age 5-14 in 2008. Despite recent government legislation, Vietnamese children wear motorcycle helmets significantly less often than adults. However, barriers to helmet use in children have been identified in some surveys and research.

CONCLUSIONS: There are gaps in the current documentation and understanding of the disability burden from motorcycle crashes in Vietnamese children. As a result, meaningful analysis or estimation of the child disability burden related to motorcycle injuries is difficult. Future research on RTIs among Vietnamese children should include a case-control study to determine the burden of disability secondary to motorcycle crashes. This work will direct future efforts to quantify the benefits of proven child injury prevention interventions, including motorcycle helmet use, in Vietnam. In addition, initial research efforts could target the known barriers to helmet use in children that were identified in past studies.
A Qualitative Study of Pediatricians’ Approach to Treating Childhood Obesity in Wisconsin

Authors: Benjamin Traun, BA; Tracy Flood, MD, PhD; Amy Meinen, MPH, RD; Mike Daniels, BS; Patrick Remington, MD, MPH

Department: Department of Population Health Sciences, University of Wisconsin School of Medicine and Public Health

Mentor(s): Patrick Remington, MD, MPH; Tracy Flood, MD, PhD; Amy Meinen, MPH, RD

Support: Shapiro Summer Research Program; Farrell Public Health Research Award

BACKGROUND: Over the past three decades, rates of childhood obesity have tripled, and now, nearly two-thirds of Americans are overweight or obese. The health consequences of obesity are abundant, costing the U.S. healthcare system almost $150 billion annually. Given the gravity of this health concern, it is important for physicians to intervene. The current literature shows that physicians under-diagnose and under-treat childhood overweight and obesity. The barriers to successful obesity treatment and management have been well-documented in previous studies. The purpose of this study was to assess the current beliefs and experiences of Wisconsin pediatricians regarding pediatric obesity and to locate areas for improvement.

METHODS: Seventeen, one-on-one interviews with pediatricians were used to accomplish the study objectives. The interviewer used open-ended questions to guide the conversation and a second member of the study staff transcribed the responses. Seven different health systems in Wisconsin were represented in the study sample. The interview transcripts were analyzed using Grounded Theory, a qualitative data analysis tool.

RESULTS: Pediatrician responses were divided into four categories; Identification and Diagnosis, The Physician/Patient Interaction, Referrals within the Healthcare System, and The Community. According to our results, pediatricians are comfortable identifying and diagnosing pediatric obesity. They also have several tools and strategies at their disposal for the treatment and management of obesity, but do not often achieve the desired outcome of decreasing patient BMI. Most pediatricians lack connections to community resources and the ability to effectively communicate with referral systems outside of their clinic, such as with dietitians. Obesity is overwhelming to many physicians due to the immense role that family and the community play on weight-related outcomes, and the perceived small role that the health care system and they physician play.

CONCLUSIONS: Given the large role that environment plays in weight-related outcomes, it is important for the health care system to improve upon its ability to catalyze changes that benefit that environment as a whole. By building connections between the healthcare system and it’s local community, physicians will become more empowered when it comes to issues, such as obesity, that are greatly influenced by factors outside of the healthcare system.
Rheumatoid Arthritis Patient Cardiovascular Disease Prevention Experiences: Qualitative Analysis and Implications

Authors: Sarah Tweddell, MS; Christie Bartels, MD, MS; Barbara Bowers, PhD, RN; Elizabeth Jacobs, MD, MAPP; Tonya Roberts, PhD, RN

Department: Department of Medicine, Division of Rheumatology, University of Wisconsin School of Medicine and Public Health

Mentor(s): Christie Bartels, MD, MS; Tonya Roberts, PhD, RN

Support: Shapiro Summer Research Program, UW Cardiovascular Research Center

BACKGROUND: Although rheumatoid arthritis (RA) increases cardiovascular disease (CVD) risk, RA patients receive less CVD preventive care than peers. Bartels, et al. previously showed gaps in lipid testing and hypertension diagnosis despite more clinic visits in RA patients compared to peers. This qualitative study aimed to examine the processes by which RA patients experience CVD preventive care in order to inform patient-centered interventions to close these gaps.

METHODS: Ten adult RA patients were recruited from 3 local rheumatology clinics for interviews to evaluate CVD preventive care experiences. Interviews were recorded, transcribed, dual coded and team reviewed using NVivo software to facilitate grounded theory analysis and interpretation (Strauss 1994).

RESULTS: Interviewed RA patients were 70% female, ages 23-81 (mean 57). Most RA patients were unaware of increased CVD risk while all patients were aware of RA medication side effects. Those who had experienced CVD risk management described two processes by which they received CVD preventative care: 1) identifying risk and 2) action. The number of steps and likelihood of actions were related to the physician who identified risk. Primary care physicians were not specifically described as identifying RA-CVD risk, but if they identified traditional CVD risks were most likely to actively manage them. However, many patients described rarely seeing their PCP, which is consistent with national reports. Rheumatologists more often identified RA-specific risk, but rarely provided active CVD risk treatment or monitoring. Therefore, a particularly concerning finding was that 60% of participants perceived their rheumatologist as their main provider, since the reliance on this provider may delay or decrease treatment likelihood. A few participants alternatively described steps in which they themselves identified RA-specific risk and self-advocated care. Future work should examine actual rheumatologist and PCP CVD risk identification and actions, and provider perceptions to inform future interventions. Optimizing roles may include RA patient activation and rheumatologist communication/co-management to catalyze CVD risk identification and management.

CONCLUSIONS: Patients with RA do not report receiving consistent CVD preventive care. Most described their rheumatologist as their main doctor and noted infrequent PCP visits, though rheumatologists were less likely than PCP’s to actively manage CVD risks. This suggests that RA patient activation, rheumatologist communication/co-management and advocating regular PCP care should be studied as potential interventions to close CVD-preventive care gaps in RA.

Involvement of a Surgical Service Improves Patient Satisfaction After a Small Bowel Obstruction Admission
Involvement of a Surgical Service Improves Patient Satisfaction
After a Small Bowel Obstruction Admission

Authors: Xia Vang, BS; Ryan K. Schmocker, MD; Linda Cherney Stafford, MPH; Glen Leveson, PhD; Emily R. Winslow, MD

Department: Department of Surgery, University of Wisconsin School of Medicine and Public Health

Mentor(s): Emily R. Winslow, MD; Linda Cherney Stafford, MPH

Support: Department of Surgery NIH T35 Training Grant DK062780

BACKGROUND: Patient reported outcomes have been emphasized with implementation of the Affordable Care Act. The Hospital Consumer Assessment of Healthcare Providers and Systems (HCAHPS) survey is widely used to measure patient satisfaction. Despite impending financial implications of patient experience scores, little is known about their clinical and structural determinants. Since small bowel obstructions (SBO) are managed across an array of hospital settings, analysis of patient satisfaction in this subgroup was undertaken to identify structural processes that could be targeted for improvement.

METHODS: Patients admitted between 2009-2012 and completed the HCAHPS survey were identified using ICD-9 codes for SBO. Exclusions included age <18, readmits within 30 days, and those discharged to a skilled nursing facility. Charts from 92 eligible patients were identified. Retrospective review abstracted demographic and clinical variables. To improve homogeneity, only patients (n=47) with SBO due to adhesions or hernias were analyzed. Relationships between HCAHPS patient satisfaction domains and patient/system level variables were assessed using univariate analyses. Topbox and composite scores were determined using HCAHPS standards.

RESULTS: Of the 47 patients, 52% were female; mean age was 63±17 yrs; length of stay was 6±5 days; 96% had prior surgery. Of all 47 patients, 72% (n=34) were admitted to a surgical service. 44% (n=15) of these required surgeries. Of the 28% (n=13) admitted to a medical service, 54% (n=7) had surgical consultation. Of those with surgical consultations, 57% required surgery. Patients who had surgical service (SURG) involvement (either as a consulting/primary service) had significantly higher overall hospital satisfaction HCAHPS scores when compared to those on the medical service without surgical consultations (MED) (TopBox score: 80% SURG; 33% MED, p=0.015). When examining patient satisfaction with physician communication, SURG patients trended towards higher scores (TopBox MD Communication Composite: 71% SURG; 44% MED; p=0.1). Each physician communication domain had a similar pattern.

CONCLUSIONS: Involvement of a surgical service during admission for SBO is associated with increased patient reported satisfaction. These findings have implications for a hospital system’s efforts to improve HCAHPS scores. Further investigation is needed to elucidate specific factors that impact patient satisfaction for a variety of surgical diagnoses.
Maternal Attitudes and Coverage Rates of Childhood Immunizations in Rural Uganda

Authors: ¹Bryan Vonasek, BA; ²Laura Jacobson, BS; ³Leonidas Twesigye BS; ³Francis Bajunirwe, MBChB, MS, PhD; ²Ajay Sethi, PhD, MHS; ¹James Conway, MD, FAAP

Department: ¹Department of Pediatrics, University of Wisconsin School of Medicine and Public Health; ²Department of Population Health Sciences, University of Wisconsin School of Medicine and Public Health; ³Department of Community Health, Mbarara University of Science and Technology, Uganda

Mentor(s): Ajay Sethi, PhD, MHS; James Conway, MD, FAAP

Support: Shapiro Summer Research Program; Department of Pediatrics, University of Wisconsin School of Medicine and Public Health; Global Health Institute, University of Wisconsin-Madison

BACKGROUND: Although childhood immunizations prevent over 2 million deaths per year worldwide, 1.5 million children still die each year from vaccine-preventable diseases. In rural areas of developing countries, there has been relatively little research into mothers' knowledge and attitudes towards childhood immunizations. In the Sub-Saharan African country of Uganda, vaccine coverage rates are below the WHO goal of 90%, with 82% of children having completed the diphtheria, tetanus, pertussis (DTP) series and only 75% coverage with measles-containing vaccine in 2011. The aims of this study are to survey the coverage of immunizations for children under the age of five (U5s) and to survey mothers' attitudes towards and knowledge of childhood immunizations in rural Western Uganda.

METHODS: To identify barriers that prevent women in rural Uganda from vaccinating their children, we are conducting a cross-sectional survey of the attitudes and knowledge of vaccine-preventable diseases and immunizations with 500 mothers of U5s living in 10 rural, under-served villages in Sheema District in Western Uganda. We are also collecting the immunization history on the health cards for the U5s from these mothers so that we will have an accurate estimate of local vaccine coverage for BCG, Polio, DTP, hepatitis B, Hib, and measles in this underserved area on the periphery of an outstretched healthcare system.

RESULTS: The cross-sectional survey is ongoing and will be completed over the next 2-4 months. Initial data analysis will explore perceptions of immunizations from parous women in rural Uganda and possible barriers to improving coverage. Final data analyses will evaluate relationships between demographic characteristics, attitudes towards childhood immunizations and immunization coverage.

CONCLUSIONS: Results of this study will help determine childhood immunization coverage rates and possible barriers to improving childhood immunization coverage in this population.
Evaluating the Effects of an Interventional Resistance-Training Program on Strength and Lean Mass Acquisition in Adolescent Girls

Authors: Vuong Vu, BA; Brittney Bernardoni, BS; Lindsay Raab, BS; Tamara A. Scerpella, MD

Department: Department of Orthopedics and Rehabilitation, University of Wisconsin School of Medicine and Public Health

Mentor(s): Tamara A. Scerpella, MD

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

BACKGROUND: A 20-month school-based interventional resistance-training program was tested for lean mass and strength gains in peri-menarcheal girls. Because of rapid growth during this maturity phase, gains were expected to be significant.

METHODS: 68 girls, aged 11-12 years, were enrolled in a controlled, randomized resistance training intervention in fall 2011. The intervention focused on progressive loading exercises using dumbbell weights and resistance bands; it was completed 2-3 times per week for 10-15 minutes per session. The intervention was embedded in physical education (PE) classes at one middle school; a second middle school with standard PE classes served as a control.

At baseline (BL) and 20-month follow-up (FU), subjects were assessed as follows: 1) strength at non-dominant (ND) elbow flexion/extension (flex/ext), ND shoulder flex/ext, hip flex/ext, dominant and ND grip using a hand-held dynamometer; 2) total body and regional lean mass by dual energy X-ray absorptiometry (DXA, Lunar iDXA); 3) height by wall-mounted stadiometer; 4) weight by electronic force plate; 5) Tanner breast by self-staging via line drawings.

Percent gains were calculated for strength and lean mass changes BL to FU. Student t-tests (p<0.05) evaluated for significant differences between groups.

RESULTS: 62 subjects (21 control-CON, 41 intervention) provided BL and FU data. The intervention group was further divided into HIGH (n=23) and LOW (n=18) groups based on effort minutes assessed during the first 8 months of intervention. For this analysis, HIGH and CON groups were compared. Subject characteristics are presented in Table 1. There were no statistically significant differences in strength gains or lean mass acquisition, although trends were evident for greater percent lean mass acquisition in HIGH vs. CON (Table 2).

CONCLUSIONS: In this group of peri-menarcheal girls, percent gains in lean mass acquisition tended to be greater in the intervention group. The lack of significant differences may be attributed to several factors including measurement error associated with methodology (hand-held dynamometer), differential maturational/somatic growth, differential outside physical activity (PA) between groups, and the limited statistical evaluation presented here. Future analyses will utilize mixed linear models to control for time-varying covariates such as body size change, maturity status, and outside PA.
Increased lysozomal B-galactosidase Expression is a Senescence Marker and Identifies Indolent Prostate Cancer

Authors: Jennifer Wagner¹, BA; Matthew Truong¹, MD; Bing Yang¹, PhD; Nathan Damaschke¹, BS; Chad Guenther¹, MA; Wei Huang², MD; David Jarrard¹, MD

Department: ¹Department of Urology and ²Department of Pathology and Laboratory Medicine, University of Wisconsin School of Medicine and Public Health

Mentor(s): David Jarrard, MD

Support: Shapiro Summer Research Program; Department of Urology; Department of Defense Prostate Cancer Research Program

BACKGROUND: Senescence is terminal growth arrest that functions as a tumor suppressor in aging and precancerous cells. Therapy-induced senescence (TIS) is also a response to selected anticancer compounds or radiation. One limiting factor in monitoring senescence is the lack of markers, especially in formalin-fixed paraffin-embedded (FFPE) tissues. Lysosomal-β-galactosidase (GLB1) is a lysosomal enzyme that hydrolyzes the terminal β-galactose from ganglioside substrates and other glycoconjugates. GLB1 has been identified as the origin of senescence associated-β-gal activity (SA-β-gal). GLB1 expression was interrogated in prostate tissues utilizing a new antibody directed towards the lysozomal portion of SA-β-gal to assess whether expression levels changed in prostate cancer (PCa) and with senescence.

METHODS: Tissue microarrays consisting of 159 FFPE cores in duplicate from 86 PCa patients, 25 high-grade prostatic intraepithelial neoplasia (HGPIN), and 48 benign prostate tissues were deparaffinized and subjected to immunoflorescent staining. Vectra™, a quantitative imaging platform, was used to quantify the expression of the GLB1 protein. To further confirm ability of this antibody to recognize senescent cells, GLB1 expression was assessed by western blot in several well-described models including primary prostate epithelial cell cultures passaged to replicative senescence and TIS using low dose doxorubicin (25nm) or Diazequone (AZQ; 250nM) in PCa lines.

RESULTS: GLB1 expression was greater in HGPIN specimens in both nuclear and cytoplasmic compartments compared to benign and cancer specimens (all p<0.0001). Expression levels also discriminate PCa and metastases from benign tissue (p<0.0001, p=0.004 respectively). Primary PCa samples with associated metastatic disease had lower expression than those with localized disease (0.97 vs.1.93 nuclear, p=0.003 and 0.37 vs.0.75 cytoplasmic, p=0.01). Furthermore, higher GLB1 expression was found in primary tumor specimens with lower Gleason Score (p=0.001) and lower T stage (p=0.01). Western blot analysis of cell culture models demonstrated a cumulative increase in GLB1 expression in models of replicative senescence and TIS.

CONCLUSIONS: GLB1 is a useful marker in FFPE primary prostate tissue samples to identify reduced metastatic potential. Elevated GLB1 expression represents increased senescence, a tumor suppressor mechanism. This antibody may also be useful in PCa tissues to assess the senescence response to chemotherapy.
Effect of a Supervised Physical Therapy Program for Post-concussion Syndrome

Authors: Alyssa Walker, BS; John Wilson, MD, MS; Patrick Grabowski, PT, PhD; Dan Enz, PT, LAT; Sijian Wang, PhD

Department: Department of Orthopedics and Rehabilitation, University of Wisconsin School of Medicine and Public Health

Mentor(s): John Wilson, MD, MS

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

BACKGROUND: The majority of patients with sport-related concussion recover within 7-10 days. A small percentage of patients, however, experience post-concussion syndrome (PCS). It has become standard practice for PCS patients to refrain from physical exertion despite the fact that physical inactivity may also precipitate secondary symptoms of fatigue, depression, anxiety, and physical deconditioning. While current PCS treatments show little effectiveness, there is growing evidence to suggest exercise and a multi-faceted approach to concussion rehabilitation may be efficacious. This study evaluated the effectiveness and safety of a multidisciplinary, supervised physical therapy program, with a sub-symptom threshold exercise program (SSTEP) component, in the treatment of 25 patients suffering from PCS.

METHODS: Patients performed supervised physical therapy consisting of a sub-symptom cardiovascular exercise protocol, vestibular/visuomotor and cervical spine therapeutic exercise, and manual therapy for the spine as determined by the treating therapist. Subjects were queried at baseline, and at regularly scheduled follow-up clinic visits regarding daily symptoms using a standardized post concussion symptom scale. Graded exercise test (GXT) to symptom exacerbation threshold (ST) and Balance error scoring system (BESS) assessment were completed at initiation of the rehabilitation program, and at follow-up visits if deficits identified.

RESULTS: No statistically significant change was seen in PCSS scores from the patients’ first medical visit post-concussion and their last medical visit prior to beginning the physical therapy program (P = 0.23). Yet over the course of treatment, there was a significant decreasing trend of total scores (P = 0.008). Maximal symptom free HR was 1.3 times greater at the last GXT than at baseline testing prior to treatment (P < 0.0001). Duration of exercise was 2.3 times greater at the last GXT when compared to baseline (P < 0.002). BESS testing also showed an improvement in symptoms, with a 56.1% decrease in scores from baseline to the last BESS assessment (P = 0.001).

CONCLUSIONS: A multidisciplinary physical therapy and exercise program is determined to be safe and effective for alleviating PCS symptoms while avoiding negative repercussions of both physical inactivity and premature return to full activity. We recommend that further research be conducted on long-term progress of PCS patients undergoing a physical therapy rehabilitation program, as well as the efficacy of such a program, ideally on a larger scale.
The Novel Histone Deacetylase Inhibitor Thailandeepsin-A Inhibits Anaplastic Thyroid Cancer Growth

Authors: Eric Weinlander, BA; Yash Somnay, BS; April Harrison, BS; Maria Georgen; YiQiang Cheng, PhD; Xiao-Min Yu, MD, PhD; Herbert Chen, MD, FACS

Department: Department of Surgery, University of Wisconsin School of Medicine and Public Health

Mentor(s): Herbert Chen, MD, FACS

Support: Department of Surgery NIH T35 Training Grant DK062780

BACKGROUND: Anaplastic thyroid cancer (ATC) remains refractory to available chemotherapies and surgical interventions. Histone deacetylase (HDAC) inhibitors are an emerging targeted therapy with anti-proliferative activity in thyroid cancer cell lines. Thailandepsin-A (TDP-A) is a novel class I HDAC inhibitor whose efficacy remains largely unknown in ATC. Therefore, we aimed to characterize the effect of TDP-A on ATC.

METHODS: Human-derived ATC cells were treated with TDP-A. IC₅₀ was determined by a dimethylthiazol-diphenyltetrazolium bromide (MTT) rapid colorimetric assay and cell proliferation was measured by viable cell count. Cellular mechanisms were investigated by Western blot analysis. Canonical apoptosis markers, intrinsic and extrinsic apoptosis regulators, and cell cycle regulatory proteins were investigated. Cell cycle staging was determined with propidium iodide flow cytometry.

RESULTS: TDP-A reduced cell proliferation in a dose- and time-dependent manner. Cleavage of the apoptosis markers Caspase 9, Caspase 3, and poly ADP Ribose Polymerase increased with TDP-A treatment. Levels of the intrinsic apoptosis pathway proteins BAD, Bcl-XL, and BAX remained unchanged. Importantly, cleavage of the extrinsic apoptosis activator Caspase 8 increased dose-dependently. The anti-apoptotic proteins Survivin and Bcl-2 decreased dose-dependently. Among the cell cycle regulatory proteins, levels of CDK inhibitors p21/WAF1 and p27/KIP1 increased. Cyclin D, increased, but its coenzyme CDK4 decreased dose-dependently. CDK2 remained constant, but Cyclin A, and Cyclin B, both decreased. Flow cytometry demonstrated G2/M arrest.

CONCLUSIONS: TDP-A induces a notable anti-proliferative effect on ATC in a dose- and time-dependent manner. This effect is mainly attributed to extrinsic apoptosis with concomitant cell cycle arrest. This anti-proliferative activity occurs with high potency and demonstrates TDP-A’s therapeutic potential in ATC.
Examining the Role of Cervical Ultrasound in Detecting Thyroid Pathology in Patients with Primary Hyperparathyroidism

Authors: Deena Weiss, BS; Herbert Chen, MD, FACS

Department: Department of Surgery, University of Wisconsin School of Medicine and Public Health

Mentor(s): Herbert Chen, MD, FACS

Support: Shapiro Summer Research Program; Department of Surgery

BACKGROUND: Minimally invasive parathyroidectomy for primary hyperparathyroidism is made possible with accurate preoperative imaging. In addition to the detection of parathyroid adenomas, cervical ultrasound also provides concomitant assessment of the thyroid gland, and many surgeons believe that it is essential. However, the incidental identification of thyroid nodules may then subject patients to further workup and potentially invasive thyroid procedures. We sought to determine the long-term consequence of omitting preoperative ultrasound on the development of thyroid pathology and cancer.

METHODS: At our institution, 222 patients with primary hyperparathyroidism underwent parathyroidectomy without preoperative cervical ultrasound from 1990 to 2001. Thyroid pathology discovered by follow-up after parathyroidectomy, as well as subsequent biopsy and surgical interventions were analyzed.

RESULTS: Of the 222 patients who underwent parathyroidectomy, the mean age was 55 ± 1 years and 149 (67%) were female. In the course of their follow-up after parathyroidectomy, 13 (6%) patients received a cervical ultrasound, and 7 of the 13 (3%) underwent fine-needle aspiration of a thyroid nodule. Only 1 of the 7 (0.4% of all patients) was ultimately diagnosed with thyroid cancer. Four additional patients were discovered to have thyroid malignancies as a result of intraoperative decision-making. All five patients are currently alive, with an average follow-up time of 14.9 ± 1.6 years. No patients in this series had an unnecessary thyroid intervention.

CONCLUSIONS: In patients who undergo parathyroidectomy without a pre-operative ultrasound, only a small number (0.4%) subsequently were diagnosed with thyroid cancer. Furthermore, omission of ultrasound during the localization of parathyroid glands does not have a negative impact on the diagnosis of thyroid pathology as all patients who had thyroid cancer had good outcomes, and in fact, may prevent unnecessary thyroid interventions. Therefore, the use of cervical ultrasound for parathyroid localization should be considered optional rather than essential.
Psychometric Properties of the Sport Concussion Assessment Tool (SCAT3)

Authors: Andrew Wiederhold, BS; Jon Erickson, BS; Elizabeth Pretto; Tim McGuine, PhD, LAT; Alison Brooks, MD, MPH

Department: Department of Orthopedics and Rehabilitation, University of Wisconsin School of Medicine and Public Health

Mentor(s): Tim McGuine, PhD, LAT; Alison Brooks, MD, MPH

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

BACKGROUND: Sport-Related Concussion (SRC) is increasingly recognized as a major public health concern in the US. An estimated 70000 SRCs occur each year within the population of US high school athletes. Recently, the newest version of the Sport Concussion Assessment Tool 3rd edition (SCAT3) has been developed as an assessment tool to evaluate the presence of SRC. The SCAT3 takes approximately ten minutes and measures Concussion Symptoms (CSI, CSS), Immediate Memory (IM), Orientation (OR), Concentration (CO), Delayed Recall (DR) and Balance (BESS). The psychometric properties (baseline values, reliability, responsiveness) of the SCAT3 have not been determined in high school athletes.

METHODS: The SCAT3 test battery was administered at six Wisconsin high schools during the summer of 2013. Subjects also completed a short survey to provide information regarding their sport participation status and previous history of SRC. Student T tests were used to determine if significant differences in component and summary scores existed based on sex and previous history of SRC.

RESULTS: A total of N = 757 high school athletes (male = 570 male; female = 187, grades 9-12) were enrolled as subjects. The component scores and summary scores (Mean + SD) for the CSI = 1.32 ± 2.23, CSS = 2.15 ± 4.7, OR = 4.69 ± 0.53, IM = 14.25 ± 1.0, CO = 3.25 ± 1.25 BESS = 13.46 ± 5.1, DR = 3.93 ± 1.01 and Summary SAC score = 26.2 ± 1.9. There were no differences in the scores based on sex: CSI (p =0.001) CSS (p =0.001), OR (p =0.021), IM (p =0.583), CO (p =0.384), BESS (p =0.661), DR (p =0.221), Summary score = (p =0.026). There were no differences in the scores based on previous history of SRC: CSI (p =0.028) CSS (p =0.021), OR (p =0.278), IM (p =0.127), CO (p =0.826), BESS (p =0.348), DR (p =0.993), Summary score = (p =0.320).

CONCLUSIONS: This study established normative data and representative baseline SCAT3 values for high school athletes, and is the first phase in determining the psychometric properties of the SCAT3. The study is ongoing to measure the reliability (test, re-test) on a subsample of the subjects and responsiveness (change in scores post injury) in subjects who sustain a SRC during their sport participation.
Is Comprehensive Miscarriage Management Offered in Wisconsin?

Authors: Hope Wilkinson, MS; Jess Dalby, MD

Department: Department of Family Medicine, University of Wisconsin School of Medicine and Public Health

Mentor(s): Jess Dalby, MD; Ronnie Hayon, MD

Support: Department of Family Medicine

BACKGROUND: Early pregnancy failure or miscarriage occurs in up to 20% of recognized pregnancies (4) and is commonly managed in family medicine practice. Treatment options include expectant waiting, medical management and surgical evacuation, either in the office or in the operating room. Current research indicates that all three treatment options and surgical settings are equally safe, though of variable efficacy, and best practice includes providing all women not experiencing hemorrhaging or contraindications with all of these options. Provider opinions about these treatment options do not always match with the latest evidence and research shows that women are often influenced by what they believe their provider believes is best.

METHODS: We performed a retrospective chart review of patients experiencing miscarriage that were seen at Access Community Health Centers (ACCESS) in Madison, Wisconsin, between December 1, 2011, and November 30, 2012. We surveyed physician providers in the University of Wisconsin Department of Family Medicine who treat women experiencing a miscarriage. Providers were asked about their training experience, what types of gynecological procedures they perform, and their practices in miscarriage.

RESULTS: The majority of family medicine providers in Wisconsin (94%) do not offer comprehensive miscarriage management. Of women experiencing miscarriages who were treated at ACCESS, 3% received comprehensive miscarriage care. Additionally 51% of women experiencing a miscarriage who received care at ACCESS made at least one visit to the Emergency Department.

CONCLUSIONS: Family medicine physicians in Wisconsin lack the ability, training and/or resources to offer comprehensive miscarriage management. Most women are not offered medical management and uterine aspiration in the office. Miscarriage is an opportunity to improve the patient experience and the distribution of health care resources by decreasing emergency department visits and decreasing operating room uterine aspiration.
Resolution of Thyroglobulin Antibodies after Total Thyroidectomy for Cancer

Authors: Jimmy Xu, BS; Ryan Bergren, BS; David Schneider, MD; Herbert Chen, MD, FACS; Rebecca S. Sippel MD, FACS

Department: Department of Surgery, Division of General Surgery, University of Wisconsin School of Medicine and Public Health

Mentor(s): Rebecca S. Sippel, MD, FACS

Support: Department of Surgery NIH T35 Training Grant DK062780

BACKGROUND: Thyroglobulin (Tg) levels can be used post-operatively to identify residual or recurrent thyroid cancer after surgical treatment. Thyroglobulin antibodies (TgAb) are produced by 10-25% of thyroid cancer patients and can interfere with thyroglobulin measurement. The purpose of the study was to describe the time course of TgAb resolution and the significance of a persistently elevated level in antibody positive patients after thyroidectomy.

METHODS: A database of 247 consecutive patients with preoperative TgAb measured who underwent surgical treatment of differentiated thyroid cancer (DTC) between January 2007 and May 2013 was reviewed. Patients were stratified based on TgAb status (positive or negative) and disease recurrence (defined by biopsy proven disease or unplanned second surgery). Survival and regression analysis was used to determine the time course of TgAb resolution. Log Rank (Mantel-Cox) was used to determine an association between persistently elevated antibody levels and cancer recurrence. SPSS statistical software was used for analysis.

RESULTS: Of 247 patients (77% women, 23% men; mean age ± SE, 45.7 ± 1.0 years) with TgAb measured preoperatively, 34 (14%) had positive preoperative TgAb levels (greater than or equal to 20 IU/ml) (mean 298.1 ± 99.2 IU/ml). The median time to TgAb resolution was 11.0 ± 2.3 months, and the majority resolved by 32.4 months. Regression analysis of the patients with completely resolved antibodies yielded an average decline of -11% IU/ml per month ± 2.2%. Disease free survival was equivalent between TgAb positive and TgAb negative groups (p = 0.4). In 9 of 34 patients, antibodies had not resolved at last follow up but imaging could not identify recurrent disease.

CONCLUSIONS: TgAb are common in patients with thyroid cancer but they resolve after successful treatment at approximately -11% IU/ml per month from their preoperative levels with median resolution at 11.0 months. Persistently elevated levels after thyroidectomy were not associated with disease recurrence in our series.
Peripheral Blood Mononuclear Cell Immune Response

Authors: Megan Yanny, BS; Mark K. Devries, BS; Daniel J. Jackson, MD

Department: Department of Pediatrics, Division of Allergy and Immunology, University of Wisconsin School of Medicine and Public Health.

Mentor(s): Daniel J. Jackson, MD

Support: Shapiro Summer Research Program; Department of Pediatrics IRB H-2007-0044-CR002

BACKGROUND: Human rhinovirus (HRV) species is an important factor in the severity of respiratory illnesses and asthma exacerbations. In young children, HRV-A and HRV-C are more likely to cause lower respiratory illness than HRV-B. In older asthmatic children, HRV-C is the most common cause of exacerbations. Plasmacytoid dendritic cells (pDCs) respond to infection with a type 1 cytotoxic immune response by secreting IFN-α and IFN-λ. However, in allergic asthma, pDCs function abnormally, altering cytokine production to a type 2 antibody response. We hypothesize that HRV-A, HRV-B, and HRV-C will induce differential antiviral cytokine responses in PBMCs.

METHODS: Peripheral blood samples were obtained from 40 children enrolled in the Childhood Origins of ASThma (COAST) study. PBMCs were separated by density-gradient centrifugation and incubated overnight at 37°C with 2.5x10⁶ pfu equivalent/mL of HRV-A36, HRV-B52, HRV-C15, or media control. After 22 hours, the supernatants were collected and frozen at -80°C. Immune responses were measured using a multiplex ELISA for interferons (IFN-α2, IFN-γ, IFN-λ) and additional cytokines/chemokines (TNF-α, IL-4, IL-5, IL-6, IL-8, IL-10, IL-13, IP-10, MCP-1, MIP-1β).

RESULTS: HRV-A36 stimulation led to consistently increased antiviral and inflammatory immune responses when compared to HRV-B52 or HRV-C15 (p<.0001). For the majority of the cytokines/chemokines, HRV-B52 led to greater responses than HRV-C15. HRV-C15 led to significantly greater responses than the media control for IFN-α2, IFN-γ, IP-10, IL-6, IL-10, TNF-α, and MIP-1β.

CONCLUSIONS: Comparison of immune responses in PBMCs varied by HRV species. HRV-C15 stimulation led to significantly less cytokine/chemokine production than other HRV species. It is important to determine whether other types of HRV-C lead to a similar diminished immune response. If so, this suggests that HRV-C may evade the immune response of mononuclear cells which could lead to greater illness severity during HRV-C infections.
Altered Mesenchymal Stem Cell Osteogenesis Contributes to Type I Diabetic Bone Loss

Authors: Michael Ziegele, BS; Wan-Ju Li, PhD

Department: Department of Orthopedics and Rehabilitation, University of Wisconsin School of Medicine and Public Health

Mentor(s): Wan-Ju Li, PhD

Support: Shapiro Summer Research Program; Department of Orthopedics and Rehabilitation

BACKGROUND: Type I diabetes (T1D) is an increasing worldwide epidemic, affecting over 800,000 people within the United States alone. Conditions such as retinopathy, nephropathy, neuropathy, and stroke are established complications of this disorder. Recently however, gathering evidence has revealed a new complication of T1D: reduced bone mineral density (BMD) or osteoporosis. One study of 94 patients with T1D demonstrates significantly reduced BMD at the femoral head (-9.1%), lumbar spine (-12%), and Ward’s triangle (-16.3%). Increased fracture risk is additionally noted; 2.3 fold at the lumbar spine, 2.6 fold at the femoral neck, and 1.8 fold at the distal radius in one meta-analysis.

METHODS: We conducted an extensive review of available literature regarding bone loss in response to T1D, specifically focusing upon the contribution and mechanism of altered osteogenic differentiation of mesenchymal stem cells (MSCs).

RESULTS: MSCs serve as the common progenitor for both osteoblasts and adipocytes. Osteoblastogenesis is repressed in response to T1D. Diabetic-rodent models demonstrate significant reductions in osteogenic marker expression, including runx2 (18% non-diabetic control), ALP (25% non-diabetic control), and OC (10% non-diabetic control). Adipogenesis in contrast, is upregulated in response to T1D. Markers of adipogenesis, including PPAR-γ and ap2 increase two-fold within the bone marrow of diabetic mice compared to controls. The Wnt signaling pathway exerts dual control over these two pathways, inhibiting adipogenesis and stimulating osteoblastogenesis. Studies show repressed Wnt signaling activity in T1D, revealing reductions in phosphorylated GSK3B (40% non-diabetic control) and cytoplasmic B-catenin levels (85% non-diabetic control) within bones from diabetic mice. Preliminary research suggests increased FOXO transcriptional activity, reduced signaling through the insulin receptor, and amplified expression of Wnt signaling inhibitors Sost and Dkk1 to all be potential mediators of a T1D-induced reduction in Wnt-signaling. No studies were discovered reporting alterations in BMP signaling.

CONCLUSIONS: Bone loss is a serious and legitimate complication of T1D. Altered lineage selection of MSC precursors away from osteoblasts towards adipocytes provides an explanation for T1D bone loss. Reductions in Wnt signaling appear to be responsible for this lineage shift. Multiple theories behind this reduction are available, further research will need to be undertaken in order to better understand these potential mechanisms.
ACKNOWLEDGEMENTS
We gratefully acknowledge the generous support for student research in 2013 provided by:

The Herman and Gwendolyn Shapiro Foundation

UW Hospitals and Clinics
William S. Middleton Memorial Veterans Affairs Hospital
University of Wisconsin Medical Foundation
Marshfield Clinic Research Foundation
Dan and Ellie Albert Research Traineeship Award
Farrell Public Health Research Award
Wisconsin Academy for Rural Medicine

SMFH Departments, Centers, and Institutes

Anesthesiology
Biostatistics and Medical Informatics
Carbone Cancer Center
Cardiovascular Research Center
Cell and Regenerative Biology
Center for Women’s Health Research
Dermatology
Family Medicine
Institute for Clinical and Translational Research
McArdle Laboratories
Medicine
Neurological Surgery
Neurology
Oncology
Ophthalmology and Visual Sciences
Orthopedics and Rehabilitation
Pediatrics
Population Health Sciences
Psychiatry
Radiology
Surgery
Urology

Deans
Robert N. Golden, MD
Elizabeth Petty, MD
Patrick McBride, MD, MPH
Patrick Remington, MD, MPH
Byron Crouse, MD
Marc Dresner, MD
Richard Moss, PhD
ACKNOWLEDGEMENTS

Student Research Committee
Herbert Chen, MD, Chair
Nizar Jarjour, MD
Paul Anderson, MD, MS
Elizabeth Burnside, MD
Susan Thibeault, PhD
Gary Lyons, PhD
John Kuo, MD
Elizabeth Jacobs, MD
Steven Rose, MD
Michael Kim, MD

Administrative Staff
Lynne Cleeland
Kristi Herritz
Christine Ayers
Karin Silet
Kathy Holland
Laurie Schumacher
Mike Ashmore
Gabrielle Rochester