34th Annual Research Forum

Friday, April 15, 2016
8:00am to 9:30am
208 Light Hall

Established and Sponsored by the Vanderbilt University House Staff Advisory Council
Vanderbilt University Medical Center’s Research Forum provides an opportunity for non-faculty VUMC personnel to present research conducted at Vanderbilt. This Forum is open to all Vanderbilt University House Staff and Medical Students.

Research must have been performed at Vanderbilt. Unpublished work is eligible and encouraged. Work already published, or presented at another meeting, is also eligible and encouraged. All submitted abstracts are published in the Vanderbilt University Medical Center Research Forum book.

Abstracts are reviewed and selected for either an oral or a poster presentation by a panel of Vanderbilt School of Medicine faculty members who are actively involved in clinical and basic science research. The top three abstracts will be selected for oral presentation. The oral presentations will be judged by non-scientifically/non-medically trained professionals and will be judged grossly on the ability to effectively communicate to a lay audience. Following the oral presentations at the Forum, the best overall project will be awarded an Elliot V. Newman Award.

The Grant W Liddle Award, which honors a faculty member who demonstrates exemplary leadership in the promotion of scientific research at Vanderbilt University Medical Center, is presented annually at the Forum.
THIRTY-FOURTH ANNUAL RESEARCH FORUM

CHAIRPERSONS

Nichelle I. Winters, MD, PhD
Resident in Internal Medicine

Vance L. Albaugh, MD, PhD
Resident in Research Trainee, General Surgery

MODERATOR

Keith T. Wilson MD, AGAF
Thomas F. Frist Sr., Professor of Medicine
Professor of Cancer Biology, Pathology, Microbiology, & Immunology
REVIEW COMMITTEE

Basic Science Research

JOSHUA A. BAUER, PhD
Research Assistant Professor
Department of Biochemistry

SMRITI SMRITI, PhD
Research Instructor
Department of Molecular Physiology & Biophysics

RAMEELA CHANDRASEKHAR, PhD, M.A.
Assistant Professor
Department of Biostatistics

RYAN J. STARK, M.D.
Assistant Professor
Division of Pediatric Critical Care

VITO QUARANTA, M.D.
Professor
Cancer Biology

MICHAEL L. FREEMAN, PhD
Professor and Interim Chair
Department of Radiation Oncology

DANIEL S. PERRIEN, PhD
Research Instructor
Department of Orthopaedics & Rehab

KATTY (JING QIONG) KANG, PhD, M.D.
Assistant Professor
Department of Neurology

ARTHUR C. FLEISCHER, M.D.
Chief of Ultrasound, Professor
Department of Radiology & Radiological Sciences

ALEXANDER I. ZAIKA, PhD
Associate Professor
Department of Surgery Admin

CIRIA Q. HERNANDEZ, M.D., PhD
Res Asst Professor
Department of Neurology

Oral Presentation Judges

BRETT V. BENSON, PhD
Professor, Political Science Department

GEORGE TODD MORTON, A.B., E.D.M., E.D.D.
Asst. Dean and Dean of Admissions, Law School–Student Services

CHERRIE CLAY CLARK, M.B.A., B.A.
Professor, Managerial Studies (A&S)

RUSSELL M. MCINTIRE, JR., PhD
Associate Dean, College of Arts and Science

Clinical Science Research

ARIE L. NETTLES, PhD
Associate Professor
Department of Developmental Medicine

RAMEELA CHANDRASEKHAR, PhD, M.A.
Assistant Professor
Dept. of Biostatistics

MATTHEW R. DANTER, M.D.
Assistant Professor
Department of Cardiac Surgery

ANDRIES ZIJLSTRA, PhD
Assistant Professor
Department of Pathology, Microbiology, Immun

BAXTER P. ROGERS, PhD
Research Assistant Professor
Department of Radiology & Radiological Sciences

HEINRICH J G MATTHIES, PhD
Research Assistant Professor
Department of Molecular Physiology & Biophysics

ALBERT ATTIA, M.D.
Assistant Professor
Department of Radiation Oncology Center

JAMES L. BLAIR, D.O.
Assistant Professor
Department of Anesthesiology - Division of Neuroanesthesia

LAN L. GELLERT, PhD, M.D.
Assistant Professor
Department of Pathology, Microbiology, Immun.

ANNA R. HEMNES, M.D.
Assistant Professor
Allergy/Pulmonary & Critical Care Medicine

MEREDITH EVANS PUGH, M.D.
Assistant Professor of Medicine
Allergy/Pulmonary & Critical Care Medicine

QUINN S. WELLS, M.D., PharmD, M.S.C.I.
Assistant Professor of Medicine
Cardiovascular Medicine Division

KIMBERLY C. BRENNAN, M.D.
Assistant Professor
Radiology & Radiological Sciences
GRANT W. LIDDLE AWARD

The Grant W. Liddle Award was established in 1983 by the Vanderbilt University Medical Center house staff to recognize faculty members who demonstrate exemplary leadership in the promotion of scientific research at the Vanderbilt University Medical Center.

A native of American Folk, Utah, Dr. Liddle graduated first in his class from the University of Utah in 1943. After obtaining an M.D. degree from the University of California, San Francisco, in 1948, he served as a post-doctoral fellow at the newly formed Metabolic Research Unit at the NIH. In 1956, Dr. Liddle was recruited by Dr. Hugh J. Morgan to become Director of Endocrinology at Vanderbilt University. He was named Chairman of the Department of Medicine in 1968, a position he held until 1983.

Dr. Liddle’s career was marked by commitment to excellence in research, patient care, and the teaching of house staff and medical students. His research accomplishments include developing the dexamethasone suppression test and metyrapone test for assessing pituitary-adrenal gland function; describing a new form of hypertension, pseudohypoaldosteronism (Liddle’s Syndrome); developing spironolactones as useful aldosterone antagonists; and systematically improving methods for treating Cushing’s disease. In 1982, he was elected to the National Academy of Sciences and to the Royal College of Physicians in England.

Past Recipients of the Grant W. Liddle Award are:

2016  Michael F. Vaezi, MD, PhD, MS
2015  Keith T. Wilson, MD, AGAF
2014  Jonathan G. Schoenecker, MD, PhD
2013  Terence S. Dermody, M.D.
2012  Russell Rothman, M.D., MPP
2011  Alfred L. George, Jr., M.D.
2010  Harold L. Moses, M.D.
2009  D. Brent Polk, M.D.
2008  Dennis Hallahan, M.D.
2007  Nancy J. Brown, M.D.
2006  Adrian Jarquin-Valdivia, M.D., R.D.M.S.
2005  Marshall L Summar, M.D.
2004  Denis M. O’Day, M.D.
2003  Herbert S. Schwartz, M.D.
2002  John A. Zic, M.D.
2001  Kathryn M. Edwards, M.D.
2000  R. Michael Rodriguez, M.D.
1999  David H. Van Buren, M.D.
1998  Charles Wright Pinson, M.D., M.B.A.
1997  Steven Leach, M.D.
1996  Jason D. Morrow, M.D.
1995  Robert H. Ossoff, M.D., Ph.D.
1994  William O. Richards, M.D.
1993  Barney S. Graham, M.D.
1992  Gordon Bernard, M.D.
1991  Achilles Demetriou, M.D., Ph.D.
1990  David Robertson, M.D.
1989  Robert Collins, M.D.
1988  Stanley Cohen, Ph.D.
THE ELLIOT V. NEWMAN PRIZE

Elliot Voss Newman was a distinguished cardiologist, scientist, medical scholar and teacher. A graduate of Harvard College and Medical School, Dr. Newman came to Vanderbilt from Johns Hopkins University in 1952 to establish a program of clinical physiology and research. The author of the electrocardiography chapter in Harrison’s Textbook of Medicine and of the renal physiology chapter in Cecil and Loeb’s textbook, Dr. Newman was a pioneer in the development of medical engineering and the use of applied mathematics and computer science for clinical problems. Dr. Newman was the first Joe and Morris Werthan Professor of Experimental Medicine at Vanderbilt and was founder of the Clinical Research Center, which bears his name. He was a friend and mentor to medical students and house officers alike and helped to promote the scientific careers of many.

Recent Elliot V. Newman Award recipients:

2015
Paul Whiting, MD—BMI as a predictor of perioperative complications following Orthopaedic Trauma Surgery: An ACS-NSQIP analysis.

2014
Emily Zern, B.A., VMS III—B cell responses to HIV antigen are a potent correlate of viremia in HIV-I infection and improve with PD-1 blockade

Ciara M. Shaver, M.D., Ph.D.—New-onset atrial fibrillation is independently associated with increased mortality in critically ill patients

2013
Bobak Parang, B.A.—VMS II, BVES Suppresses Inflammatory Carcinogenesis

Young Min Lee, B.S.P.H.—VMS III, Recovery from Sports-Related Concussion: Days to Return To Neurocognitive Baseline in Adolescents vs. Young Adults

2012
Jonathan Kropski, M.D.—Clinical Fellow, Allergy, Pulmonary & Critical Care Medicine “Murine Herpesvirus-68 Infection Exacerbates Endoplasmic- reticulum Stress in Alveolar Epithelial Cells and Acts As a “second-hit” in the Development of Lung Fibrosis”

Patrick C. Drayna, M.D.—Ketamine Sedation is not Associated with Clinically Meaningful Elevation of Intraocular Pressure”

2011
Stephen Tourjee, B.A.—The Impact of Nerve Blocks on Opioid Use and Hospital Length of Stay in Patients with Traumatic Lower-Extremity Injury”

Yong I. Cha, M.D., Ph.D.—“Sensitivity of HPV (+) Oropharyngeal Head and Neck Cancers to Poly(ADP-ribose) Polymerase, PARP, Inhibition, Due to Defective DNA Damage Response”

2010
Daniel J. Moore, M.D., Ph.D.—Clinical Fellow, Pediatrics and Microbiology & Immunology “Targeting the Nuclear Import Shuttle Resolves Insulitis and Arrests Type 1 Diabetes”

Joyce P. Granger, M.D.—“Reliability of End Tidal CO2 Monitoring in Acute Pediatric Asthmatic Attack”

2009
James M. Dies, M.D.—“Parental Knowledge and Use of Preventive Asthma Care Measures”

Shih-Hsin Eddy Yang, M.D., Ph.D.—“Inhibition of GSK3β Enhances Repair of Radiation-Induced DNA Double Strand Breaks in Hippocampal Neurons”
THIRTY-FOURTH ANNUAL
VANDERBILT UNIVERSITY RESEARCH FORUM
Friday, April 15, 2016 • 8:00am – 9:30am • 208 Light Hall

8:00 OPENING REMARKS.............................................. Vance L. Albaugh, MD, PhD
WELCOME.................................................................Donald W. Brady, MD
INTRODUCTION OF FORUM MODERATOR............... Nichelle Winters, MD, PhD
FORUM MODERATOR..................................................Keith T. Wilson, MD

8:05 Assessment of Peripheral Nerve Regeneration with Diffusion Tensor Imaging in Reverse and Forward Autografts
Ashkan Afshari, Lyly Nguyen, Nathaniel Kelm, Justine Kim, Ravinder Bamba, Richard Boyer, Nancy Cardwell, Alonda Pollins, R. Bruce Shack, Mark Does, Wesley Thayer

8:25 Induced Differentiation Inhibits Sphere Formation In Neuroblastoma
Brian T. Craig, Eric J. Rellinger, Alexandra L. Alvarez, Jingbo Qiao, Yan Guo, Dai H. Chung

8:45 Similar Clinical Severity and Outcomes for MRSA and MSSA Pediatric Musculoskeletal Infection
Thomas An, Michael Benvenuti, Megan Mignemi MD, Issac Thomsen MD, Jonathan Schoenecker MD Ph.D.

9:05 Excuse Judges for Deliberation...........................................Keith T. Wilson, MD

9:10 Poster Presentation Awards...........................................Vance L. Albaugh, MD

9:15 Grant W. Liddle Award...................................................Nichelle Winters, MD, PhD.
Michael F. Vaezi, MD, PhD, MS (Award Winner)

9:20 Elliot V. Newman Awards..............................................Keith T. Wilson, MD
2016 ORAL PRESENTERS

(Alphabetically by presenter’s last name)

ASHKAN AFSHARI, M.D.
Fellow
Department of Plastic Surgery

BRIAN T. CRAIG, M.D.
Resident
Department of General Surgery

THOMAS J. AN
Medical Student
VMS3
Assessment of Peripheral Nerve Regeneration with Diffusion Tensor Imaging in Reverse and Forward Autografts

Ashkan Afshari, Lyly Nguyen, Nathaniel Kelm, Justine Kim, Ravinder Bamba, Richard Boyer, Nancy Cardwell, Alonda Pollins, R. Bruce Shack, Mark Does, Wesley Thayer

PURPOSE:
Nerve autograft is the gold standard for peripheral nerve injury repair in segmental nerve defects. However, the effect of autograft polarity is unclear, with no consensus on autograft orientation during repair. Diffusion tensor imaging (DTI) is an emerging magnetic resonance technology that can non-invasively image peripheral nerves and assess nerve fiber regeneration. Some studies have demonstrated expected DTI outcomes secondary to crush or single cut nerve injury, however none have evaluated this in nerve gaps. In this study we evaluate nerve regeneration utilizing DTI in autografts after nerve gap injury. We also compare outcomes between reverse and forward autografts.

METHODS:
Thirty-six female Sprague Dawley rats were divided into 3 groups: 1) Control- left sciatic nerve isolation without injury, 2) Reverse Autograft- 10mm cut left sciatic nerve segment reoriented 180° and used to coapt the proximal and distal ends, or 3) Forward Autograft- 10mm cut nerve segment kept in its normal orientation for coaptation. Animals underwent validated behavior studies, Sciatic Function Index and Foot Fault, at 72 hours, then weekly. At 6 weeks, axons proximal, within, and distal to the autograft were evaluated using DTI and axon motor staining using immunohistochemistry. Bilateral gastrocnemius/soleus muscle weights were compared to obtain a net wet weight to assess the degree of muscle atrophy.

RESULTS:
Fractional anisotropy (FA) along the control nerve was significantly higher compared to proximal, within, or distal segments of the autograft group, while radial diffusivity ($\lambda_3$) was lower. There was no difference in axon count between the control and the proximal autograft segment. Among autografts, FAProx was lower than FAgraft; axial diffusivity $\lambda_{IIprox}$ higher than $\lambda_{IIgraft}$ and $\lambda_{IIIdistal}$; and $\lambda_{IIIprox}$ higher than $\lambda_{IIIgraft}$ and $\lambda_{IIIdistal}$. Axon counts decreased distally along the nerve segments. Lastly, when reverse and forward autograft were compared to each other, no differences were seen in muscle weight, behavior scores, motor axon count, or DTI.

CONCLUSION:
At 6 weeks axonal regeneration is seen within the graft and distal segments. The proximal segment of the injured nerves demonstrated decreased FA, while maintaining normal motor axon counts, which may be attributed to edema or inflammation. Secondly, there was no difference in autograft orientation, which was further confirmed with DTI.
Induced Differentiation Inhibits Sphere Formation In Neuroblastoma

Brian T. Craig, Eric J. Rellinger, Alexandra L. Alvarez, Jingbo Qiao, Yan Guo, Dai H. Chung

OBJECTIVES:
Neuroblastoma arises from neural crest precursor cells, and differentiation status is a key factor used for clinical decision-making. Metastatic relapse in bone marrow is the leading cause of mortality in children with this devastating disease, and the differentiating agent 13-cis-retinoic acid is used as post-therapy maintenance to decrease the risk of relapse. Neuroblastoma tumor-initiating cells have been isolated from the bone marrow of patients in remission using sphere culture, which also promotes growth of neural crest stem cells. Sphere culture may therefore enrich for a cancer stem cell phenotype in neuroblastoma. We sought to test whether sphere formation depends on differentiation status and to elucidate the molecular mechanisms responsible for the sphere-forming phenotype.

METHODS:
Four human neuroblastoma cell lines were cultured in low attachment, serum-free media with EGF (20 ng/ml) and bFGF (40 ng/ml) and tested for sphere-forming frequency by limiting dilution analysis. Cellular differentiation was induced by treatment with 13-cis-retinoic acid (5 mM). Gene expression profiling of sphere-cultured cells was performed by paired-end RNA sequencing and validated by RT-qPCR. ANOVA and Student’s t test were used for multiple and two-group comparisons, respectively.

RESULTS:
MYCN-amplified LAN-1 (6.1%) and BE2C (4.9%) had much higher sphere-forming frequency than non-MYCN-amplified SK-N-SH (1.7%) or SK-N-AS (0.7%) (p<0.001). Inducing differentiation inhibited sphere formation in BE2C and LAN1 to the level of the non-MYCN-amplified cells. Gene expression profiling was used to contrast the high sphere-forming BE2C to the low sphere-forming SK-N-SH cells to identify potentially novel regulators of sphere formation. Interestingly, the hematopoietic progenitor cell marker CD34 and the TGF-b family member GDF15, important in glioblastoma and multiple other cancers, were the two most highly differentially expressed transcripts.

CONCLUSIONS:
Sphere culture in neuroblastoma correlates with MYCN amplification, depends on the cellular differentiation state and is associated with increased expression of progenitor cell markers. Taken together, these data suggest that frequent sphere formation may represent a cancer stem cell phenotype in neuroblastoma, and that this in vitro model system could shed light on the critical mechanisms that lead to metastatic bone marrow relapse after therapy.
Similar Clinical Severity and Outcomes for MRSA and MSSA Pediatric Musculoskeletal Infection

Thomas An, Michael Benvenuti, Megan Mignemi MD, Issac Thomsen MD, Jonathan Schoenecker MD Ph.D.

OBJECTIVES:
Studies on pediatric musculoskeletal infection have suggested that methicillin resistant Staph. aureus (MRSA) causes worse hospital outcomes than methicillin susceptible Staph. aureus (MSSA). Based on these results, clinical prediction algorithms have been developed to differentiate between MRSA and MSSA early in a patient’s clinical course. This study compares hospital outcomes for pediatric patients with MRSA and MSSA musculoskeletal infection presenting to the emergency department at Vanderbilt. The authors hypothesized that there would be no significant differences in in the severity of infections caused by MRSA and MSSA.

METHODS:
An IRB-approved retrospective study was conducted to identify pediatric patients with S. aureus musculoskeletal infection over a 5-year period (2008-2013). The patient population was identified through sequential review of the pediatric orthopedic consult list. Demographic information, laboratory values, and clinical outcomes were obtained from the electronic medical record. Statistical analysis performed with GraphPad Prism 6 (La Jolla, Ca) and STATA 14 (College Station, TX).

RESULTS:
Of the 92 identified cases of S. aureus pediatric musculoskeletal infection, there were 49 cases of MRSA (53%) and 43 cases of MSSA (47%). There were no significant differences between MRSA and MSSA infections in median hospital length of stay (4.8 vs. 5.7 days, p=0.50), febrile days (0.0 vs. 1.5 days, p=0.10), and peak CRP (117 vs. 103 ug/ml, p=0.52). However, a higher proportion of MRSA infections required operative intervention compared to MSSA infections (85% vs. 62%, p=0.015*). A predictive logistic regression model based on CRP, temperature, WBC, pulse and respiratory rate at presentation demonstrated poor ability to differentiate between MRSA and MSSA infection, with an area under the receiver operator characteristic of 0.676.

CONCLUSIONS:
The results demonstrated no significant difference in most hospital outcomes between MSSA and MRSA musculoskeletal infection. In addition, a predictive model based on severity markers obtained at presentation was unable to effectively differentiate between MRSA and MSSA infection. Therefore, the clinical utility and capacity for early differentiation between MRSA and MSSA depends on regional virulence patterns that may be specific for each institution. Given the changing trends in S. aureus virulence and resistance patterns, algorithms to differentiate between strains will need to be updated regularly with clinical data.
BASIC SCIENCE RESEARCH

ABSTRACTS

(Alphabetically by last name)
2016 Basic Science Research Abstracts

Page #:

15. Kristie I. Aamodt, Medical Student
16. Ashkan Afshari, Fellow
17. Ravinder Bamba, MD, Resident
18. Melissa H. Bloodworth, Medical Student
19. Melissa H. Bloodworth, Medical Student
20. Michael Chi, MD, Resident
21. Edward Roberdeau Cochran III, MD, Resident
22. Brain T. Craig, MD, Resident
23. Nicholas A. Harris, Medical Student
24. Jonathan A. Hemler, MD, Fellow
25. Tracey S. Hong, Medical Student
26. Valerie Jansen, MD, Ph,D, Fellow
27. Lilian Juttukonda, Medical Student
28. Lilian Juttukonda, Medical Student
29. Eric J, Rellinger, MD, Resident
30. Kelsie Riemenschneider, Medical Student
31. Rafal Sobota, Medical Student
32. Rafal Sobota, Medical Student
2016 Basic Science Research Abstracts

Page #:

33. Blair Stocks, MD, Fellow
34. Blair Stocks, MD, Fellow
Deconstructing the Pancreatic Islet Microenvironment to Identify Signals that Promote β Cell Proliferation

Kristie I. Aamodt, Diane Saunders, Nripesh Prasad, Radhika Aramandla, Zoya Khan, Shawn E. Levy, Marcela Brissova, Alvin C. Powers

Reduced pancreatic β cell mass is a hallmark of diabetes, which makes the ability to increase or re-store β cell mass a major therapeutic goal. However, factors that effectively stimulate β cell proliferation have not been identified. While testing the hypothesis that increased endothelial cell (EC) signaling would increase β cell mass using a model of inducible vascular endothelial growth factor-A (VEGF-A) overexpression in β cells (βVEGF-A mouse), we found that increased VEGF-A leads to reduced, not increased, β cell mass. Surprisingly, withdrawal of the VEGF-A stimulus is followed by robust β cell proliferation, leading to islet regeneration, normalization of β cell mass, and reestablishment of the intra-islet capillary network.

Using islet and bone marrow (BM) transplantation approaches we found that β cell proliferation and regeneration is dependent on the local microenvironment of ECs, β cells, and macrophages (MΦs) recruited to islets upon VEGF-A induction. We then established that clodronate-mediated depletion of MΦs (86%) prevents β cell proliferation during the recovery phase, thus demonstrating that these recruited MΦs are essential to regeneration.

Since the islet microenvironment dynamically changes through phases of quiescence, β cell loss and recovery, we performed transcriptome analysis on purified β cells, ECs, and MΦs isolated at these time points to identify mechanisms through which these cell populations interact with each other to promote β cell regeneration. These data indicate that MΦs are recruited to islets by increased expression of cell adhesion molecules on both MΦs and ECs, and increased production of chemokines and cytokines involved in leukocyte extravasation by MΦs already located in islets. In addition, MΦ phenotype shifts, due in part to β cell-derived signals (Il4, Csf1) driving their transition from a pro-inflammatory to a tissue reparative phenotype.

Based on integrated analysis of RNA-Seq data, we further found: (1) increased growth factor expression by β cells (e.g., Igf1, Tgfb1/2, Fgf1/7), ECs (e.g., Ctgf, Pdgfa), and MΦs (e.g., Ctgf, Igf1, Pdgfc), (2) increased expression of growth factor receptors (e.g., Pdgfra/b, Igf1r, Tgfbr2, Fgfr1) and integrins on β cells, and (3) evidence of increased integrin activation by the extracellular matrix and simultaneous activation of the PI3K/Akt and MAPK signaling pathways. These results suggest a new β cell regeneration paradigm where β cell self-renewal is mediated by coordinated interactions between MΦs recruited to the site of β cell injury, intra-islet ECs, and β cells.
OBJECTIVE:
Peripheral nerve repairs have been a topic of much discussion and account for billions of health care dollars. To date, the gold standard for segmental loss has been the utilization of nerve autografts. However, this method leads to donor site morbidity and increased operative time to harvest the graft. Therefore various types of conduits have been developed to augment these repairs and bridge nerve gaps. Porcine derived extracellular matrix has been utilized as a scaffold in several reconstructive fields and has demonstrated remarkable outcomes. Due to its versatility and ability to serve as a regenerative scaffold, we compare engineered conduits, constructed from porcine-derived urinary bladder matrix (UBM), to the gold standard, nerve autografts.

METHODS:
Twenty-four Sprague Dawley rats were divided into 2 groups. All underwent left sciatic nerve injury, leaving a 10mm gap. The injury was repaired using either: 1) Reverse autograft – the 10mm cut segment was oriented 180° and used to coapt the proximal and distal ends or 2) UBM conduit - the 10mm nerve gap was bridged with UBM conduit. Postoperatively, at 72 hours, and then weekly, up to 6 weeks, validated behavior/functional assessments were performed including Sciatic Function Index (SFI) and Foot Fault Asymmetry Scores (FF). At 6 weeks, the repaired nerves as well as bilateral gastrocnemius/soleus muscles were harvested from each animal. Nerves were evaluated using immunohistochemistry for motor axon staining, proximal, within, and distal to the graft. The net wet muscle weights were calculated to assess the degree of muscle atrophy.

RESULTS:
The UBM group demonstrated significantly improved FF scores at 72 hours, 1 week, 2 weeks, and 4 weeks. This pattern was also observed for SFI scores, although not statistically significant. At 6 weeks, motor axon counts proximal/within/distal to the graft was similar between UBM conduits and reverse autografts (1635/817/416 vs 1539/780/432, p=ns). Likewise, the net gastrocnemius/soleus weights in the UBM group was similar between the two groups (1.36g vs 1.37g, p=ns).

CONCLUSION:
UBM conduits prove to be at least similar to nerve autografts for the repair of peripheral nerve injuries. They have the potential to become the new gold standard for gap nerve injury repairs. In a clinical setting, these promising results can eliminate the donor site morbidity and increased operative time associated with nerve autografting.
Hydrophilic Polymers Restore Axonal Continuity as Assessed by Diffusion Tensor Imaging

Ravinder Bamba MD, D. Colton Riley, Richard Boyer PhD, R. Bruce Shack MD, Wesley Thayer MD PhD

OBJECTIVES:
Hydrophilic polymers such as polyethylene glycol (PEG) have been hypothesized to rejoin the axolemma of the cut ends of severed proximal and distal axons, inducing both morphological and functional axonal continuity. We hypothesize that PEG immediately restores axonal continuity and can be demonstrated by MR diffusion tensor imaging (DTI).

METHODS:
The objective of this study was to evaluate the efficacy of PEG-fusion using DTI parameters in both a rat and porcine model. The left sciatic nerves of female rat and porcine were completely transected and repaired using standard microsurgical techniques. Following repair, PEG was injected into the neurorrhaphy; negative controls did not receive PEG. Nerves were immediately excised and MR imaging was obtained.

RESULTS:
PEG rapidly restores axonal continuity as assessed by diffusion tensor imaging. The rat model included a control (n=6), PEG (n=6), and PEG [device] (n=6). The porcine model included an unoperated control (n=4), negative control (cut+repair; n=4), and PEG treated (cut+repair+PEG; n=4). FA was significantly decreased at the site of injury in both PEG and negative control groups compared to unoperated controls (p<0.01). The drop in FA at the zone of injury indicates a loss in axonal continuity. However, PEG treated nerves were associated with a statistically significant increase in FA (p<0.05) at the site of injury compared to negative controls. Additionally, PEG treated nerves demonstrated a significant increase in the number of DTI tracts that traveled through the zone of injury compared to negative controls. While an increase in FA and DTI tracts at the site of injury compared to negative controls indicate that PEG successfully restores axonal continuity, the decrease in FA and DTI tracts compared to unoperated controls suggest that PEG does not restore continuity to all axons. Principle diffusion vectors in negative control animals appeared more homogenous at the zone of injury compared to PEG treated. However, in unoperated control nerves, principle diffusion vectors were homogeneous throughout.

CONCLUSIONS:
The introduction of PEG into neurorrhaphy rapidly restores axonal continuity. The aforementioned data suggest that high-resolution DTI is capable of detecting acute peripheral nerve injuries. Use of PEG fusion and DTI might produce a paradigm shift in the treatment of traumatic injuries to peripheral nerves.
IL-4 Signaling Attenuates IL-17-Producing γδ T Cells During Klebsiella Pneumoniae Infection


OBJECTIVE:

Patients with asthma have innate immune defects with pathogens, which may partially explain why these individuals are at increased risk for invasive bacterial infections and bacterial pneumonia. γδ T cells reside at the interface of epithelial-environmental interfaces such as the respiratory and gastrointestinal tracts, and are a critical first line of defense against bacterial and fungal pathogens. A subset of γδ T cells are the γδ17 cells which produce large quantities of IL-17, a cytokine crucial to the anti-bacterial and anti-fungal function of these cells. IL-4 is produced at high levels in the airway of asthma patients. We hypothesized that IL-4 inhibits innate γδ17 cells during acute Klebsiella pneumoniae (KP) infection.

METHODS:

γδ T cells were purified from the spleens of Balb/c mice. To induce IL-17 production, γδ T cells were cultured with IL-1β and IL-23 for 3 days in the presence or absence of IL-4. For in vivo experiments, WT or STAT6 knockout (KO) mice were infected with 10^3 CFU KP by retropharyngeal instillation and sacrificed 36 hours later. The type I IL-4R, STAT6 phosphorylation, and γδ17 cells were detected by flow cytometry. Cytokine production was evaluated by ELISA, and IL-23R and Sgk1 expression were determined by RT-PCR.

RESULTS:

γδ T cells express the type I IL-4R, and IL-4 increased STAT6 phosphorylation in γδ T cells. IL-4 inhibited γδ17 cell production of IL-17. IL-4 also decreased γδ17 expression of the IL-23R and its positive regulator, Sgk1. To determine whether IL-4 regulates γδ17 in vivo, we used a mouse model of KP in STAT6 KO mice, which lack the ability of IL-4 to signal through the IL-4R. Acute lung infection with KP resulted in a significant increase in the number of γδ17 cells in STAT6 KO mice compared to WT mice.

CONCLUSIONS:

γδ T cell expression of the type I IL-4R is functional, as IL-4 induces STAT6 phosphorylation in γδ T cells. IL-4 inhibits γδ17 cell production of IL-17. IL-4 also decreases Sgk1 expression, which may lead to destabilized IL-23R expression on γδ17 cells. Endogenous IL-4 reduces lung γδ17 cell numbers during acute KP infection. IL-4 inhibition of γδ17 cells provides a possible explanation for why asthmatic patients are at greater risk for invasive bacterial disease.
Liraglutide Abrogates Respiratory Syncytial Virus (RSV)-Induced Inflammation and Airway Dysfunction

Melissa H. Bloodworth, Jian Zhang, Shinji Toki, Lindsey C. Morris, Martin L. Moore, Kevin D. Niswender, R. Stokes Peebles Jr.

OBJECTIVE:
RSV is the leading cause of hospitalization in infants. Severe RSV infection is a risk factor for the subsequent development of asthma. During severe RSV illness, the type 2 response mediates mucus production, which directly contributes to airway obstruction and respiratory failure. The type 2 response is also the most common immunologic phenotype of inflammation in asthma. The RSV strain 12/12-6 was isolated from a hospitalized patient with severe lower respiratory tract infection and bronchiolitis. We hypothesize that RSV 12/12-6 induces a strong type 2 response with subsequent mucus production, and that this immune-associated pathology is inhibited by the GLP-1R agonist liraglutide.

METHODS:
Balb/c WT mice were infected with the RSV clinical isolate 12/12-6. Escalating doses of the GLP-1R analog liraglutide starting at 0.05 mg/kg with a 2-fold daily increment until the final dose of 0.2 mg/kg weight was reached or 0.1% BSA in PBS (vehicle) was administered subcutaneously beginning 2 days prior to infection and given twice daily until the mice were euthanized. Throughout the 8 days following infection, mice were euthanized and BALs and lungs were collected for protein measurements via ELISA, cellular analysis by flow cytometry, or histopathology.

RESULTS:
RSV 12/12-6 induced the highest reported murine lung production of the type 2 cytokine IL-13 and mucus during RSV infection. Liraglutide treatment resulted in a 2-fold decrease in RSV-induced IL-13, inflammation, and mucus production with concurrent decreases in the Th2 chemokines CCL17 and CCL22. Liraglutide also significantly decreased epithelial-associated cytokines TSLP, IL-33, and IL-1α, which induce Th2 proliferation and activation. Liraglutide did not enhance viral load and concurrently increased IFNλ.

CONCLUSION:
Our findings demonstrate that the GLP-1R analog liraglutide protects against RSV 12/12-6-induced inflammation and mucus production. Liraglutide has immunoregulatory functions that decrease inflammatory responses, and could be used to treat RSV bronchiolitis, a disease for which there is currently no cure.
ROS-Responsive Microspheres for On-Demand Relief of Chronic Pain

Michael Chi, Taylor Kavanaugh, Kristin O'Grady, Kelli Boyd, Jerod Denton, Craig Duvall

OBJECTIVES:

Chronic pain (CP) is a leading cause of disability, loss of quality of life and socioeconomic burden, yet its treatment is often ineffective and fraught with adverse effects such as tolerance, addiction, somnolence and constipation. Inflammation plays an important role in the development and maintenance of CP via different mediators including reactive oxygen species (ROS). Our objective is to develop a novel drug delivery system for use in the treatment of chronic pain by delivering drugs in a targeted fashion to sites of inflammation. Poly(propylene sulfide) (PPS) microspheres could be used to encapsulate analgesics and release them locally in response to ROS. A recent study, however, indicated that poly(lactic-co-glycolic acid) (PLGA) microspheres loaded with bupivacaine caused pronounced myotoxicity. Thus, our first objective was to test if ROS-responsive, bupivacaine-loaded PPS microspheres also induce myotoxicity or other tissue damage.

METHODS:

PPS and PLGA microspheres loaded with and without bupivacaine were synthesized and injected into the gastrocnemius muscle of healthy, wild-type mice. Samples were harvested after two weeks and scored for myotoxicity.

RESULTS:

Blind myotoxicity scoring revealed no myotoxicity in either the PPS or PLGA microsphere injected groups, regardless of if they were loaded with bupivacaine or not. However, the muscle samples from the PLGA microsphere injected groups showed accumulation of macrophages and free microspheres between muscle fibers that was independent of drug loading. This accumulation of macrophages and free microspheres was not seen in either of the PPS microsphere injected groups.

CONCLUSIONS:

We have shown that the use of PPS as a drug delivery system has benefits over the commonly used polymer, PLGA, by causing less of an immune response. We are currently 1) using PPS-bupivacaine microparticles to test the analgesic efficacy on bone cancer pain, and 2) developing PPS microparticles containing other molecules to evaluate their efficacy in reducing inflammatory pain.
Creating Reproducible Deformation in Breast MRI for Collecting Elastographic Data on Breast Tumors

Edward Roberdeau Cochran III, MD, Micah Fritsche, MD, Rebekah H. Griesenauer, Jared A. Weis, PhD, Michael Miga, PhD

OBJECTIVES:

Current imaging methods assess tumor response to therapy on the basis of changes in tumor size, enhancement patterns, and metabolic activity (PET). Clinical studies have demonstrated that cancer progression is also accompanied by changes in tissue stiffness, which can be an early marker of tumor response to therapy. The field of elastography has established methods to assess tissue stiffness using different imaging modalities, and provides a potential avenue to detect early tissue changes in response to therapy. The objective of this study is to design a device that can consistently and reproducibly compress tissue in order to assess changes in soft tissue stiffness. Specifically, we will target breast tissue utilizing MRI. We aim to utilize this ability to reproducibly compress breast tissue in combination with a newer elastographic method, Modality Independent Elastography (MIE), to qualitatively and quantitatively assess tissue stiffness. Eventually our goal is to detect early changes in tumor stiffness as a response to therapy.

METHODS:

A device that could compress breast tissue from within a breast MRI coil was desired. A 3D modeling program was used to design and simulate our device. The compression device consists of a base plate on which an inflatable balloon rests. The base plate contains upright guiderods on which a compression plate apparatus is mounted over a balloon. The balloon is then manually inflated, and the compression plate rises upward towards the patient to compress the overlying breast. Reproducibility of compression is then tested on a phantom breast model.

RESULTS:

Currently a device that is compatible with an MRI and fits within the breast coil has been designed and fabricated. The next step of this project will be to test the function of this compression device and document reproducible compression forces on a phantom breast model. Ultimately, we aim to test this device on human volunteers to document reproducible compression forces in breast tissue.

CONCLUSIONS:

Finding an additional and earlier imaging biomarker to evaluate response to therapy could give clinicians additional data to detect earlier responders undergoing chemotherapy, helping guide management. Our compression device another step towards introducing MRI elastography as an imaging biomarker in the oncologic evaluation.
**Induced Differentiation Inhibits Sphere Formation In Neuroblastoma**

*Brian T. Craig, Eric J. Rellinger, Alexandra L. Alvarez, Jingbo Qiao, Yan Guo, Dai H. Chung*

**OBJECTIVES:**
Neuroblastoma arises from neural crest precursor cells, and differentiation status is a key factor used for clinical decision-making. Metastatic relapse in bone marrow is the leading cause of mortality in children with this devastating disease, and the differentiating agent 13-cis-retinoic acid is used as post-therapy maintenance to decrease the risk of relapse. Neuroblastoma tumor-initiating cells have been isolated from the bone marrow of patients in remission using sphere culture, which also promotes growth of neural crest stem cells. Sphere culture may therefore enrich for a cancer stem cell phenotype in neuroblastoma. We sought to test whether sphere formation depends on differentiation status and to elucidate the molecular mechanisms responsible for the sphere-forming phenotype.

**METHODS:**
Four human neuroblastoma cell lines were cultured in low attachment, serum-free media with EGF (20 ng/ml) and bFGF (40 ng/ml) and tested for sphere-forming frequency by limiting dilution analysis. Cellular differentiation was induced by treatment with 13-cis-retinoic acid (5 mM). Gene expression profiling of sphere-cultured cells was performed by paired-end RNA sequencing and validated by RT-qPCR. ANOVA and Student’s t test were used for multiple and two-group comparisons, respectively.

**RESULTS:**
MYCN-amplified LAN-1 (6.1%) and BE2C (4.9%) had much higher sphere-forming frequency than non-MYCN-amplified SK-N-SH (1.7%) or SK-N-AS (0.7%) (p<0.001). Inducing differentiation inhibited sphere formation in BE2C and LAN1 to the level of the non-MYCN-amplified cells. Gene expression profiling was used to contrast the high sphere-forming BE2C to the low sphere-forming SK-N-SH cells to identify potentially novel regulators of sphere formation. Interestingly, the hematopoietic progenitor cell marker CD34 and the TGF-b family member GDF15, important in glioblastoma and multiple other cancers, were the two most highly differentially expressed transcripts.

**CONCLUSIONS:**
Sphere culture in neuroblastoma correlates with MYCN amplification, depends on the cellular differentiation state and is associated with increased expression of progenitor cell markers. Taken together, these data suggest that frequent sphere formation may represent a cancer stem cell phenotype in neuroblastoma, and that this in vitro model system could shed light on the critical mechanisms that lead to metastatic bone marrow relapse after therapy.
Non-canonical activating effects of alpha2a adrenergic receptor agonism in the bed nucleus of the stria terminalis

Nicholas A. Harris, Austin T. Isaac, Stephanie A. Flavin, Elias K. Awad, Yuval Silberman, Danny G. Winder

Drug addiction is a major health concern. Patients often go untreated, leading to relapse with stress cited as a major cause. During abstinence, norepinephrine (NE) engages maladaptive stress circuitry to promote reinstatement. Agonism at α2-adrenergic receptors (α2-ARs) can dampen elevated NE tone. Clonidine and guanfacine are α2-agonists with positive preclinical results dampening stress-induced reinstatement of drug seeking behavior. However, treatment does not change ultimate relapse rates. We hypothesize that this is due to competition among the effects of α2-AR agonism beyond its commonly cited role as an inhibitory autoreceptor on NE terminals. We aim to investigate these effects in the bed nucleus of the stria terminalis (BNST), a component of the extended amygdala implicated in stress and reward behaviors. In rodent models, intra-BNST administration of α2 agonists reduces stress-induced reinstatement. In the BNST, α2-AR agonism presynaptically inhibits release of both norepinephrine and glutamate Recently, we have found that α2-AR agonism enhances excitability in BNST. However, the mechanism underlying these effects, as well as the specific identification of the cells activated, are critical unknowns. We aim to determine the mechanism underlying α2-AR agonism-induced enhancement of glutamatergic transmission in BNST neurons and its relevance to circuit activity, and to begin to determine the impact of this regulation. We hypothesize that activation of postsynaptic α2A-ARs enhances excitatory responses through inhibition of HCN channels. To test this hypothesis, we combine electrophysiological studies aimed at uncovering the mechanism of guanfacine activating effects within the BNST with anatomical studies aimed at identifying the guanfacine-activated population of BNST neurons. Here, we show that guanfacine-activated BNST neurons show a high prevalence of the hyperpolarization-activated current Ih, suggesting a role for HCN channels in the activity-enhancing effects of α2A-AR agonism. In addition, HCN channel inhibition mimics guanfacine effects on postsynaptic field potential responses in the BNST. Complementary anatomical data shows that postsynaptic α2A-AR mRNA expressing BNST neurons are largely distinct from HCN1 subunit-expressing neurons, suggesting the HCN2 subunit mediates guanfacine enhancing effects. Through these experiments, we hope to better understand non-canonical effects of α2-AR agonism in the BNST and its behavioral and circuit relevance.
A Study of Immunogenetic Associations with Peanut Allergy utilizing a Novel DNA Repository

Jonathan A Hemler, MD, Elizabeth S Marston, MD, Jason H Karnes, PhD, Andrew M Glazer, PhD, Elizabeth J Phillips, MD, Simon A Mallal, MBBS, Peggy L Kendall

OBJECTIVES:
A fundamental knowledge gap exists regarding genetic causes of peanut allergy (PA). Large genetic databases now make it possible to conduct detailed human genome studies to identify contributors to disease.

METHODS:
BioVU, a unique biorepository of >200,000 DNA samples matched to de-identified electronic medical records (EMR), was used to identify subjects for study of HLA alleles associated with peanut allergy (PA). 65 PA patients and 170 peanut tolerant controls (PC) were identified in BioVU using an algorithm ratified by expert review. Of these, 16 PA and 43 PC self-identified White patients had genotypic data available for analysis. HLA alleles were imputed from Illumina® HumanExome BeadChip data using SNP2HLA. HLA allele associations were tested in a dominant model with PLINK with significance considered at alpha=0.05.

RESULTS:
No significant associations (p<0.05) were detected. Suggestive associations included HLA-DQB1*05*02 (p=0.07, OR 1.25), which correlated with increased risk of PA, and HLA A*68 (p=0.10, OR 0.70), which correlated with decreased risk of PA.

CONCLUSIONS:
The trend in HLA-DQ associating with PA risk conforms with previous studies localizing risk to the HLA class II HLA-DR/DQ region. HLA sequencing amongst all PA and PC will be performed to increase the power to detect associations within the HLA locus. The BioVU repository has provided: 1. A novel platform for studying genetic contributions to PA with the goal of creating a model to define its specific immunopathogenesis and 2. An algorithm for a specific PA phenotype that can now be validated across a large network of EMRs with DNA repositories.
Pelvic Acceleration as an Objective Means of Quantifying Gait Asymmetry

Tracey S. Hong, Gerasimos Bastas, MD PHD, Karl E. Zelik, PHD

OBJECTIVES:
There are over 1 million Americans living with lower limb loss. Lower limb amputees (LLA) often exhibit gait asymmetries, which can be worsened by poorly fitted prosthetics and can lead to secondary disabilities like back pain and osteoarthritis. To mitigate these risks, frequent reassessment and gait monitoring tools are needed to better inform clinical interventions. Observational gait analysis is most commonly used in the clinical setting, but can have low inter-observer reliability. Motion capture and force plate use is the gold standard for quantitative assessment, but it is too time consuming and costly for outpatient settings. Inertial measurement units (IMU) may offer a solution, as they are portable, inexpensive, and can provide objective movement data of both lower limbs. We propose that tracking pelvic movement with an IMU may be useful for assessing amputee gait asymmetry.

METHODS:
A comparative instrumented analysis was performed to study the potential of a pelvis-mounted IMU (affixed at L5) to estimate sound vs. residual limb force asymmetries experienced during walking. We tested 1 able-bodied control, 1 unilateral transtibial amputee (TTA), and 1 unilateral transfemoral amputee (TFA) while they walked on a force-treadmill. Force and acceleration data were collected simultaneously, filtered, and stride-averaged. Pearson correlation between the fore-aft ground reaction forces (GRF) and pelvic acceleration was used to assess how well pelvic motion tracked center-of-mass motion. We estimated asymmetries in right vs. left leg loading behavior by quantifying braking/deceleration ratios. In the clinical setting, we collected unilateral IMU data from 16 TTA and 14 TFA. We tested walking performance across different speeds and dates, and pre vs. post intervention when feasible.

RESULTS:
We observed a strong correlation (R>0.6) between pelvic acceleration and net GRF waveforms for each of the 3 subjects, suggesting that pelvic motion may be a useful surrogate for assessing net limb loading. However, LLA braking asymmetry ratios derived from IMU pelvic acceleration data showed poor correspondence with treadmill-derived force asymmetry ratios. This could be due to IMU sensing limitations or pelvis affixation methods. Alternatively, this may reflect methodological limitations in estimating individual limb braking with a single IMU, due to challenges in parsing leading vs. trailing limb contributions during double support. Clinically, we observed that IMU pelvic acceleration waveforms remained patient specific and consistent across different speeds and dates.

CONCLUSIONS:
We posit that an inexpensive, portable measure of walking performance would aid in clinical decision-making by alerting practitioners to gait deviations and enabling timely intervention. The consistency and observed similarity in waveforms between pelvic acceleration and GRF highlight the potential utility of IMUs. Efforts are ongoing to identify what can be reliably gleaned from these sensors.
Inhibition of 3-phosphoinositide dependent protein kinase 1 (PDK1) synergizes with CDK4/6 inhibitors against ER-positive breast cancer

Valerie Jansen, Neil Bhola, Josh Bauer, Valeria Estrada, Carlos Arteaga

OBJECTIVE:
Dysregulation in cell cycle checkpoints is common in cancer. Small molecule inhibitors that target the CDK4/6/cyclinD1 pathway of the cell cycle are in clinical development. However, as for other targeted therapies, development of resistance to CDK4/6 inhibitors is anticipated. Thus, there is a need to develop potent therapeutic strategies to circumvent drug resistance.

METHODS:
We performed a high-throughput RNA interference kinome screen to identify targetable molecules whose inhibition, in combination with the CDK4/6 inhibitor LEE011, induced synthetic lethality in MCF7 breast cancer cells. PDK1 RNAi oligonucleotides and the PDK1 inhibitor GSK2334470 in combination with the CDK4/6 inhibitors, palbociclib and LEE011, were tested against ER+ breast cancer cells. In vivo anti-tumor efficacy of LEE011 and GSK2334470 was assessed in mice bearing MCF7 xenografts.

RESULTS:
A siRNA kinome screen identified PDK1 as the top RNA whose downregulation sensitized MCF7 cells to CDK4/6 inhibitors. This was confirmed with independent siRNAs in ER+ MCF7, T47D, HCC1428 and HCC1500 breast cancer cells. Pharmacological inhibition of PDK1 with the ATP-competitive small molecule inhibitor GSK2334470 in combination with the CDK4/6 inhibitors synergistically inhibited proliferation of MCF7 and T47D cells. LEE011-resistant MCF7 and T47D cells were generated by chronic treatment with LEE011. Drug-resistant cells displayed increased levels of PDK1 and phosphorylated S6 ribosomal protein (pS6), an effector of the PDK1 substrate p70S6K, compared to parental drug-sensitive cells. Inhibition of PDK1 re-sensitized the LEE011-resistant cells to the CDK4/6 inhibitors. Genetic and pharmacological inhibition of PDK1 abrogated pS6 levels whereas inhibition of AKT did not affect pS6 levels, suggesting PDK1 can induce resistance to CDK4/6 inhibitors via p70S6K/pS6 signaling in an AKT-independent manner. The effects observed in cell lines in culture were recapitulated in vivo using MCF7 xenografts established in ovariectomized nude mice. Treatment with GSK2334470 and LEE011 induced tumor regressions more potently than either drug alone.

CONCLUSIONS: These data support a critical role for PDK1 in mediating acquired resistance to CDK4/6 inhibitors in ER+ breast cancer cells. Co-targeting of the PDK1 and CDK4/6 pathways may overcome resistance to CDK4/6 inhibitors and is worthy of further translational and clinical investigation in patients with ER+ breast cancer.
Acinetobacter baumannii coordinates metabolism with metal import to infect the lung

Lillian Juttukonda, Eric Skaar

OBJECTIVE:
Acinetobacter baumannii is a gram-negative bacterium associated with pneumonia in critically ill patients. Infections are commonly caused by strains of A. baumannii that are resistant to most antibiotics, making treatment challenging. Neutrophils are essential for host defense during A. baumannii infection of the lung, and the neutrophil protein calprotectin inhibits A. baumannii growth by binding manganese (Mn) and limiting Mn availability in the lung. Like many bacterial pathogens, A. baumannii requires Mn for growth. We sought to identify the mechanisms that A. baumannii employs to combat calprotectin-mediated Mn sequestration during infection of the lung.

METHODS:
A Mn transporter was identified using an orthologue database search. This transporter is encoded within an operon containing genes required for catabolizing urea to ammonia, herein named the manganese and urea metabolism (mum) operon. Gene-deletion strains were constructed and their phenotypes were evaluated.

RESULTS:
Deletion of the Mn transporter mumT impairs A. baumannii growth in the presence of calprotectin. Interestingly, deletion of urea carboxylase mumC also decreases growth in the presence of calprotectin. Inactivation of mumC impairs restricts utilization of certain carbon and nitrogen sources, demonstrating an important role for mumC in A. baumannii metabolism. These findings suggest that the mum operon combats both Mn starvation and metabolic stress. To interrogate the significance of this system in vivo, a murine pneumonia model of A. baumannii was utilized. In this model, the mumT-inactivated strain is significantly out-competed by wild-type A. baumannii in both the lung and the liver. Intriguingly, the mumT-inactivated strain remains attenuated in the lungs of calprotectin-deficient mice, which suggests that mumT is required to overcome additional stresses that exist in the lung.

CONCLUSIONS:
These findings reveal that A. baumannii has sophisticated mechanisms to subvert host-mediated metal sequestration and expose a connection between metal starvation and metabolic stress in the lung. This connection may be exploited by future combination antimicrobial therapies that target both metal homeostatic mechanisms and metabolic pathways.
Dietary manganese and the host protein calprotectin synergize to promote Staphylococcus aureus infection of the heart

Lillian Juttukonda, Eric Skaar, Jessica Moore, Yaofang Zhang

OBJECTIVES:
Staphylococcus aureus is a leading cause of bacterial infection worldwide. Like many bacterial pathogens, S. aureus must acquire nutrient manganese (Mn) during infection. Mn levels vary in humans depending on dietary intake. Humans release the Mn-binding protein calprotectin at the site of infection. Calprotectin is thought to inhibit S. aureus growth by sequestering Mn. The goal of this study is to understand how Mn levels the diet alter the ability of calprotectin to prevent S. aureus infection.

METHODS:
Wild-type and calprotectin-deficient (CP-/-) mice were fed diets containing low, normal, or high levels of Mn and infected intravenously with S. aureus.

RESULTS:
Mice fed a high Mn diet exhibit increased mortality from S. aureus infection, enhanced bacterial burdens in the heart, and increased surface-exposed cardiac abscesses. Mice on high Mn diet and infected by a S. aureus strain lacking Mn importers survived, indicating that Mn import by the bacterium is essential for the dramatic enhancement of virulence in conditions of high Mn. Laser ablation inductively coupled plasma mass spectrometry was employed on heart sections, confirming that Mn levels at the site of infection were altered by diet. Calprotectin abundance in infected hearts was analyzed via matrix-assisted laser desorption imaging mass spectrometry, revealing that calprotectin is recruited to cardiac S. aureus lesions. Contrary to known antibacterial role of calprotectin in the liver, CP-/- mice were found to have lower bacterial burdens in the heart than WT mice. Furthermore, CP-/- mice fed a high Mn diet are protected from mortality. Because calprotectin has a reported role in neutrophil chemotaxis, inflammatory cell recruitment to S. aureus-infected hearts was evaluated. CP-/- mice fed a high Mn diet have substantially fewer neutrophils in infected hearts compared to WT mice.

CONCLUSIONS:
These results demonstrate that dietary Mn is an important determinant of S. aureus infection and has significant implications for nutrient supplementation in patients at risk for S. aureus infection. Furthermore, these findings reveal that calprotectin promotes neutrophil accumulation in S. aureus-infected hearts and suggest that neutrophils exacerbate S. aureus replication in this organ.
ML327 Blocks N-MYC Expression and Tumor Formation in MYCN-amplified Neuroblastomas

Eric J. Rellinger, Chandrasekhar Padmanabhan, Brian T. Craig, Hanbing An, Jingbo Qiao, Alex G. Waterson, R. Daniel Beauchamp, Dai H. Chung

OBJECTIVES:
Neuroblastomas (NB) arise from the neural crest and are the most common extracranial solid tumor in children. Epithelial-to-mesenchymal transition (EMT) is heralded by loss of E-cadherin expression and is a critical feature of both neural crest migration and epithelial cancer metastasis. A novel class of chemical probes that reverse EMT in colon cancer cells has been identified through a high-throughput screen of 83,200 compounds. It is posited that NBs arrest in a mesenchymal phase that fails to differentiate. As such, we hypothesized that forced reversal of EMT using the chemical probe ML327 could induce NB differentiation.

METHODS:
We utilized six MYCN-amplified NB cell lines for our initial characterization of ML327. Cellular viability was measured using MTT and clonogenesis assays. Soft agar colony formation was our measure of anchorage-independent growth. Protein and mRNA were quantified by Western blotting and RT-PCR. Cell cycle analysis was completed using propidium iodide and flow cytometry. Murine subcutaneous xenografts were performed to measure tumor-initiating capacity and tumor progression.

RESULTS:
ML327 markedly inhibits the growth of all tested MYCN-amplified NBs in the low micromolar range by inducing G1 cell cycle arrest. Anchorage-independent growth was completely blocked with ML327 treatment. E-cadherin expression in NB cells is induced 24h following treatment with ML327. These changes are preceded by a decrease in N-MYC protein and mRNA levels at 2h, suggesting that N-MYC is an early mediator of ML327-induced arrest. Repression of N-MYC is followed by induction of P21cip1 mRNA (4h) and protein expression. ML327 induces a polarized phenotype in NB cells that is accompanied by decreased neuronal and enhanced Schwann cell marker expression. Pretreatment with ML327 prevented NB xenograft tumor development tumors in mice (p=0.0007) and ML327 treatment arrests growth of established xenografts.

CONCLUSIONS:
The EMT inhibitor, ML327, blocks N-MYC expression, followed by induction of p21cip1 expression and G1 cell cycle arrest. ML327 abrogates NB xenograft growth in mice and is a promising lead compound for the treatment of MYCN-amplified pediatric cancers. Further characterizing its effects on MYC signaling may have broad-reaching implications given the paucity of inhibitors for this critical oncogene family.
New therapeutic approaches for NRAS-mutant melanoma: MDM2, CDK4/6, and MEK inhibitors, alone vs. in combination

Kelsie Riemenschneider, Anna Vilgelm, Andrew Johnson, Ann Richmond

OBJECTIVES:
Up to 20% of melanomas are characterized by NRAS driver mutations, but effective therapies targeting NRAS are not available. We sought to determine the utility of targeting molecules activated downstream of NRAS that would interrupt the oncogene’s effect on tumor growth. Effects of MDM2 (Nutlin3A/CGM097), CDK4/6 (LEE011), and MEK (AZD6244) inhibitors on the growth of NRAS-mutant melanoma were analyzed in vitro and in vivo.

METHODS:
In vitro studies utilized NHEM (normal human melanocytes), C790 (NRAS-mutant mouse melanoma cells), WC00075A and WC00126A (NRAS-mutant human melanoma cells). After determining IC50 values for each inhibitor, cells were treated with vehicle (DMSO), each drug alone, or various combinations for a total of 11 treatment groups. Cell viability was quantified by CellTiter Blue assay and visualized with crystal violet staining. For in vivo experiments, NRAS-mutant melanoma patient-derived xenografts (PDXs) were implanted into athymic nude mice. Mice were randomized into 4 treatment groups (5-6 mice per group): vehicle, MDM2 inhibitor (50 mg/kg), CDK4/6 inhibitor (100 mg/kg), or MDM2 and CDK4/6 inhibitors combined. Drug was delivered daily by oral gavage 5 days/week for 3 weeks. We followed mouse weight and response to therapy based on PDX tumor volumes calculated from microcaliper measurements made twice a week.

RESULTS:
Decreased melanoma cell viability was observed in response to IC50 concentrations of MDM2, CDK4/6, or MEK inhibitors. Notably, viability was further decreased with combined MDM2 + CDK4/6 or MDM2 + MEK treatments. Cell cycle analysis showed that combination therapy induced an increased percentage of cells in G1 and a decreased percentage in S phase, suggesting an induction of G1 cell cycle arrest. Preliminary in vivo experiment data showed that some NRAS-mutant PDXs responded minimally. However, others exhibited up to 90% inhibition of tumor growth with combined therapy, and this was significantly greater than the response to either treatment alone.

CONCLUSIONS:
Our in vitro findings demonstrate that combining an MDM2 inhibitor with either a CDK4/6 or MEK inhibitor resulted in greater induction of cell cycle arrest and more reduced viability of NRAS-mutant melanoma cells than with either drug alone. Furthermore, our PDX experiments suggest that combined use of MDM2 and CDK4/6 inhibitors is more effective than either therapy alone for some NRAS-mutant human melanomas. We are currently working to identify genetic markers that will predict patient responses to this therapy to inform future clinical trials.
Regulatory locus near IL12B confers resistance to tuberculosis in highly susceptible patients

Rafal Sobota, Nuri Kodaman, Sarah Tishkoff, Ford von Ryan, Catherine Stein, Giorgio Sirugo

The immunosuppression resulting from HIV infection increases the risk of progression to active tuberculosis disease (TB), both in patients newly exposed to Mycobacterium tuberculosis (MTB) and in those with latent infections. We hypothesized that HIV-positive patients who do not develop TB despite living in areas where it is hyperendemic provide a model of natural resistance. We performed a genome-wide association study of TB resistance, using 581 HIV-positive Ugandans and Tanzanians enrolled in prospective cohort studies of TB, 267 of whom developed active TB, and 314 did not. A common variant, rs4921437, in locus 5q33.3 was significantly associated with TB (odds ratio = 0.37, p = 2.11 x 10^-8). This variant lies within a region of the genome that includes IL12B and is embedded in an active regulatory region, an H3K27Ac histone mark. The locus also displays consistent patterns of linkage disequilibrium across African populations and has signals of strong selection in populations from equatorial Africa. Along with prior studies demonstrating that therapy with IL12, the cytokine encoded in part by IL12B, associated with longer survival following MTB infection in CD4-T-cell deficient mice, our results suggest that this pathway may be an excellent target for development of new TB treatment modalities, especially for HIV-positive patients. Our results also indicate that studying extreme disease resistance in the face of extensive exposure can increase the power to detect associations in complex infectious disease.
Epigenetic and genetic variation in GATA5 is associated with gastric disease risk

Rafal Sobota, Barbara Schneider, Nuri Kodaman, Keith Wilson, Pelayo Correa, Robertino Merar, Blanca Piazzuelo, Luis Eduardo Bravo, Wael El-Rifai, Alberto Delgado, Douglas Morgan, Scott Williams

OBJECTIVE:
The prevalence of gastric cancer varies considerably among geographic regions with comparable rates of Helicobacter pylori infection, smoking prevalence, and antibiotic availability. We hypothesized that genetic variation plays a role in gastric disease and tested this using a genotyping array with approximately 200,000 SNPs.

METHODS:
We recruited endoscopy patients residing in two regions of Colombia that vary widely in incidence of gastric cancer. We assessed the relationship between immune system-related SNPs to gastric histopathology scores in a Discovery cohort of 130 patients and in an independent Replication cohort of 159 patients. The promoter methylation levels of a gene found to associate with gastric histopathology were quantitated in 189 samples from both cohorts.

RESULTS:
Two synonymous coding SNPs (rs6061243 and rs6587239) in nearly perfect linkage disequilibrium in the GATA5 gene were significantly associated with progression of gastric lesions after correction for multiple testing in a dominant-effects model (b=-0.863, p=2.63E-07; b=-0.815, p=7.97E-07, respectively). In the replication cohort, rs6587239 was significantly associated with histopathology (b=-0.330, p=0.050) using a dominant-effects model, and both rs6061243 and rs6587239 were significant when additively modeled (b=-0.256, p=0.021, and b=-0.239, p=0.029, respectively). Promoter methylation of GATA5 was associated with higher histopathology scores (b=0.028, p=0.001). A multivariate regression model revealed that both GATA5 methylation and the exonic SNPs were independently associated with gastric lesions. A SNP-by-methylation interaction term added to the model was also significant, but presence of this term in the model removed significance of methylation, indicating a non-linear relationship between methylation and genotype.

CONCLUSIONS:
We identified exonic variants in GATA5 that associated with gastric histopathology. Hypomethylation of the GATA5 promoter was also independently associated with gastric histopathology. The significant statistical interaction between the genetic locus and epigenetic state reported here suggests that epigenetic effects on gastric disease progression may vary across genetic backgrounds.
B Lymphocytes Prevent Transplantation Tolerance in NOD Mice by Limiting CD4 Treg Function

Blair Stocks, Chris Wilson, Andrew Marshall, Daniel Moore

OBJECTIVE:
Type 1 Diabetes is a significant barrier to islet transplantation as grafts are subject to both alloimmunity and recurrent autoimmunity. No better is this clinical scenario modeled than the T1D-prone non-obese diabetic (NOD) mouse, a model in which no therapy has ever induced permanent transplant tolerance to islet allografts or any other allograft, indicating the severity of the immunologic barrier. As B lymphocytes play a critical role in T1D progression, I hypothesized that eliminating B lymphocytes would enhance tolerance induction in NOD mice.

METHODS:
Diabetic NOD mice and B cell deficient NOD mice (NODuMT) were transplanted with C3H islets and tolerized with 100ug anti-CD45RB on days 0,1,3,5,7 or left untreated. Rejection was determined by two consecutive blood glucose readings >250mg/dL. To confirm the tolerant state, grafted islets were removed and return to hyperglycemia noted. Hyperglycemic recipients were then retransplanted with matched C3H or 3rd party Balb/c islets and the maintenance of euglycemia noted. Tolerant grafts were analyzed via IHC and lymphocyte populations were evaluated by flow cytometry.

RESULTS:
B lymphocyte deficient NODuMT mice were susceptible to tolerance induction in nearly 100% of recipients. Removal of islet allografts resulted in recurrent hyperglycemia thereby confirming graft function. Whereas retransplant of a matched C3H graft was accepted without further treatment, recipients receiving 3rd party Balb/c islets rapidly rejected these grafts. IHC analyses of tolerant islet allografts demonstrated significant infiltration of protective CD4 T Regulatory Cells (CD4 Tregs), whose expansion by anti-CD45RB therapy was restrained by B lymphocytes. Antibody mediated depletion of graft protective CD4 Tregs prior to islet transplant in NODuMT mice rendered the majority of recipients resistant to tolerance induction.

CONCLUSIONS:
My discoveries 1) represent the first instance in which permanent transplant tolerance has been achieved in NOD mice and 2) highlight the deleterious role that B lymphocyte play in the establishment of transplant tolerance in T1D.
Enhanced IL-6 Production Impedes Transplant Tolerance in Lupus-prone Mice

Blair Stocks, Chris Wilson, Mabel Seto, Andrew Marshall, Daniel Moore

OBJECTIVE:
Autoimmunity is a significant barrier to transplantation. Based on previous studies, it is apparent that there are separate genetic regions that control susceptibility to autoimmunity vs. resistance to transplantation tolerance, but these have been difficult to isolate in polygenic models. I have recently established that B6.SLE123 mice, in which a lupus phenotype is conferred by 3 genetic regions, resist tolerance induction to islet transplants in the absence of any pre-existing islet autoimmunity. Using this congenic model, I have now further traced which genetic regions contribute to tolerance resistance and their mechanisms.

METHODS:
Single congenic B6.SLE1, B6.SLE2, and B6.SLE3 mice were rendered diabetic, transplanted with C3H islets, and treated with the tolerance inducing agent anti-CD45RB (100ug/day, days 0,1,3,5,7). Rejection was determined by two consecutive blood glucose readings > 250mg/dL. Evaluation of the alloresponse was measured via ex vivo and in vivo mixed lymphocyte reactions (MLRs). IL-6 production was assessed via ELISA. IL-6 signaling blockade was achieved by administering 500ug of anti-IL-6R on days -3,-1,1,3 relative to transplant; blockade efficacy was evaluated by phosphoflow cytometry.

RESULTS:
Each single congenic strain resisted anti-CD45RB mediated transplant tolerance induction. Rejection kinetics of B6.SLE1 mice most closely resembled that of triple-congenic B6.SLE123 mice in which no recipients achieved long-term tolerance. Lymphocytes from B6.SLE123 and B6.SLE1 mice demonstrated enhanced alloreactivity during MLRs and enhanced IL-6 production. Administration of an anti-IL-6R blocking antibody reduced IL-6 mediated phosphorylation of STAT3(Y705) and enhanced CD4 T Regulatory Cell (CD4 Treg) expansion. Co-administration of anti-IL-6R with anti-CD45RB resorted long-term tolerance induction to islet allografts in 30% of B6.SLE1 recipients.

CONCLUSIONS:
Analyses of minimal genetic regions from an autoimmune background demonstrate strong effects preventing transplantation tolerance. I relate the function of one of these regions in lupus to increased IL-6. IL-6 signaling blockade may enhance organ engraftment in autoimmunity and lupus.
2015 Clinical Science Abstracts

Page #:
39.  Alexandra M. Foxx, Medical Student
40.  Emily Buittigieg, Medical Student
41.  Eric J. Hall, Medical Student
42.  J. Matthew Kynes, MD, Fellow
43.  Matthew W. Semler, MD, Fellow
44.  Peter Morone, Resident
45.  Christina Marmol, Resident
46.  Petrice M. Cogswell, Resident
47.  Cosby Stone, Jr., MD, MPH, Fellow
48.  Cosby Stone, Jr., MD, MPH, Fellow
49.  Venessa Pinto, Fellow
50.  Caroline Watnick, MD, Fellow
51.  Benjamin Li, Medical Student
52.  John Chen, Medical Student
53.  Sean Rice, Resident
54.  Christodoulos Kaoutzanis, Fellow
55.  Lyly Nguyen, Fellow
56.  Joseph W. Wick, Medical Student
57.  Adrienne Childers, Fellow
58.  Christopher Bowman, Fellow
59.  Michael Ghiam, Medical Student
60.  Colin T. Prather, Medical Student
61.  Scott L. Zuckerman, Resident
62.  Scott L. Zuckerman, Resident
63.  Vaughn Braxton, Resident
64.  Drew A. Long, Medical Student
65.  Drew A. Long, Medical Student
66.  Aaron Yengo-Kahn, Medical Student
67.  Aaron Yengo-Kahn, Medical Student
68.  Ryan Gardner, Medical Student
2015 Clinical Science Abstracts (Cont’d)

Page #:
69. Brian Holt Zalneraitis, BS, Medical Student
70. James Leathers, Medical Student
71. Ashkan Afshari, Fellow
72. Kelly Harms, Medical Student
73. Aamer Imdad, Fellow
74. Cristin Fritz, Resident
75. Adil Faqih, Medical Student
76. Julia Boll, Fellow
77. Kelly Pekala, Medical Student
78. Rob Tauscher, Medical Student
79. Sara Seghezzo, MD, Resident
80. Michael Benvenuti, Medical Student
81. Thomas An and Michael Benvenuti, Medical Students
82. Thomas An, Medical Student
83. Thomas An, Medical Student
84. Ritwik Bhatia, Medical Student
85. Han Shi, Medical Student
86. Amanda Harris, Resident
87. Romany A N Johnpulle, MD, Fellow
88. Gabriel Winberry, MD, Fellow
89. Jeffrey Friedman, Resident
90. Kristy Kummerow Broman, Resident
91. Brian T. Craig, Resident
92. Weston Langdon, Resident
93. Alexandra Ritts, Resident
94. Jaime de la Fuente, Medical Student
95. Julia Boll, Fellow
96. Brian Bingham, Medical Student
97. Jacob Ark, Resident
98. Taylor Coston, Medical Student
99. Han Shi, Medical Student
100. Brian Bingham, Medical Student
101. Justin R. Gregg, Resident
102. Heather N. Grome, Resident
103. Rohini Chakravarthy, Medical Student
104. Ravinder Bamba, MD, Resident
105. Diana G. Douleh, Medical Student
106. Loren E. Smith, Resident
107. Edward Iglesia, Resident
108. Alexander Chern, BS, Medical Student
Decline in Cervical Cancer Screening and Follow-up Procedures in Women <21 years following New Screening Guidelines

Alexandra M. Foxx, Yuwei Zhu, MD MS, Edward Mitchel, MS, Dineo Khabele, MD, Marie R. Griffin, MD MPH

OBJECTIVE:
In 2009, major US cervical cancer screening guidelines recommended no screening for women age <21 years due to concerns that harms of screening and treatment outweighed the benefits in this age group. We examined changes in annual screening and treatment procedures for cervical dysplasia after guideline introduction.

METHODS:
We identified Davidson County women age 18-20 years old enrolled in Tennessee Medicaid (TennCare), 2006-2014 with at least one Pap smear, HPV test, colposcopy, or dysplasia treatment each year via Current Procedural Terminology (CPT) coding. We also counted total numbers of these outcomes annually and estimated yearly costs based on average procedural costs from previous peer reviewed studies, adjusted for inflation using the 2014 medical component of the Consumer Pricing Index (CPI).

RESULTS:
From 2006 to 2014, about 4,000 Davidson County women age 18-20 years were enrolled in TennCare annually: 30.7% non-Hispanic White, 54.8% non-Hispanic Black, 4.5% Hispanic. The percent receiving Pap smears declined from 52.4% in 2006 to 14.2% in 2014 (rate ratio [RR] 0.27, 95% confidence interval [CI] 0.25-0.30), HPV testing declined from 12.8% to 5.4% (RR 0.42, CI 0.36-0.50), colposcopy 8.8% to 0.9% (RR 0.10, CI 0.07-0.14), and dysplasia treatment 1.2% to 0.0%. Rates of all outcomes declined similarly in non-Hispanic Whites and Blacks, and Hispanics. The estimated cost of all screening tests/procedures totaled $602,047 in 2006 and $47,763 in 2014.

CONCLUSIONS:
Since the introduction of new screening guidelines, Pap smears, HPV testing, colposcopy and treatment procedures for cervical dysplasia have decreased in young women. To our knowledge, this is the first study to demonstrate significant reduction in all screening and treatment procedures. The decline in all procedures is consistent with the guideline recommendations, however there is still room for improvement in further reduction of Pap smears, HPV testing and colposcopy. We estimate possible savings of close to $500,000 annually for Davidson County women 18-20 years old enrolled in TennCare. This represents a possible area of cost savings for the health care system. These estimates do not account for changes in visit rates or complications from these procedures.
Assessment of Body Composition in Children with Cystic Fibrosis

Emily Buttigieg

OBJECTIVES:
Compare the accuracy of the investigational BIVA Device in comparison with an FDA cleared device, the Bodystat, in measuring tissue resistance and reactance.
-Assess the use of the investigational BIVA Device in comparison with height and weight to assess nutritional status trends in children with cystic fibrosis over successive clinic visits.
-Assess the use of the investigational BIVA Device in comparison to recorded Ins/Outs and physical exam findings to assess body water status in hospitalized patients.

METHODS:
This prospective cohort study includes children aged 0-18 with cystic fibrosis. Enrolled patients have their tissue resistance and reactance measured by the BIVA device and select patients with the Bodystat device at each visit as well as during any hospitalization. This data is remotely transmitted to a smartphone where it is mapped on a BIVA nomogram for interpretation. This data is compared to recorded height, weight, ins/outs, physical exam findings and clinical nutritional assessment.

RESULTS:
The BIVA device measurements are strongly, directly correlated to the commercially available Bodystat Device with R-squared values of 0.99 and 0.80 for tissue resistance and reactance respectively. In the clinical setting, the BIVA device seems to directly correlate with the standard height and weight measurements used in clinic with the proportion of clinically malnourished patients generally increasing as body cell mass decreases and vice versa. Furthermore, the BIVA device measurements correlated with patients’ nutritional status trends over successive clinic visits. Finally, in hospitalized patients, body water changes, as indicated by recorded Ins/Outs and physical exam findings, directly correlate with trends in BIVA device measurements.

CONCLUSIONS:
The investigational BIVA device is equally accurate in comparison with the FDA cleared device, Bodystat, at measuring tissue resistance and reactance. Both in the outpatient clinic and in the hospital, the BIVA device measurements generally correlate with patients’ clinical assessment of nutritional status. Overall, use of the BIVA device, as indicated in this study, can allow for earlier, more accurate detection of nutritional deficiencies, decreased clinic visits and improved patient outcomes.
Influence of Shunt Type on Ventricular Arrhythmias in Patients with Hypoplastic Left Heart Syndrome

Eric J. Hall, Andrew H. Smith, Frank A. Fish, David P. Bichell, Bret A. Mettler, Kimberly Crum, Prince J. Kannankeril, Andrew E. Radbill

OBJECTIVES:
Hypoplastic left heart syndrome is a severe form of congenital heart disease treated with three stages of surgical palliation. Transplant-free survival for these patients remains <70% at 3 years of life. Arrhythmia burden, associated influence of shunt type at Stage I surgery (right ventricle to pulmonary artery shunt [Sano] versus modified Blalock-Taussig shunt [BTS]) on arrhythmias, and implications for mortality risk are not well defined.

METHODS:
Single center retrospective analysis of patients with single right ventricle lesions (hypoplastic left heart syndrome and anatomic variants) enrolled September 2007-2015 in an ongoing prospective study of arrhythmias after congenital heart surgery.

RESULTS:
Of 120 patients, 58 received Sano and 62 BTS at the time of surgery, with median post-Stage I follow-up of 773 days. The overall arrhythmia incidence was 79%. Amongst all types of arrhythmias, only ventricular arrhythmias (VAs) differed between groups, which were more common in patients receiving Sano (29% Sano vs. 14% BTS, P .049). VAs included 15 with monomorphic VT, 1 polymorphic VT, 3 accelerated ventricular rhythm (AVR) prompting intervention, and 7 AVR untreated. Sano was independently associated with more VAs in multivariate logistic regression (Odds Ratio 2.6, 95% confidence interval [CI] 1.01-6.6, P .048), and lower freedom from VA during follow-up by Cox regression (Hazard Ratio [HR] 2.30, CI 1.02-5.2, P .045) after accounting for other differences in the BTS and Sano cohorts. Although VA did not impact survival among all patients, among interstage survivors to Stage II palliation (n=86), a history of VA conferred >13-fold increased risk of death (HR 13.5, CI 4.2-43, P<.001).

CONCLUSION:
In this cohort, patients with single right ventricle lesions receiving the Sano shunt at the time of Stage I surgery had an increased incidence of ventricular arrhythmias as compared to patients with a Blalock-Taussig shunt. Ventricular arrhythmias may impact late mortality in patients who survive the interstage period to reach Stage II palliation.
An assessment of PACU respiratory events and interventions

J. Matthew Kynes, MD, Carrie Menser, MD, Amanda Lorinc, MD, Summer Fitts, RN, Patricia LeeAnn Inman, RN, Suanne Daves, MD, Scott Watkins, MD

OBJECTIVE:
This study assessed the incidence and types of postoperative respiratory interventions and events, which can contribute to perioperative morbidity and are likely under-reported. Using this data, we hope to identify high-risk patients and procedures to target for improvement.

METHODS:
This was a prospective observational study of pediatric patients admitted to the PACU during one month. Data was collected from standardized reports by bedside PACU nurses as well as chart review and included demographic information and adverse respiratory events (ARE) including PACU respiratory interventions and PACU respiratory events.

RESULTS:
Of 1362 PACU admissions during the study period, 162 had an ARE (11.8%). Patients with an ARE were more likely to have ASA status 3 or above (32.0% vs. 24.1%, p=0.028), and have had ENT surgery (38.8% vs. 21.1%, p < 0.001). Patients without an ARE were more likely to have had GI or general pediatric surgery procedures (10.0% vs 3.0%, p < 0.01). Male patients (55.2% vs. 62.3%, p = 0.08), urology (12.7% vs. 10.5%, p = 0.43) and radiology (12.3% vs. 12.4%, p = 0.9) procedures showed no difference in proportion of ARE.

The 162 patients with ARE had 187 PACU respiratory interventions. Interventions included chin lift after handover (82, 43.8%), positive pressure ventilation (64, 34.2%), oral airway placement (13, 6.9%) and nasal airway placement (10, 5.3%). Twelve pharmacologic interventions were recorded including albuterol (5, 41.7%), racemic epinephrine (4, 33.3%) and propofol (3, 25%). 72 respiratory-specific events were recorded including hypoxia with SpO2<90% (49, 68.1%), upper airway obstruction (21, 29.2%) and stridor (8, 11.1%). Three patients had unplanned admission due to an event.

In the nine months prior to the study the median number of PACU respiratory events reported per month by a computer registry was 15. In the month after data collection event recording increased to 70.

CONCLUSION:
Limited data on postoperative ARE are available. Our event and intervention rate of 11.8% is similar to other reported figures (Mamie C et al. Paediatr Anaesth. 2004) but higher than our current reporting system suggested. Future interventions to reduce events may focus on medically complex and ENT patients, who appear to be at greater risk.
Randomized Trial of Apneic Oxygenation during Endotracheal Intubation of the Critically Ill

Matthew W. Semler, MD, David R. Janz MD, MSc, Robert J. Lentz, MD, Daniel T. Matthews, MD, Brett C. Norman, MD, Tufik R. Assad, MD, Michael J. Noto, MD, PhD, Andrew C. McKown, MD, Emily G. Kocurek, MD, Todd W. Rice, MD, MSc

OBJECTIVES:
Hypoxemia is common during endotracheal intubation of critically ill patients and may predispose to cardiac arrest and death. Administration of supplemental oxygen during laryngoscopy (apneic oxygenation) may prevent hypoxemia. We hypothesized that apneic oxygenation would increase the lowest arterial oxygen saturation experienced by patients undergoing endotracheal intubation in the intensive care unit.

METHODS:
A randomized, open-label, pragmatic trial in which 150 adults undergoing endotracheal intubation in a medical intensive care unit were randomized to receive 15 L/min of 100% oxygen via high-flow nasal cannula during laryngoscopy (apneic oxygenation) or no supplemental oxygen during laryngoscopy (usual care). The primary outcome was lowest arterial oxygen saturation between induction and two minutes after completion of endotracheal intubation.

RESULTS:
Median lowest arterial oxygen saturation was 92% with apneic oxygenation versus 90% with usual care (95% confidence interval for the difference -1.6% to 7.4%; P = .16). There was no difference between apneic oxygenation and usual care in incidence of oxygen saturation < 90% (44.7% versus 47.2%; P = .87), oxygen saturation < 80% (15.8% versus 25.0%; P = .22), or decrease in oxygen saturation > 3% (53.9% versus 55.6%; P = .87). Duration of mechanical ventilation, intensive care unit length of stay, and in-hospital mortality were similar between study groups.

CONCLUSIONS:
Apneic oxygenation does not appear to increase lowest arterial oxygen saturation during endotracheal intubation of critically ill patients compared to usual care.
Development and Global Impact of a Mobile-based Simulator for a Decompressive Hemicraniectomy

Peter Morone, Scott Zuckerman, Michael Dewan, Robert Singer

OBJECTIVE:
Current decompressive hemicraniectomy (DHC) simulators are often expensive to construct, space occupying and not widely accessible. We sought to design a virtual, mobile-based DHC simulator that users could access on a personal handheld device.

METHODS:
A protocol for performing a DHC was devised. Using graphics software a 3D, animated version of the procedure was created. Electronic files were coded into iOS and Android platforms and a mobile application (app) was developed for the Apple App Store and Google Play Store. The DHC module employed tactile feedback to interact with users and was built with learning and test modes. The learning mode consisted of 152 animated steps and taught users how to perform the procedure. The test mode contained 123 multiple-choice questions and tested users on procedural knowledge. User data were prospectively collected from March 15, 2015 to October 21, 2015.

RESULTS:
A free, mobile-based simulator for completing a DHC was created for iOS and Android operating systems. Over a 7-month period, 32,623 users from 6 continents (66% North America, 19% Europe, 9% South America, 4% Asia, 1% Africa and 1% Australia) downloaded the module and spent 7,324 hours in simulation time.

CONCLUSION:
Creation of a mobile-based DHC simulator is achievable. We attained increased usability by making the module straightforward to download, accessible on mobile devices and cost-free. These characteristics make this type of simulator design pertinent to global neurosurgical training.
Perspectives of Latina Women Participating in an RCT Evaluating the Maternal Infant Health Outreach Worker (MIHOW) Program

Christina Marmol, Melanie Lutenbacher, Tonya Elkins

OBJECTIVES:
Many studies show that recruitment of minorities into randomized control trials is difficult. This study identified the motivation of low-income Latina women for participation in the parent RCT. The parent RCT studies the effectiveness the MIHOW home visiting program in Latino populations. MIHOW targets socially and economically disadvantaged pregnant women and provides education about pregnancies and infants, support, and referrals to resources. Latina mothers have higher rates of term births, breast-feeding and healthy parenting practices, but as populations stay in the US longer, these practices disappear and higher rates of obesity, diabetes, and maternal instability emerge. This study provided a qualitative perspective to the quantitative parent RCT, further defining the needs of the women during pregnancy and early infancy.

METHODS:
Women (n=20) were randomly selected from those who had completed the parent RCT. The women were aged 22-41 (M=30.05 years), had been in the US for 3-336 months (M=114.37), and had 0-5 (M=2.11) older children in the home. Each woman completed an individual face-to-face interview in Spanish. A standard set of culturally appropriate questions guided each interview. Field notes were taken, and all interviews were audio taped, transcribed, and translated. Data saturation was achieved after 12 interviews. Content analysis was used to identify themes and subthemes by 3 independent reviewers who met periodically to resolve discrepancies.

RESULTS:
Four major themes emerged: Learning new things, Assimilation into the US, Economic resources, and Sources of emotional/social support. Women endorsed enrolling in the program because of the desire to learn new things, because they were new to the US, or because it had been years since their last pregnancy. Many women, both new to the US and long time residents, spoke of troubles surrounding missing their families and adapting to the US health care system. The needs of most women centered on support: social, emotional, and economic.

CONCLUSION:
Latina women like our participants are eager to enroll in programs like MIHOW that answer their needs through education and access to resources. Findings underscore that Latina women thrive socially, emotionally, and economically from frequent in-home visits during pregnancy and into the early life of their infant.
Intracranial vessel wall and cerebrovascular reactivity imaging in atherosclerotic and non-atherosclerotic stenotic disease

Petrice M Cogswell, L Taylor Davis, Megan K Strother, Carlos C Faraco, Allison O Scott, Lori C Jordan, Matthew R Fusco, Blaise deB Frederick, Jeroen Hendrikse, Manus J Donahue

OBJECTIVES:

Vessel wall imaging (VWI) and cerebrovascular reactivity (CVR)-weighted mapping with MRI may provide a more complete description of structural and functional manifestations of intracranial stenotic disease when used in sequence with lumenography and structural MRI. The purpose of this work is (1) to apply a novel intracranial vessel wall imaging protocol in a group of patients with intracranial stenosis secondary to atherosclerosis and moyamoya disease (non-atherosclerotic stenosis), and (2) to quantify the impact of vessel wall disease on parenchymal impairment as defined by CVR response time and magnitude.

METHODS:

Patients with intracranial stenosis > 50% and extracranial stenosis < 70% underwent high spatial resolution VWI and BOLD imaging using a hypercapnic stimulus. A novel time regression technique was used that allows for CVR time (e.g., time for arteriole endothelium to relax in response to vasoactive stimuli) and maximum CVR (e.g., amount by which arterioles are able to increase cerebral blood flow and volume in response to vasoactive stimuli) to be separately calculated. Blinded review of the vessel wall imaging was performed for lesion determination. CVR time and maximum CVR values were compared (two-tailed Student’s t-test) between vascular territories with vs. without a proximal vessel wall lesion.

RESULTS:

36 patients were studied (16 atherosclerosis, 20 moyamoya). CVR time was significantly prolonged in flow territories with vs. those without a proximal vessel wall lesion for both the atherosclerosis and moyamoya groups. Similar analysis for maximum CVR showed a significant decrease in the moyamoya group but not the atherosclerosis group.

CONCLUSION:

Intracranial vessel wall imaging can depict lesions in patients with intracranial stenosis, and these lesions were shown to correlate with functional changes of cerebrovascular reactivity. Vascular territories with a proximal vessel wall lesion were shown to have a prolonged CVR time in both patient groups. The differences were more marked in the moyamoya group possibly indicative of different mechanisms of endothelial and smooth muscle dysfunction in atherosclerotic vs. non-atherosclerotic disease. Maximum CVR was shown to be significantly decreased in the presence of a vessel wall lesion in the moyamoya patients only, possibly indicating that it is CVR time, rather than overall reactivity, that is impaired in many patients with atherosclerotic disease.
A Three Part Over the Counter Intervention Induces Remission or Improvement in Chronic Oropharyngeal Candidiasis

Cosby Stone, Jr. MD, MPH, Jane Choi, MD

OBJECTIVE:
Oropharyngeal candidiasis is a painful condition with frequent relapses. Antibiotic containing oral products may be a risk factor favoring *Candida* over other species. We sought to determine whether antibiotic containing oral product use is common in patients with recurrent or chronic oropharyngeal candidiasis, and whether a subsequent three part intervention might achieve remission of active candidiasis without needing antifungal therapy.

METHODS:
In 8 patients with oropharyngeal candidiasis demonstrated by physical examination or direct laryngoscopy, we assessed use of antibiotic containing oral care products, inhaled corticosteroids, systemic antibiotics, antibiotic containing oral care products, and the presence of immune suppression. We then discontinued antibiotic containing oral care products, added daily liquid probiotic consumption (kefir yogurt), and encouraged oral rinses with dilute baking soda for two weeks, after which fluconazole or nystatin therapy was added.

RESULTS:
Antibiotic containing toothpaste use was present in 100% of our cases, with triclosan being the most common antibiotic (88%). Use of inhaled corticosteroids (50%), immune suppression (25%) and recent systemic antibiotic use (25%) were also common. 50% of patients achieved resolution of oropharyngeal candidiasis by intervention alone and 50% achieved remission with addition of antifungal medication. 100% reported symptomatic reduction with the intervention. During 9 months of subsequent observation, 4 out of 8 patients were able to tolerate subsequent oral antibiotic exposure without recurrence of oropharyngeal candidiasis, 1 had symptoms return with lower severity, and 3 have not yet required antibiotics. Importantly, two patients who had lived with >2 years of persistent daily candidiasis achieved remission without antifungal treatment.

CONCLUSION:
Use of antibiotic containing oral care products was common in our patients with oropharyngeal candidiasis. Cessation of antibiotic containing oral care products along with addition of probiotic kefir yogurt and rinses with dilute baking soda helped achieve remission or symptom reduction.
Anaphylaxis after Zoster Vaccine: Implicating Alpha-Gal Allergy as a Possible Mechanism

Cosby Stone, Jr. MD, MPH, Jon Hemler, MD, Scott Commins, MD, PhD, Alex Schuyler, BS, BA, Elizabeth J. Phillips, MD, R. Stokes Peebles, Jr. MD, John M. Fahrenholz, MD

OBJECTIVE:
A patient with alpha-gal allergy presented to our clinic for follow up of anaphylaxis after receiving zoster vaccine. We then sought to determine whether alpha-gal antigen was present in five selected vaccines.

METHODS:
First we characterized our case, determining specific IgE antibody levels to various alpha-gal allergy associated antigens. Then, we selected five vaccines (TDaP-Sanofi, TDaP GSK, yellow fever, MMR, and zoster), which all contained mammalian derived products. The latter three vaccines contained increasing amounts of mammalian gelatin, with zoster vaccine containing the most: 15,580 µg of porcine gelatin per dose. We performed direct biotinylation of these five vaccines in repeated samples to assess for direct binding of alpha-gal IgE from serum samples donated by three alpha-gal allergic subjects. Finally, we measured the alpha-gal titers in the donated serological samples from the same three donors and incubated the vaccines with alpha-gal containing sera overnight to evaluate for depletion of alpha-gal IgE.

RESULTS:
Our patient was tested for alpha-gal allergy with galactose-alpha-1,3-galactose IgE of 56.8 kU/L, beef IgE of 22.2 kU/L, lamb/mutton IgE of 13.1 kU/L, pork IgE of 19.8 kU/L, porcine gelatin IgE of 1.84 kU/L, and bovine gelatin IgE at 0.15 kU/L (reference range for all IgE tests <0.35 kU/L). Direct biotinylation revealed low positive binding (values were 0.27 - 0.45 kU/L) for MMR and zoster vaccine in sera from the first two subjects, though our third subject did not demonstrate binding. Incubation of the sera samples from alpha-gal patients with vaccine overnight showed depletion of the alpha-gal IgE response in sera pre-incubated with zoster vaccine and MMR in all three subjects. Both vaccines consistently removed some alpha-gal IgE response upon re-assay. We did not observe epitope binding to alpha-gal IgE with the other vaccines.

CONCLUSIONS:
Zoster vaccine and MMR vaccine, the two vaccines with the highest content of gelatin, both showed direct binding of alpha-gal IgE after biotinylation and depletion of alpha-gal IgE during overnight incubation. Our laboratory findings along with our patient’s clinical history demonstrates the presence of alpha-gal epitope in these vaccines, and that for certain patients with alpha-gal allergy, there is a risk of anaphylaxis. Further research is needed to determine the a priori risk for anaphylaxis to these vaccines for individual patients with alpha-gal allergy.
Brain MRI findings in pediatric patients post ECMO

Venessa Pinto, Sumit Pruthi, Ashly Westrick, Chevis Shannon, Brian Bridges, Truc Le

OBJECTIVE:
Neurologic complications can occur with extracorporeal membrane oxygenation (ECMO) due to a number of factors such as surgical manipulation of blood vessels, systemic anticoagulation, thromboembolic events, thrombocytopenia, and coagulopathies. Prior studies identified neonates as a population with unique neuro-imaging findings and risk factors post-ECMO. The aim of this study is to describe and classify brain MRI findings of pediatric patients treated with ECMO.

METHODS:
We conducted a retrospective study of pediatric patients, 4 weeks to 18 years of age, who underwent a comprehensive brain MRI after ECMO, between January 2000 and July 2015. Patients were identified utilizing a hospital ECMO registry from where demographic and clinical characteristics were extracted. Radiologic findings were independently analyzed by a pediatric neuroradiologist. Descriptive statistics and analyses were performed using SAS 9.4. Statistical analysis was set a priori at p <.05.

RESULTS:
After filtering for inclusion criteria, we identified 51 pediatric patients that underwent a comprehensive brain MRI after ECMO decannulation. In the study cohort, 51% were female, with a median age of 13.5 months (IQR 3-170 mo) and a median ECMO run duration of 6.9 days (IQR 3.8-10.3d). Among indications for ECMO cannulation, 13 (26.5%) were cardiac, 24 (49%) were respiratory and 12 (25%) were ECPR cannulations, with 34 (66%) being VA cannulations. Among the VA ECMO patients, 14 (41%) were transthoracic cannulations. There were 14 patients (28.5%) with an overall incidence of stroke, with 8 patients that had exclusive ischemic strokes, 2 with hemorrhagic strokes and 3 with mixed types of stroke. Of all those with any ischemic strokes, 90% were in the distribution of anterior cerebral circulation, while 60% of all hemorrhagic strokes were in the anterior circulation. The incidence of stroke in patients on VA ECMO was significantly decreased in patients undergoing transthoracic cannulation (7%) as compared to peripheral cannulation (40%, p = 0.05). There was no statistical difference noted between indication for ECMO or mode of cannulation and type of stroke.

CONCLUSIONS:
There is a high incidence of stroke in the pediatric population that could affect neuro-developmental outcomes and quality of life after ECMO. This data will be used to further classify brain lesions and identify risk factors for neurological injury after ECMO and to look for outcome predictors based on neuro-radiologic findings.
Single-dose Oral Dexamethasone is Effective in Preventing Relapse after Pediatric Acute Asthma Exacerbations

Caroline Watnick, MD, Daniel Fabbri, PhD, Donald H Arnold

OBJECTIVE:
To examine relapse rates in a large population of children treated for acute asthma exacerbations during an era of prednisone and prednisolone use compared to an era of dexamethasone use.

METHODS:
Data were extracted from electronic medical records on all patients aged 3-17 years presenting to our urban tertiary care pediatric emergency department from January 2006 to December 2014 with an ICD-9 billing code of (493.00) for acute asthma. We identified patients seen in the emergency department, treated with systemic corticosteroids, and subsequently discharged. Within that group, we identified patients that returned within a 72-hour period with continued asthma symptoms. Patients must have received a corticosteroid during the initial emergency department visit at our institution for study inclusion. Our institutional practice guideline transitioned from prednisone or prednisolone 2mg/kg for 3-5 days to single-dose dexamethasone (0.6mg/kg, maximum 16mg) in the spring of 2014. We used chi-square tests to compare relapse rates for patients receiving oral prednisone or prednisolone to those receiving oral dexamethasone, and multivariable logistic regression to examine for associations of corticosteroid formulation with relapse, adjusted for gender, age, race, ethnicity, and insurance type.

RESULTS:
Amongst 13,518 unique patient visits for asthma there were 183 (1.4%) with relapse. Data from 4,749 (35.1%) patients who received no corticosteroid or an intravenous formulation of corticosteroid were not included in the analysis. We identified 7,130 (52.7%) patients who received oral prednisone or prednisolone and 1,639 (12.1%) patients who received oral dexamethasone. There were 143 (2.01%) relapses among patients receiving oral prednisone or prednisolone and 21 (1.28%) relapses among those receiving oral dexamethasone (p = 0.05), an absolute risk reduction of 0.73% and a relative risk reduction of 36%. No demographic characteristics were associated with relapse in multivariable models.

CONCLUSION:
Single-dose oral dexamethasone is associated with a reduction of emergency department relapse for pediatric patients with acute asthma exacerbations. Though overall relapse rates for both forms of oral corticosteroid are very low, dexamethasone may be the preferred choice in the emergency department management of this population.
The Utilization of Chemotherapy and Radiation at the End of Life in Individuals with Metastatic Non-Small Cell Lung Cancer: Rethinking the Conversation

Benjamin Li, Mark Stavas, MD, Stephanie Perkins, MD, Sharon Phillips, MSPH, Sara Martin, MD, Samantha Hsieh, BS, Eric Shinohara, MD, MSCI

BACKGROUND:
To date, the majority of end of life utilization studies have been single institutional or Medicare-based models. This may lead to significant bias secondary to individual physician preferences, narrow age groups and single payer systems. Here we study more broadly trends and variables impacting the use of chemotherapy (CHT) and radiation (XRT) in the final 60, 30 and 14 days of life in individuals with metastatic non-small cell lung cancer (NSCLC).

METHODS:
The Florida Cancer Data System was used to evaluate individuals with Stage IV (M1) NSCLC between 1995-2010. We determined overall utilization and the association between patient demographics, insurance and socioeconomic status (SES) with CHT or XRT received.

RESULTS:
48,858 individuals met inclusion criteria for analysis. The median age was 69 years and survival 4.8 months. Overall use of XRT decreased from 52% to 37%, while CHT increased from 35% to 49% from 1995 to 2010. 12%, 6% and 2% of individuals received XRT in the final 60, 30 and 14 days of life, while 7%, 4% and 2% received CHT. Neither insurance status (OR, 0.852; 95% CI, 0.721 - 1.174) nor SES (OR, 1.026; 95% CI, 0.950 -1.109) was predictive for XRT received. Low SES (OR, 0.685, 95% CI, 0.633-0.741) and uninsured individuals (OR, 0.678, 95% CI, 0.572-0.804) were less likely to receive CHT. Older-unmarried females were less likely to receive CHT or XRT compared to younger married males.

CONCLUSION:
When examining a broad demographic and insurance mix, the utilization of CHT and XRT in the final 60, 30, and 14 days of life remains relatively low with rates supporting those in previously reported studies. Younger married males were most likely to receive palliative treatments. Insurance and SES did not influence the delivery of XRT, while they did influence CHT utilization.
Risk Factors for Cardiac Toxicities Associated with Proteasome Inhibitor Chemotherapy during Treatment of Multiple Myeloma


OBJECTIVE: Proteasome inhibitors bortezomib and carfilzomib are cornerstone therapies for multiple myeloma. An increased incidence of cardiac adverse events (CAEs) has been reported in patients receiving carfilzomib. However, risk factors for cardiac toxicity remain unclear. Our objective was to evaluate the incidence of CAEs associated with carfilzomib compared with bortezomib and identify risk factors for developing events.

METHODS: This is a retrospective analysis of 96 patients with multiple myeloma who received bortezomib (n=44) and/or carfilzomib (n=52). Patients receiving carfilzomib had significantly more prior lines of therapy.

RESULTS: Bortezomib-associated CAEs occurred in 12 (13%) patients while carfilzomib-associated events occurred in 13 (25%) patients. Cumulative incidence of CAEs was not significantly different between agents. Heart failure was the most common type of event for both bortezomib and carfilzomib (6% and 13%, respectively). By multivariate analysis, male gender was an independent risk factor for developing CAEs. Patients taking antithrombotic agents had a significantly reduced risk of CAEs. Patients with a prior history of cardiac events who were followed by a cardio-oncologist experienced fewer CAEs. Longer duration of proteasome inhibitor use resulted in decreasing risk of CAEs.

CONCLUSION: The incidence of CAEs associated with carfilzomib did not differ significantly from that of bortezomib. Events occurred early in therapy. Male gender was a risk factor for CAEs while use of antithrombotic therapy was a protective factor. These data suggest patients may benefit from antithrombotic therapy and follow-up by a cardio-oncologist while receiving proteasome inhibitor therapy.
Comprehensive patient education on diet prior to outpatient colonoscopy does not improve quality of bowel preparation: A prospective, randomized, controlled trial

Sean Rice, Keith Obstein, Patrick Yachimski, Chris Slaughter, Tina Higginbotham, Melanie Dean

BACKGROUND:
Successful outpatient colonoscopy (CLS) largely depends on quality of a patient’s bowel preparation. While prior studies show education on consumption of the pre-CLS purgative can improve bowel preparation quality, no study has evaluated dietary education alone. We have created an educational patient focused video on pre-CLS dietary instructions.

OBJECTIVES:
To determine if a comprehensive dietary education video pre-CLS improves outpatient bowel preparation quality.

METHODS:
A prospective randomized, blinded, controlled study of patients undergoing outpatient CLS was performed. All patients received a 4 L PEG split-dose bowel preparation and standard institutional pre-procedure instructions. Patients were then randomly assigned to watch either a 4-minute educational video detailing clear liquid diet restriction or to no video. Participants randomized to the video were provided with the video link 48-72 hours prior to colonoscopy, while tracking total number of views. Exclusion criteria were inpatient status, prior colon resection, abnormal imaging, planned therapeutic interventions, or CLS for diagnosis/therapy of GI bleeding/suspected pathology. An attending endoscopist blinded to randomization performed the CLS. The bowel preparation quality was scored using the Boston Bowel Preparation Scale (BBPS) by two nurses who were blinded to the randomization. Adequate preparation was defined as a BBPS total score of 6 with all segment scores greater than 2. Wilcoxon rank sum and Pearson chi-squared tests were performed to assess differences between groups.

RESULTS:
94 patients were randomized (video: n=43; control: n=51) with 47 total video views being tallied. There was no difference between the groups regarding age, gender, race, BMI or prior CLS. There was an increased percentage of patients with an adequate bowel preparation in the video group when compared to the control group; however, this was not statistically significant (74% v. 69%; p=0.54). In addition, BBPS total score (p=0.5) and segment scores (right: p=0.93; transverse: p=0.8; left: p=0.26) were similar between the groups.

CONCLUSION:
The addition of a patient educational video on clear liquid diet alone was insufficient to improve bowel preparation quality when compared to standard pre-procedure instruction at our institution. This study, combined with prior studies, suggests education on diet alone may not impact bowel preparation quality as much as education on the purgative itself.
Incidence and Risk Factors for Major Surgical Site Infections In Aesthetic Surgery: Analysis of 129,007 Patients

Christodoulos Kaoutzanis, Varun Gupta, Julian Winocour, Bruce Shack, James C. Grotting, Kent Higdon, Nishant Ganesh Kumar

OBJECTIVE:

Surgical site infections (SSIs) represent one of the most common postoperative complications in patients undergoing aesthetic surgery. Current literature evaluating SSIs following aesthetic surgical procedures is usually limited to single procedures, single institution or surgeon experiences with small sample size. Our objective was twofold: (1) to determine the incidence of SSIs amongst some of the most commonly performed cosmetic procedures, and (2) to delineate significant risk factors for postoperative SSIs after aesthetic surgery.

METHODS:

A prospectively enrolled cohort of patients who underwent aesthetic surgery between 2008 and 2013 was identified from the CosmetAssure national insurance database. Primary outcome was occurrence of a major SSI requiring emergency room visit, hospital admission, or reoperation within 30 days of the index operation. Univariate and multivariate analysis evaluated potential risk factors for SSIs including age, gender, body mass index (BMI), smoking, diabetes mellitus, type of surgical facility, procedure by body region, and combined procedures.

RESULTS

A total of 129,007 patients were captured in the database, of which 599 (0.46%) were diagnosed with a major SSI. Mean age (43.8±12.4 vs. 40.9±13.9, p<0.01) and BMI (27.3±5.5 vs. 24.3±4.6, p<0.01) were higher for patients with SSIs. Patients with a SSI were more likely to be smokers (10.5% vs. 8.2%, p=0.04) and diabetic (4.5% vs. 1.8%, p<0.01). Females suffered more SSI than males (0.5% vs. 0.3%, p=0.02). Trunk or extremity procedures had a higher incidence of SSI compared to breast or face procedures (0.9% vs. 0.2%, p<0.01). On multivariate analysis, independent predictors of SSI included age (Relative Risk (RR) 1.01), female gender (RR 1.86), BMI (RR 1.07), smoking (RR 1.61), diabetes mellitus (RR 1.58), hospital or ambulatory surgery center procedures (RR 1.39), trunk or extremity procedures (RR 2.42), and combined procedures (RR 1.88).

CONCLUSION:

SSIs following cosmetic surgical procedures are associated with numerous independent predictors, which should be taken into consideration when counseling patients undergoing aesthetic surgery.
Incidence and Risk Factors of Major Complications in Brachioplasty: Analysis of 2,294 Patients

Lyly Nguyen, Varun, Ashkan, R. Bruce, K. Kye, James C.

OBJECTIVES:
Brachioplasty is a popular procedure to correct upper arm ptosis. However, current literature on complications and risk factors is scant and inconclusive. Using a large, prospective, multicenter database, we report the incidence of major complications and risk factors in patients undergoing brachioplasty.

METHODS:
Patients who underwent brachioplasty between 2008-2013 were identified from the CosmetAssure database. The primary outcome was the occurrence of major complication(s), defined as complications requiring emergency room visit, hospital admission, or reoperation within thirty days of the procedure. Risk factors including age, gender, body mass index (BMI), smoking, diabetes, combined procedures, and type of surgical facility were evaluated using univariate and multivariate analysis.

RESULTS:
Within the 129,007 patients enrolled in CosmetAssure, 2,294 (1.8%) underwent brachioplasty. Brachioplasty patients were more likely to be older than 50 years (50.1%), obese (36.3%), diabetic (5.5%), but less likely smokers (5.5%). Major complications occurred in 3.4% brachioplasties with infection (1.7%) and hematoma (1.1%) being most common. Combined procedures, performed in 66.8% cases, had a complication rate of 4.4%, in comparison to 1.3% for brachioplasties performed alone. Combined procedures (RR=3.58), males (RR=3.44), and BMI ≥30kg/m2 (RR=1.92) were identified as independent risk factors for the occurrence of any complication. Combined procedures (RR=12.42), and the male gender (RR=8.89) increased the risk of hematoma formation.

CONCLUSIONS:
Complication rates from brachioplasty are much lower than previously reported. Hematoma and infection are the most common major complications. Combined procedures, male gender, and BMI ≥30kg/m2 are independent risk factors for complications.
Surgical Resection of Intradural Extramedullary Spinal Tumors: Patient Reported Outcomes and Minimum Clinically Important Difference

Joseph B. Wick, Scott L. Zuckerman, Silky Chotai, Clinton J. Devin, Scott L. Parker, David P. Stonko, Andrew T. Hale, Matthew J. McGirt, Joseph S. Cheng

OBJECTIVE:
Patient-reported outcomes (PROs) and quality of life metrics are vital in establishing value of care in spine surgery. Few studies have evaluated PROs among patients undergoing surgery for intradural extramedullary (IDEM) tumors. We sought to provide validity, responsiveness, and minimum clinically important difference (MCID) thresholds in PROs for patients undergoing IDEM tumor resection.

METHODS:
Forty patients enrolled in a single center, prospective, longitudinal registry were analyzed. PROs recorded at baseline, 3-, and 12-months post-operatively included: Oswestry Disability Index (ODI) or Neck Disability Index (NDI), EuroQol-5D (EQ-5D), Short-form-12 item health survey (SF-12), numeric rating scale pain scores (NRS), and North American Spine Society (NASS) satisfaction questionnaire. Responders were those who reported being “much better” or “somewhat better” after surgery on the SF-12 health transition index (HTI). Validity of PROs were assessed with receiver-operating characteristic curves, and differences between standardized response means (SRMs) in responders vs. non-responders were used to determine each PRO’s relative responsiveness. MCID thresholds were derived using the minimal detectable change (MDC) approach.

RESULTS:
Significant improvement across all PROs at 3- and 12-months follow-up was noted. Over 86% of patients were able to return to work, and 85% were satisfied with their outcome. Using the MDC approach, derived MCID thresholds were 13.9 points for ODI/NDI, 0.14 quality adjusted life years for EQ-5D, 2.8 points for SF-12 physical component score (PCS) and 10.7 points for SF-12 mental component score (MCS), 1.9 points for back/neck pain, and 1.8 points for leg/arm pain. PCS was the most accurate discriminator of meaningful improvement (AUC-0.83) and most responsive (SRM-1.36) to postoperative improvement. EQ-5D, ODI/NDI, NRS-BP and LP were all accurate discriminators (AUC-0.7-0.8) and responsive measures (0.97-0.67) of meaningful postoperative improvement. MCS was neither a valid discriminator (AUC-0.48) nor a responsive measure (SRM: -1.5) of outcome.

CONCLUSIONS:
Resection of IDEM tumors provides significant, sustained improvement in quality of life, health, disability, and pain at 12-months following surgery. Surgically resected IDEM-specific clinically meaningful thresholds for PROs reported in this study can accurately discriminate responders and non-responders based on SF-12 HTI for all PROs except MCS.
Infantile Fibrosarcoma of the Sublingual Space: A Rare Entity

Adrienne Childers, Edward Penn

OBJECTIVE:
To review the case of infantile fibrosarcoma (IF) of the sublingual space in a neonate with discussion focused on clinical management of this rare entity.

METHODS:
Case report and literature review.

RESULTS:
A 39 week neonate delivered via cesarean section was initially noted to have significant hemorrhage from a right sublingual mass. After airway was secured with nasal intubation, she was transferred to a tertiary facility for further management. Patient underwent tracheostomy with biopsy of mass on first day of life with preliminary report concerning for hemangioma. Propranolol therapy as well as methylprednisolone were initiated with no significant improvement. On further pathologic evaluation, a spindle cell neoplasm with hemanigopericytoma-like branching vascular channels was seen, and genomic testing revealed trisomy 20 and ETV6-NTRK3 fusion with the diagnosis of IF established. Imaging studies obtained at time of diagnosis did not reveal metastatic disease. Patient was subsequently treated with chemotherapy, radiation therapy and surgical excision of residual mass once it was determined to be adequately resectable.

CONCLUSIONS:
Infantile fibrosarcoma is an uncommon diagnosis in the head and neck region (~9% of cases of IF) and is often misdiagnosed as hemangioma on initial presentation. Once the diagnosis is established, treatment options include primary surgical resection versus chemotherapy +/- radiation with subsequent resection. Other considerations in management of IF include multidisciplinary team approach, genomics and airway management. It is imperative to consider a broad differential diagnosis when evaluating neoplasms of the head and neck given extensive variability in treatment algorithms.
MRI in Recent-Onset Type 1 Diabetes (T1D) Shows Reduced Pancreatic Volume and Altered Pancreatic Microstructure

Christopher Bowman, John Virostko, Jonathan Williams, William Russell, Daniel Moore, Alvin Powers

Recent studies have shown a reduced pancreas volume in adults with recent-onset T1D. Since islets account for only 1-2% of pancreatic mass, this suggests that pancreatic exocrine tissue is also altered in early T1D. These important initial studies did not include children, measured only total pancreatic volume, and did not perform longitudinal measurements in the same individual. To investigate pancreatic volume and microstructure shortly after the onset of T1D, we used a Philips 3 Tesla magnetic resonance imaging (MRI) scanner and advanced quantitative MRI techniques, including apparent diffusion coefficient (ADC), T2 relaxation mapping, and magnetization transfer ratio (MTR), to assess the pancreas in age-matched, healthy controls and individuals with recent-onset T1D (ages 8-35 yrs, avg. 13.2 ± 3.4). The same individual was scanned within 100 days of T1D diagnosis (Dx, avg. 55 d, range 31-98), at 6 months after Dx, and at 12 months after Dx. The MRI scan data from 13 T1D patients within 100 days of T1D Dx and 11 controls showed a trend towards a smaller pancreas volume index (PVI) (T1D vs controls = 0.78 vs 1.04, 25% decrease, p=0.08). Longitudinal pancreatic MRI measurements were reproducible in controls. In two individuals with T1D scanned at the three time points, the PVI was progressively smaller at 6 and 12 months after Dx, while a third individual with T1D displayed similar PVI longitudinally. The ADC, a measure of water diffusion which may reflect cell density, also showed a trend to being higher in T1D (1.45e-3 mm^2/s vs 1.37e-3 mm^2/s, 6% increase, p=0.17), suggesting a decline in cell density. Neither the T2 relaxation time nor MTR were different in the T1D pancreas. These results suggest that children and adolescents with recent-onset T1D have reduced pancreatic volume and altered pancreas microstructure.
Retention in HIV care and viral suppression at the Vanderbilt Comprehensive Care Clinic, 1999-2013

Michael Ghiam, Peter Rebeiro, April Pettit

OBJECTIVE:
Describe the percentage of patients retained and virally suppressed at the Vanderbilt Comprehensive Care Clinic (VCCC), and determine which factors confer risk of being poorly retained or not virally suppressed.

METHODS:
This retrospective observational study followed HIV-1 infected adults in care at the VCCC from 1999-2013. Retention was ≥2 HIV care encounters in the year of interest, ≥90 days apart, using either (A) CD4 or viral load (VL) measurement dates or (B) visit dates. Viral suppression was a VL of ≤200 copies/mL at the last measurement in the year of interest. Modified Poisson regression was used to obtain adjusted relative risks (RR) and 95% confidence intervals (CI) of retention and viral suppression by age, race (White, African American, Hispanic, or Other), sex, and HIV transmission risk (injection drug use [IDU], men who have sex with men [MSM], heterosexual contact [Hetero], or Other).

RESULTS:
Among 4794 patients included throughout the study, 78% were retained and 66% were virally suppressed. Since 2012, the proportion virally suppressed has surpassed the proportion retained (85% vs. 83% in 2012, respectively; p<0.05 for trend). Patients 18-24 (RR=1.2; 95% CI:1.1,1.4) and 25-34 (RR=1.2; 95% CI:1.1,1.3) vs. 35-44 years old, of African American race (RR=1.3; 95% CI:1.2,1.4) vs. White, and with IDU as HIV risk factor (RR=1.2; 95% CI:1.0,1.4) vs. Hetero were at increased risk of not being retained, while MSM (RR=0.8; 95% CI:0.7,0.9) were protected. Similarly, patients 18-24 (RR=1.3; 95% CI:1.1,1.4) and 25-34 (RR=1.2; 95% CI:1.1,1.2) vs. 35-44 years old, of African American race (RR 1.3; 95% CI:1.2,1.3) vs. White, and with IDU as HIV risk factor (RR 1.3; 95% CI:1.2,1.4) were at increased risk of not being virally suppressed.

CONCLUSION:
Retention in care and viral suppression are critical in reducing HIV-associated morbidity and mortality. Prior studies employed cross-sectional models which may have limited ability to identify disparities or describe temporal trends. Because HIV disease burden varies geographically and demographically, appropriate analysis and increased collaboration among local HIV care centers are necessary to identify populations most at risk of poor retention or suboptimal viral suppression. At the VCCC these populations include patients <35 years old, of African American race, and with IDU HIV risk factor. Care visits should be routinely included in retention definitions in future CoC studies.
Sport-related structural brain injury associated with arachnoid cysts: a systematic review and quantitative analysis

Colin T. Prather, Scott L. Zuckerman, Aaron M. Yengo-Kahn, Gary S. Solomon, Allen K. Sills, Christopher M. Bonfield

OBJECTIVE:
Arachnoid cysts (AC) are congenital, intracranial lesions bordered by an arachnoid membrane filled with spinal fluid. ACs demonstrate a higher rate of structural brain injury after trauma. Given the potential consequences of a structural brain injury, we performed a systematic review of sport-related structural-brain injury associated with ACs with a corresponding quantitative analysis.

METHODS:
Titles and abstracts were searched systematically across the following databases: PUBMED, Embase, CINAHL, and PsycINFO. The review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. Peer-reviewed case reports, case series, or observational studies that reported a structural brain injury due to a sport with an associated AC were included. Patients were excluded if they did not have an AC, suffered a concussion without structural brain injury, or sustained the injury during a non-sport-related activity. Descriptive statistical analysis and time to presentation data were summarized. Univariate logistic regression models assessing for predictors of neurologic deficit, open craniotomy, and cysto-peritoneal shunt were completed.

RESULTS:
After an initial search of 994 original articles, 64 cases of sport-related structural brain injury associated with an AC were identified. The median age at presentation was 15 years. Headache was the most common presenting symptom (98%), followed by nausea and vomiting (50%). Open craniotomy was the most common form of treatment (50%). Eight patients (13%) received a cysto-peritoneal shunt. No significant predictors were found for neurologic deficit or open craniotomy. In the univariate model predicting the need for a cysto-peritoneal shunt, the odds of receiving a shunt decreased as age increased (p=0.005, OR=0.61, 95%CI 0.58-0.92). Of the 55% of studies that mentioned an outcome, all were good, and 6% of studies mentioned return to play status.

CONCLUSIONS:
The current systematic review yielded 64 cases of sport-related structural brain injury associated with ACs. The majority of cases presented with chronic symptoms and recovery was reported generally to be good. Though the review is subject to publication bias, we do not find at present that there is contraindication to participate in sports in patients with an AC, although parents and children should be counseled appropriately.
INTRODUCTION:
Sport-related concussion (SRC) has emerged as a public health problem, especially among student-athletes. Whereas most concussions resolve by two weeks, a minority of patients experience post-concussion syndrome (PCS), with persistent symptoms for months. The objective of our study was to elucidate predictive factors of PCS among a sample of NCAA student-athletes from the 2009/10 to 2014/15 academic years.

METHODS:
SRC data originated from the NCAA Injury Surveillance Program (ISP) during the 2009/10-2014/15 academic seasons. The NCAA ISP is a prospective database made up of a convenience sample of schools across all divisions. All SRCs are reported by certified athletic trainers (ATs). The PCS group consisted of concussed individuals with concussion-related symptoms lasting 4 weeks or longer. The non-PCS group consisted of concussed individuals with symptom resolution ≤2 weeks. Individuals with symptoms resolving in the intermediate area of 2-4 weeks were excluded. Logistic regression estimated adjusted odds ratios (OR).

RESULTS:
During the 2009/10-2014/15 seasons, 1507 individuals reported concussions were sustained among NCAA athletes. One hundred and twelve (7.4%) individuals had PCS (i.e., concussion-related symptoms lasting ≥4 weeks). Men’s ice hockey contributed the largest proportion of individuals to the PCS group (28.6%), whereas men’s football made up the largest proportion of individuals in the non-PCS group (38.6%). In multivariate analysis, recurrent concussion was associated with increased odds of PCS (OR=2.08, 95%CI 1.28-3.36). Concussion symptoms also associated with increased odds of PCS included: retrograde amnesia (OR=2.75, 95%CI 1.34-5.64), difficulty concentrating (OR=2.35, 95%CI 1.23-4.50), sensitivity to light (OR=1.97, 95%CI 1.09-3.57), and insomnia (OR=2.19, 95%CI 1.30-3.68). Contact level, gender, and loss of consciousness were not associated with PCS.

CONCLUSION:
PCS represents one of the most impactful sequelae of SRC. In this study of exclusively collegiate student-athletes, we found recurrent concussions and various concussion-related symptoms were associated with PCS. The identification of initial risk factors for the development of PCS may assist sports medicine clinicians in timely interventions and treatments to prevent morbidity and shorten recovery time after SRC.
Mechanisms of injury as a predictor of sport-related concussion severity in football, basketball, and soccer: Results from a regional concussion registry

Scott L. Zuckerman, Douglas J. Totten, Kolin E. Rubel, Andrew W. Kuhn, Aaron M. Yengo-Kahn, Gary S. Solomon

OBJECTIVES:
The objectives of the current study were: 1) to provide a descriptive analysis of mechanisms of sport-related concussion (SRC) in football, basketball, and soccer; and 2) to determine if mechanism of injury was associated with symptom duration.

METHODS:
A retrospective cohort study was conducted through patient interviews from the Vanderbilt Sports Concussion Center (VSCC) outcomes registry. From 2012 – 2015, 941 patients were seen, 699 of which were eligible for inclusion. Complete data were collected for 295 patients (42%). Mechanism of injury was divided into 3 domains: 1) contact mechanism (what initiated contact with the athlete’s head); 2) player mechanism (the sport specific action the concussed athlete was performing); and 3) awareness mechanism (whether the athlete was aware of the oncoming collision). Mechanisms were compared via One-Way Chi-Square ($\chi^2$) Analyses For Goodness of Fit. Kaplan-Meier plots and Cox Proportional Hazards models were run to estimate the relationship between our exposure (concussion mechanism) to the time variable outcome (days of symptom duration). Covariates were controlled for using propensity score analysis.

RESULTS:
A total of 92 football players, 42 basketball players, and 47 soccer players were included. Seventy percent of athletes were males. Within the contact mechanism, the most common mechanisms were helmet-to-helmet contact in football (74%), elbow-to-head in basketball (35%), and player (non-head)-to-head in soccer (33%). Within the player mechanism, tackling (33%) and blocking (32%) were most common in football, rebounding (45%) and defense/loose-ball (33%) were most common in basketball, and loose-ball (44%) and heading (40%) were most common in soccer. In the awareness mechanism, being unaware of the oncoming collision was associated with a 2.54 times increase in the hazard of not achieving asymptomatic status.

CONCLUSION:
Several themes arose in the current study of concussion mechanisms across a regional SRC outcomes registry: (1) a helmet-to-helmet collision was the most common contact mechanism in football; (2) ground and surrounding equipment and player elbows caused the majority of basketball concussions; (3) challenging a player, fighting for a loose-ball, and heading (not necessarily with ball contact) were proportionally the most common mechanisms of SRC in soccer; and (4) “awareness” of an oncoming collision in soccer was the only sports mechanism that decreased the risk of prolonged symptom recovery.

*Vaughn Braxton, Paula Donahue, Rachelle Crescenzi, Allison Scott, Manus J. Donahue*

**OBJECTIVES:**
To determine whether MRI can provide additional quantitative information not available from conventional measures of lymphatic compromise in patients with breast-cancer-treatment-related lymphedema (BCRL) and if MRI can be used to evaluate response to standard-of-care manual lymphatic drainage (MLD) therapy.

**BACKGROUND:**
BCRL affects 20-30% of women following breast cancer with lymph node dissection, resulting in increased medical costs and requiring lifelong management. BCRL is partially managed with MLD, yet uncertainty remains regarding optimal initiation and frequency of therapy.Insensitive imaging methodologies and conventional metrics are barriers to addressing these concerns. Developing a reproducible imaging protocol may provide a tool for diagnosis and individualized BCRL treatment.

**METHODS:**
Healthy controls (n=25; age=23-74yrs) and unilateral BCRL (n=15; age=33-77yrs) participants were scanned at 3T with multiparametric MRI. Volunteers underwent bilateral measures of upper limbs by perometry, tissue dielectric, and bioimpedance spectroscopy. Measurements were performed immediately before and after a 50 min MLD session. Deep tissue regions of interest over the upper arm were identified for analysis of T2 relaxation times. Internal comparison to unaffected extremities and to healthy controls was performed using a Wilcoxon signed-rank test.

**RESULTS:**
Non-MRI metrics showed no significant changes before vs. after MLD. Mean combined upper extremity deep tissue T2 for controls was 36.7±0.2 ms compared to 36.9±0.3 ms for the affected arms of patients. In comparing deep tissue T2 of affected to unaffected extremities, there was no significant difference either before or after MLD. However, a significant T2 increase for the unaffected extremities following MLD (36.5±0.2ms vs. 39.4±0.3ms; p<0.01) and a trend for increased T2 in affected arms following MLD was observed (36.9±0.3ms vs. 38.6±0.3ms; p=0.07).

**CONCLUSION:**
Significant increase in T2 relaxation times in the extremities of BCRL patients may indicate a mechanism of lymphedema mobilization via collateral lymphatics or changes in local chemical environment (e.g., sodium or histamine release). Ongoing work that incorporates chemical and multi-nuclear imaging is focused on understanding these effects. The long-term goal is to develop imaging biomarkers of lymphatic dysfunction that can be used for clinical trial endpoints.
Evaluating the Quality of Life and Functional Outcomes of Patients with Diffuse Axonal Injury Post Traumatic Brain Injury

Drew A. Long, Mayur B. Patel, Jonathan C. Siktberg, Miya A. Smith, Taylor C. Leath, Laura D. Wilson, Aashim Bhatia

OBJECTIVE:
The presence of Diffuse Axonal Injury (DAI) is broadly associated with poor outcomes in patients suffering from traumatic brain injury (TBI). However, this relationship is not well understood, nor is the prognostic value of identifying DAI on MRI or CT. The purpose of this study is to compare long-term quality of life and functional outcomes between patients with and without radiological evidence of DAI. Furthermore, we aim to correlate long-term outcomes to lesion location and severity.

METHODS:
Participants included in this retrospective cohort study were patients age ≥ 18 who suffered a TBI and received a brain MRI and/or CT within 2 weeks of admission at Vanderbilt University Medical Center (VUMC) between January 1, 2000 and June 30, 2013. The Extended Glasgow Outcome Scale (GOSE) and Quality of Life After Brain Injury—Overall Scale (QOLIBRI-OS) were conducted on eligible patients who agreed to participate in order to assess the primary outcomes of quality of life and functional outcomes in patients post-TBI.

RESULTS:
Follow-up was completed on 122 patients; 68 were DAI positive while 51 were DAI negative. The mean GOSE was 5.71 in the DAI positive group compared to 6.35 in the DAI negative group. Univariate statistical analysis of QOLIBRI scores showed that the DAI negative group had significantly higher QOLIBRI than the DAI positive patients. These models will be adjusted for the following covariates: age, sex, time post TBI, Injury Severity Score, Glasgow Coma Scale, and Marshall Class.

CONCLUSION:
Preliminary unadjusted results point towards worsened functional outcomes and quality of life in the DAI positive group compared to the DAI negative group. These results agree with previous literature suggesting worsened outcomes in patients with radiological evidence of DAI. To complete the data analysis and the results, the radiologists involved in this study must first interpret the remaining MRI and CT scans. Once the MRI and CT scans are read, the DAI positive cohort can be stratified into the severity and location of DAI to further specify our results before we carry out biostatistical analysis.
ICU Antioxidant supplementation and atrial arrhythmias

Drew A. Long, Susan Hamblin, Paul Moore, Jonathan Pouliot, Judith M. Jenkins, Wei Wang, Ram-eela Chandrasekhar, Mayur Patel

OBJECTIVES:
Antioxidant supplementation may improve outcomes in intensive care unit (ICU) patients, and may decrease atrial arrhythmias. The purpose of this study is to determine if the incidence of atrial arrhythmias is reduced in ICU patients receiving high-dose antioxidant supplementation. We hypothesize that ICU antioxidant supplementation decreases the incidence of atrial arrhythmias.

METHODS:
In this retrospective pre-post study, injured patients ≥18 years of age and admitted to a single-center ICU for ≥48 hours were eligible for inclusion. The control group consists of patients admitted from January 2000 to September 2005, prior to antioxidant supplementation. The antioxidant group consists of patients admitted from October 2005 to June 2011 who received an antioxidant protocol for ≥48 hours. The primary outcome is the incidence of atrial arrhythmias in the first two weeks of hospitalization or prior to discharge. Secondary outcomes include the time from admission to arrhythmia occurrence and in-hospital mortality.

RESULTS:
Of the 4,699 patients, 1,622 patients were in the antioxidant group and 2,414 patients were in the control group. Adjusted for age, sex, year, injury severity, past medical history (hypertension, myocardial infarction, coronary artery disease, cardiac surgery, and congestive heart failure) and medication administration (beta-blockers, amiodarone, diltiazem), the unadjusted incidence of atrial arrhythmias was 3.02% in the antioxidant group versus 3.31% in the control group, with no adjusted difference in atrial arrhythmias among those exposed to antioxidants (OR: 1.31 [95% CI: 0.46, 3.75], P = 0.62). The expected adjusted survival time of patients in those without antioxidant therapy was lower than those receiving antioxidant therapy (OR = 0.65 [95% CI: 0.43, 0.97], P = 0.04).

CONCLUSIONS:
ICU antioxidant supplementation did not decrease the incidence of atrial arrhythmias nor alter the time from admission to development of arrhythmia. A longer expected survival time was observed in the antioxidant group compared to the control group.
OBJECTIVE:
Over the last two decades, sport-related concussion (SRC) has garnered significant attention. Even with increased awareness and athlete education, sideline recognition and real-time diagnosis remain crucial. The need for an objective and standardized assessment of concussion, led to the eventual development of the Sideline Concussion Assessment Tool (SCAT) during the second International Conference on Concussion in Sport in 2004, which is now in its third iteration (SCAT3). In an effort to update our understanding of the most well known sideline concussion assessment, we conducted a systematic review of the SCAT and the evidence supporting its use to date.

METHODS:
English-language titles and abstracts published between 1995 and October 2015 were searched systematically across four electronic databases and a review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines, adapted for the review of a heterogeneous collection of study designs. Peer-reviewed journal articles were included if they reported quantitative data on any iteration of SCAT, Standardized Assessment of Concussion (SAC) or modified Balance Error Scoring System (mBESS) data at baseline or following concussion in an exclusively athlete population with any portion aged >13. Studies which included non-athletes, only children <13 years-old, exclusively BESS data, exclusively symptom scale data, or a non-SCAT related assessment were excluded.

RESULTS:
The database search process yielded 549 abstracts and 105 full-text articles were reviewed with 36 meeting criteria for inclusion. Nineteen studies were associated with the SAC, one was associated with the mBESS exclusively and sixteen studies were associated with a full iteration of the SCAT. The majority of these studies were prospective cohort studies (53%). Male football players were the most common athletes studied. An analysis of the studies focused on baseline differences associated with age, gender, concussion history, and the ability to detect a SRC.

CONCLUSION:
Looking towards the upcoming Concussion in Sport Group meeting in 2016, one may expect further revision to the SCAT3. However, based on this systematic review, we propose further, in-depth study of an already comprehensive concussion test, with acute, diagnostic as well as long-term use.
Player Performance After Returning From Concussion in the National Football League (NFL): A Pilot Study

Aaron Yengo-Kahn, Scott L. Zuckerman, Weston Gentry, Romil D. Patel, Andrew W. Kuhn, Gary S. Solomon

OBJECTIVE:

Little is known about player performance after concussion in the National Football League (NFL). The objective was to explore the impact of sports-related concussion (SRC) on player performance after return to play among NFL players.

METHODS:

A retrospective, case-control study was conducted. A comprehensive list of all NFL players who suffered concussions from 2007-2014 (7 seasons) was compiled from publically available sources (mostly sports websites such as nfl.com and fox.com). A 2:1 matched control group was formed based on position, age, BMI, experience, and missed games. Players were excluded if they did not have 3 games prior to concussion/absence and 3 games post-concussion/absence. To assess change in performance, two analyses were performed for each position group: 1) intra-player analysis using univariate analysis of covariance (ANCOVA), and 2) inter-player analysis, comparing cases to controls using linear regression with multiple covariates.

RESULTS:

A total of 932 NFL players with concussion were collected from 2007-2014. A final cohort of 122 concussed were included as cases. Offense: the following cases: controls were obtained for each position: QB (9:18), RB (10:20), WR/TE (26:52), OL (21:42). Within the intra-player analysis, the only significant difference was yards/reception among WR/TE declining after concussion (p=0.049). The inter-player analysis revealed no significant differences. Defense: the following cases/controls were obtained for each position: DL (14:28), LB (9:18), CB/S (38:76). Neither the intra-player nor inter-player analysis revealed any pre- to post-concussion differences in player performance.

CONCLUSIONS:

In a pilot study assessing residual effects of SRC in NFL players upon return to play, only 1 of 78 intra- and inter-player comparisons revealed a decline in game performance (yards/reception among WR/TE). This study serves as a preliminary analysis in assessing the short-term effects of SRC in professional football.
Publication and Level of Evidence Trends of the Sport-Related Concussion Literature Published Between 2005 and 2015 in the American, British, and Clinical Journals of Sports Medicine

Ryan Gardner, Andrew W. Kuhn, BA, Brian H. Zalneritis, BS, Andrew T Hale, BA MSc, Scott L. Zuckerman, MD, Gary S. Solomon, PhD

OBJECTIVE:
Recent public responses to sport-related concussion (SRC) research include policy implementation, litigation, and perhaps a decrease in youth sports participation. Ideally, these responses are evidence-based. However, the SRC literature has yet to be characterized in relation to evidence-based medicine. This paper evaluates the SRC literature published over the last decade in the American (AJSM), British (BJSM), and Clinical (CJSM) Journals of Sports Medicine.

METHODS:
SRC studies published in AJSM, BJSM, and CJSM between January 1, 2005 and December 31, 2014 were collected for analysis. Two independent reviewers recorded the study design, subject matter, country of the corresponding author, financial funding, and conflicts of interest and level of evidence (Oxford criteria) for each study. To assess outcome measures, studies were grouped into two 5-year interval time periods and proportions were analyzed via chi-square ($\chi^2$) contingency tables.

RESULTS:
Over the last decade in these three journals, the number of SRC publications increased significantly, ($\chi^2=12.571$, df=1, $p<0.001$) particularly in the United States. ($\chi^2=20.745$, df=11, $p=0.036$) Conflicts of interest ($\chi^2=8.829$, df=1, $p=0.003$) and financial funding also increased substantially ($\chi^2=13.188$, df=1, $p<0.001$) with a greater proportion of higher-level studies receiving funding. ($\chi^2=14.687$, df=2, $p<0.001$) The overall level of evidence for the SRC literature [3.30 (±1.12)] did not increase in strength. ($t=0.24$, df=130, $p=0.81$) Study designs did not change and only 3 randomized controlled trials were published. ($\chi^2=7.391$, df=7, $p=0.389$)

CONCLUSION:
Efforts should be made towards continuing to fund and pilot studies with stronger, more robust experimental designs and methodology.
Performance Following Concussion Among National Basketball Association Players

Brian Holt Zalneraitis, BS, Aaron M. Yengo-Kahn, BS, Scott L. Zuckerman, MD, Jeff Stotts, MAT

OBJECTIVE:
Basketball is a physical game played on a hardwood floor among high-jumping athletes at risk for injury. It is currently unknown how sports-related concussion (SRC) affects player performance after injury among professional basketball players. The objective of this study is to explore the impact of SRC on basketball performance among National Basketball Association (NBA) players.

METHODS:
We performed a retrospective, archival cohort study that compared NBA player performance following concussion to pre-concussive performance. A comprehensive NBA injury database, compiled from publically available sources, was queried for NBA players who suffered concussion from 2005-06 to 2014-15 (10 seasons). Intra-and inter-player analyses were performed against a matched control group of players who missed time for personal reasons.

RESULTS:
Following application of inclusion/exclusion criteria and a matching process, 51 concussed players and 51 control players were included in analysis. There were no statistically significant decrements in baseline to post-concussion performance metrics in intra-player or player vs. control after 5 return games. After 20 return games concussed players demonstrated a statistically significant decrease in “plus/minus“ from baseline (-1.65 vs. 1.61, p=.023) and compared to control players (-1.65 vs 3.31, p=0.001).

CONCLUSIONS:
Our findings suggest that at the NBA level, an athlete’s initial post-injury 5 game performance does not suffer from the after-effects of concussive
A Retrospective Analysis of Patients With Systolic Left Ventricular Heart Failure Following Participation in Glial Growth Factor 2 Phase 1 Clinical Trial

James Leathers`, Trafina Jadhav, Daniel Lenihan

OBJECTIVES:
Patients diagnosed with systolic left ventricular dysfunction and symptomatic heart failure, were enrolled in a single dose Phase I study conducted at Vanderbilt University Medical Center. Some of these patients experienced a transient improvement in ejection fraction following a single treatment with GGF2. This study represents the first study to assess long-term benefits and risks of single-dose GGF2 administration.

METHODS:
Patient follow-up was performed using information from phone interviews and electronic medical records. Data collected included age, race, gender, living status, total number of hospitalizations, time to first hospitalization, total number of heart procedures, GGF2 or placebo administration status and the drug dosage administered.

RESULTS:
The mean follow-up time was 49.62 months (~4 years) from drug or placebo administration. Of the total 30 patients enrolled in the study 19 (66.6%) received varying dose of GGF2 and 11 (33.33%) received the placebo. Patients were randomized to GGF2 or placebo in 7 ascending dose cohorts. Of those receiving GGF2, 5 (26.3%) received 0.007mg, 3 received 0.021mg (15.8%), 4 received 0.063mg (21.05%), 1 received 0.189mg(4.76%), 2 received 0.378mg (10.52%), 1 received 0.756mg (4.76%) and 2 received 1.512mg (10.52%). At the 4 year follow-up, 73.6% (14/19) of the GGF2 patients were alive compared to 100% (11/11) of the placebo patients. GGF2 patients had a mean number of total hospitalizations per patient of 4.00, compared to 3.64 for placebo patients. GGF2 patients had a mean of 10.17 months till first hospital admission, compared to 19.75 months for placebo patients. GGF2 patients underwent on average 0.684 total heart procedures compared to 0.636 for placebo patients. Females, regardless of treatment, had an average of 4.13 hospitalizations per patient, compared to 2.82 for males. Females, regardless of treatment, had a time to first hospitalization of 7.36 months, compared to males 12.35 months.

CONCLUSION:
These data suggest that GGF2 is associated with higher incidence of death, earlier mean time till first hospital admission and mean number of hospitalizations when compared to placebo. Regardless of treatment, women were had earlier time to first hospitalization and higher number of mean hospitalizations, compared to males. More long-term studies should be performed to further assess the safety of GGF2.
2.5% Mafenide Acetate: A Cost-Effective Alternative to the 5% Solution for Burn Wounds

Ashkan Afshari, Lyly Nguyen, Steven Kahn, Blair Summitt

OBJECTIVES:
Mafenide acetate is an antimicrobial agent used to decrease bacterial load in significant full thickness burns, burns over cartilage, and/or over post- burn excision mesh autografts. In-vitro studies have demonstrated equal efficacy of 2.5% mafenide acetate compared to higher concentrations. Despite this, the 5% concentration is more commonly used and is double the cost of its 2.5% counterpart. This study aims to evaluate outcomes and costs associated with the use of 2.5% versus 5% mafenide acetate formulation.

METHODS:
Adult patients (≥18 years) receiving 2.5% mafenide acetate during an eleven-month period between 2014 and 2015, corresponding to a policy change in favor of the use of 2.5% mafenide acetate, were queried. Historical controls, patients receiving 5% mafenide acetate, were also reviewed during an eleven-month period between 2013 and 2014. Exclusion criteria included: pediatric patients, non-burn, infection prior to mafenide therapy, and those who received both concentrations of mafenide. A retrospective review was performed comparing outcomes and the cost of mafenide therapy between the two groups. The primary outcome evaluated was wound infection, while secondary outcomes included bacteremia/sepsis, pneumonia (PNA), duration of mafenide therapy, hospital length of stay (LOS), and mortality.

RESULTS:
A total of 107 patients received 2.5% mafenide acetate solution and 137 patients received the 5% concentration. After exclusion, 54 and 65 patients were included in each group, respectively. The mean age among the 2.5% group was 45.06 versus 54.11 (p=0.009), while there was no difference in gender, diabetes, tobacco use, BMI or TBSA burn. There was no difference in wound infection (31.5% vs 29.2%, p=0.84), bacteremia/sepsis (24.1% vs 29.2%), PNA (16.7% vs 24.6%), duration of treatment (10.69 days vs 12.82 days), LOS (18.35 days vs 22.23 days), and mortality (9.3% vs 15.4%) between the two groups. Candida and Staph species were the two most common isolates in the 2.5% group, while Pseudomonas and Staph species were the most common in the 5% arm. The mean cost of 2.5% mafenide therapy was $2115.11 compared to $5270.03 for 5% mafenide acetate.

CONCLUSIONS:
The 2.5% mafenide acetate solution is a cost-effective alternative to the 5% concentration without increasing wound infection rate, bacteremia/sepsis, PNA, LOS, duration of mafenide therapy, or mortality.
Excessive Postoperative Narcotic Prescriptions Contribute to Aberrant Opioid Behavior in Pediatric Orthopaedic Patients

Kelly Harms, Jeff Martus, MD

OBJECTIVES:
The purpose of this study was to determine the amount of narcotics prescribed postoperatively in pediatric orthopaedic patients and to assess the incidence of aberrant opioid behavior.

METHODS:
After IRB approval, data was retrospectively collected from patients aged 3 months to 18 years who were seen between January 1, 2013 and June 30, 2015 and underwent one of 25 common pediatric orthopaedic procedures. Patient demographics, including mental health diagnoses, procedure type and length of stay, narcotics in the pre-, intra-, and postoperative periods, refill requests, complications, postoperative pain phone calls, and aberrant opioid behaviors were recorded. Patient’s narcotics prescriptions in the preoperative and postoperative period were recorded using the Tennessee Controlled Substance Monitoring Database (CSMD).

RESULTS:
Ten patients were reviewed from each of the 25 procedures (n=250). The average age was 10.9 years (range 0.5 to 18, SD=4.9) and 58.8% were male. Mental health diagnoses (MHD) were seen in 13.1% of patients. The most commonly prescribed narcotic at discharge was hydrocodone-acetaminophen (91.2%). The average number of discharge doses by procedure ranged from 29.8 to 84.4 doses. Within each individual procedure, the range of discharge doses varied widely. The average narcotic dose by weight was 0.101 mg/kg (SD=0.016) with substantial variation per procedure. Overall, 16.8% of all patients showed at least one aberrant opioid behavior (AOB). The most common AOBs observed were seeing multiple physicians for pain medication (10.8%), obtaining pain medication from the emergency department (6%), and claiming to have lost pills or prescriptions (2%). Patients with MHD were more likely to exhibit AOB (21.2% vs. 16.2%, p=0.47), though this difference was not statistically significant. A greater mean number of discharge doses was significantly associated with an increased risk for AOB (60.5 vs. 51.1, p=0.05).

CONCLUSION:
This study showed that prescriptions given at discharge varied considerably within and between each procedure. This is most likely due to the fact that physicians do not have guidelines outlining the proper amount of narcotics to prescribe. The patients in this study who exhibited aberrant opioid behavior were prescribed significantly more narcotics at discharge, suggesting that excessive narcotic dosing may be an exacerbating factor which contributes to this concerning behavior.
Can telephone be used for promotion and support of breastfeeding? A meta-analysis

Aamer Imdad, Uzma Rani, Sari Acra

OBJECTIVE:
To assess the effectiveness of breastfeeding counseling given via telephone to promote breastfeeding.

METHODS:
A literature search was conducted on PubMed, Cochrane library, WHOLIS, African Index Medicus, LILACS and Central register of trials. No limits were applied to language or date of publication. Last date of literature search was November 12, 2015. Only randomized trials were included. Data were abstracted into an excel sheet and a meta-analysis were performed. Primary outcomes were exclusive breastfeeding at 4-6 weeks and 6 months. Secondary outcomes were any breastfeeding and predominant breastfeeding. The quality of evidence was graded according to the GRADE criteria.

RESULTS:
A total of 23 studies were included in the review. There was a significant increase in the rates of exclusive breastfeeding [relative risk (RR) 1.14 (95 % confidence interval (CI) 1.07-1.21, quality of evidence: moderate] and any breastfeeding [RR 1.07 (95 % CI 1.03-1.10) quality of evidence: moderate] at 4-6 weeks postpartum in those receiving the intervention compared to controls. A similar effect was noticed at 3-4 months postpartum; however, the effect size was decreased at 6 months.

CONCLUSIONS:
Breastfeeding counseling given via telephone could be helpful to increasing rates of breastfeeding in early postpartum period. Telephone counseling is advantageous as it can reduce access barriers, transportation costs and childcare costs and can be an effective way to reach many more breastfeeding mothers than finding the human resource to do the same.
Comprehensiveness of Care Provided at Global HIV Treatment Sites in the IeDEA Network: 2009-2014

Cristin Fritz, C. William Wester, Mary Lou Lindegren, Meridith Blevins

OBJECTIVES:
An important determinant of the effectiveness of HIV care and treatment programs is the capacity of sites to implement recommended services and to identify systematic changes needed to ensure that resources invested in HIV translate into improved patient outcomes. We conducted a survey in 2014 of all HIV care and treatment sites in the 7 regions of the International epidemiologic Database to Evaluate AIDS (IeDEA) collaboration to evaluate facility characteristics, HIV prevention, care and treatment services provided, laboratory capacity, and trends in the comprehensiveness of care compared to data obtained in the 2009 baseline survey.

METHODS:
Clinical staff from 262 adult treatment sites in 45 countries in IeDEA completed a site survey from September 2014 to January 2015, including Asia Pacific (n=50), Latin America and the Caribbean (n=11), North America (n=45), Central Africa (n=17), East Africa (n=36), Southern Africa (n=87), and West Africa (n=16). For the 55 sites with complete data from both the 2009 and 2014 survey, we evaluated change in comprehensiveness of care.

RESULTS:
The majority of the 262 sites (61%) offered all seven essential services (antiretroviral therapy adherence, nutritional support, PMTCT, CD4+ cell count testing, Tuberculosis screening, prevention, and outreach). Comprehensiveness of care services significantly increased across all regions from 2009 to 2014 (p < 0.001). Sites offering all services were most often in an urban setting, publicly-funded, cared for adults and children, and received PEPFAR support. CD4+ count testing was universally available but offered onsite by only 62% of clinics. Approximately two thirds (69%) of sites reported having viral load testing routinely available, with only 39% having it on site. The capacity to monitor antiretroviral-related toxicity and diagnose opportunistic infections varied widely by testing modality and region.

CONCLUSION:
The ability of sites to provide comprehensive care increased substantially over the past 5 years and was related to locale (urban) and type of funding received (publicly funded and PEPFAR supported). However, the availability of viral load monitoring remains suboptimal and should be a focus for site capacity, particularly in East and Southern Africa, where the majority of those being initiated on ART reside.
Frequency of endoscopic surveillance for Barrett's esophagus is not influenced by urban-rural designation: results from a large database analysis

Adil Faqih, Patrick Yachimski, MD, Benjamin Poulose, MD, Kristy Kummerow, MD, Michael Holzman, MD, Richard Pierce, MD, Sharon Phillips, MSPH, Li-Ching Huang, Ph.D.

INTRODUCTION:
Practice guidelines for surveillance of non-dysplastic Barrett’s Esophagus (BE) allow for some latitude in determining the optimal surveillance interval. Factors which influence the frequency of surveillance endoscopy are not well understood. The objective of this study was to assess frequency of endoscopic surveillance for BE by geographic region, with the hypothesis that frequency would vary by the patient’s urban-rural designation.

METHODS:
Cases of non-dysplastic BE undergoing esophagogastroduodenoscopy (EGD) with biopsy were identified within the Healthcare Utilization Project State Inpatient Database and the State Ambulatory Surgery Database for three states (CA, FL, and NY) in 2005-2006. Longitudinal follow up through 2011 was performed to determine frequency of endoscopic surveillance. The threshold for appropriate surveillance utilization was defined as two to four surveillance EGDs over a standardized 5 year period. Patients were censored during follow up for death or incident esophageal cancer. Urban-rural designation was determined by National Centers for Health Statistics criteria.

RESULTS:
36,646 cases of non-dysplastic BE were identified. Among these, 4,632 patients (12.6%) underwent between two and four surveillance EGDs in 5 years of follow-up with no significant difference between urban and rural populations (12.6% urban vs 13.1% rural; p = 0.43). 31,975 patients (87.3%) underwent fewer than two EGDs during follow-up, with no difference in urban vs rural surveillance (urban 86.7% vs rural 87.3%; p = 0.31). Thirty-nine patients underwent more than four endoscopic procedures per 5 years, with a greater proportion being rural patients versus urban patients (0.23% rural; 0.09% urban; p < 0.05). More patients underwent fewer than two EGDs per 5 year follow up (31,975 patients) than underwent between two and four EGDs (87.3% [31,975/36,646] vs 12.6% [4,632/36,646]; p < .0001). 40 patients (0.11%) were censored during the study for development of esophageal cancer.

CONCLUSION:
This study identified no difference in performance of surveillance EGD for BE by urban-rural designation. The majority of patients with non-dysplastic BE underwent fewer than two endoscopic surveillance procedures in five years of follow-up, below published guidelines for appropriate surveillance. A more robust system for tracking and assessing surveillance of BE needs to be developed.
Acute dissections involving the aortic arch: appropriate for medical management?

Julia Boll, R. James Valentine, Thomas C. Naslund, Clifford L. Garrard, John A. Curci, Colleen M. Brophy

OBJECTIVES:
Medical management of acute aortic dissections of the descending thoracic aorta (AD-desc) is associated with acceptable outcomes. It remains uncertain whether acute aortic dissections involving the aortic arch (AD-arch) have an increased risk of retrograde extension into the ascending aorta or other dissection-related complications. Compared to acute AD-desc dissections, medical management of acute AD-arch dissections is associated with a reduced intervention-free survival.

METHODS:
Retrospective analysis of patients admitted 2005-2014 with acute aortic dissections not involving the ascending aorta were evaluated. Primary endpoints included dissection-related death and operative intervention.

RESULTS:
Ninety-nine subjects with acute aortic dissections were evaluated. Dissections began distal to the left subclavian artery in 79 (80%) cases (AD-desc), while 20 (20%) had proximal extension involving the left subclavian (n=16), left common carotid (n=1) or innominate (n=3) arteries (AD-arch). During medical management, 2 AD-arch and one AD-desc subjects had proximal extension into the arch (P<.05), but only one AD-arch had proximal dissection into the ascending aorta. Compared to AD-desc, subjects with AD-arch had more early interventions (40% vs 19%, P=.047), cardiac complications (35% vs 11%, P<.01), and neurologic events (25% vs 6%, P<.01). Seven (35%) AD-arch subjects vs. 9 (11%) AD-desc subjects suffered dissection-related deaths (P<.01). Among subjects who did not undergo early interventions, late interventions were performed in 4 (50%) of 8 AD-arch subjects vs. 6 (10%) of 58 AD-desc subjects (P=.02). Medical treatment was successful in 4 (20%) of AD-arch subjects compared to 52 (66%) AD-desc subjects (P<.001). Multivariate logistic regression identified arch involvement as the sole predictor of dissection-related death (95% CI, 1.3-13.4, OR=4.2) and failure of medical treatment (95% CI, 2.5-29, OR= 7.7).

CONCLUSIONS:
Acute aortic dissections involving the arch are associated with a higher risk of cardiac complications, neurologic events, need for early intervention, and dissection-related death compared to those beginning distal to the left subclavian artery. While proximal dissection into the ascending aorta was rare in this study, medical management does appear to be safe as initial treatment of AD-arch dissections. However, surgeons should be aware of the increased risk of complications and the potential need for urgent interventions in these patients.
DOES THE PRIMARY ETOLOGY OF BLADDER DYSFUNCTION FOLLOWING AUGMENTATION CYSTOPLASTY CORRELATE WITH IMPROVED POST-OPERATIVE OUTCOMES?

Kelly Pekala, Deborah L. Jacobson, John C. Thomas, Stacy T. Tanaka, Douglass B. Clayton, John C. Pope, John W. Brock, Mark C. Adams

OBJECTIVES:
To determine differences in post-operative course and overall complication rates in patients with neurogenic as opposed to non-neurogenic bladder following initial augmentation cystoplasty.

METHODS:
We have previously presented our extensive database that documented post-operative demographics and outcomes in patients undergoing lower tract reconstruction. All complications were graded by a modified Clavien–Dindo system. This retrospective database includes 100 children who underwent augmentation cystoplasty between January 2002 and January 2014. Specifically, we included patients who underwent primary bladder augmentation with a minimum of one year follow-up. Patients were classified as neurogenic (NG) or non-neurogenic (NNG) on the basis of primary urologic diagnosis. We excluded all patients who underwent secondary augmentation or any patient with less than one year follow-up. We used the Wilcoxon rank-sum test with statistical significance set a priori at p < 0.05.

RESULTS:
83 patients met inclusion criteria. 65 had a neurogenic diagnosis while 18 had a non-neurogenic etiology of bladder dysfunction. The average length of hospital stay was 9.45 days for NG patients and 10.44 days for NNG patients. (p=0.92) NG patients had a mean of 3.1 surgeries whereas NNG patients had a mean of 2.77 surgeries. (p=0.68) NG patients had a mean of 2.95 complications whereas NNG had a mean of 2.27 complications. (p=0.65) The mean time from date of surgery to first complication in new bladder augmentation patients was 295 days. There was no difference in time to first complication in both groups of patients (p=0.38). When stratified to number of complications per patient year of follow-up, there were no differences between the groups (p=0.67).

CONCLUSIONS:
This study represents a comprehensive review and long-term follow up in pediatric patients who underwent augmentation cystoplasty. Contrary to our hypothesis, there were no differences in overall outcomes, including hospital stay, number of additional surgeries, and complication timing or rate when stratified per year of follow-up. This study may facilitate better informed discussions prior to surgical intervention in both groups of patients.
OBJECTIVES:
To investigate the role of skeletal muscle, visceral fat, and subcutaneous fat on hospital length of stay (LOS), complications, ICU stay, and readmissions in patients undergoing hepatic resection in one academic medical center in the United States.

METHODS:
All patients undergoing hepatic resection at Vanderbilt University between January 2006 and December 2013 were identified (N=449). Of these, only patients with a high-quality CT scan at the L3 vertebrae within 3 months prior to their operation were included (N=396). From CT, the L3 axial slice was analyzed using an automated version of Slice-O-Matic software and images were manually adjusted for attenuation errors. Electronic medical record review was conducted for demographics, tumor characteristics, and outcome measures. Univariate and multivariate analyses evaluating potential predictive factors of short-term outcomes were performed using SPSS version 23.

RESULTS:
In males, of the four body composition variables – skeletal muscle area (SM), visceral adipose tissue area (VAT), subcutaneous adipose tissue area (SAT), and skeletal muscle attenuation (SMA) – only low VAT was significantly associated with worse short-term outcomes. Specifically, low VAT was associated with longer hospital LOS (p=0.007), longer ICU LOS (p=0.01), more post-operative complications (p=0.07), and more readmissions (p=0.008). In females, low SMA was significantly associated with worse outcomes, specifically longer hospital LOS (p=0.03), longer ICU LOS (p=0.007), and more post-operative complications (p=0.09). Logistic regression analysis revealed that visceral adiposity is a strong and independent risk factor for ICU stay (p=0.04) and readmissions (p=0.01). Sex was a strong and independent prognostic factor of readmissions (p=0.002), with males having a greater likelihood of readmission than females.

CONCLUSIONS:
Overall, the body composition component that was the most robust prognostic factor for adverse short-term outcomes in patients undergoing hepatic resection was the amount of VAT. In males, increased VAT seems to be protective against adverse short-term outcomes. However, in females, it appears that low SMA – a reflection of muscle quality – is more associated with adverse short-term outcomes.
Outcome Comparisons for Dexamethasone vs. Prednisone in Pediatric Patients Hospitalized with Acute Asthma Exacerbations

Sara Seghezzo, MD, Donald Arnold, MD, MPH, Jim Gay, MD, MMHC, Paul Moore, MD, David Johnson, MD

BACKGROUND:
Systemic steroids are an important component of acute asthma exacerbation treatment, classically provided as a 5-7 day course of short-acting steroids, but studies show a significant proportion of families fail to fill systemic steroid prescriptions after hospital discharge. Longer acting steroids, such as dexamethasone, have the potential to obviate the need for prescription filling, thereby improving compliance. However outcome comparisons to short-acting systemic steroids in hospitalized patients are lacking.

OBJECTIVE:
To compare the relapse rate, length of stay (LOS) and 7-day readmission rate following discharge from an acute asthma exacerbation in patients treated with prednisone versus dexamethasone.

DESIGN/METHODS:
We performed a retrospective analysis of children ages 2-18 years hospitalized at Monroe Carell Jr. Children's Hospital from January 2012-March 2015 using Pediatric Health Information Systems and internal pharmacy data for oral medication administration. Patients who received both dexamethasone and prednisone, and those requiring ICU care were excluded. LOS, 7- and 30-day asthma ED relapse rates, and 7-day asthma readmissions were compared between dexamethasone and prednisone groups using appropriate statistical analysis.

RESULTS:
Of the 1257 children hospitalized for a primary diagnosis of asthma during the study period, 792 met inclusion criteria. Of those, 293 (37%) received only dexamethasone and 499 (63%) only prednisone. There were no differences between the dexamethasone and prednisone groups in regards to 7-day asthma readmissions [3 (1.02%) vs 4 (0.80%) p=.75], 7-day asthma relapses [6 (2.05%) vs 7 (1.40%) p=.49], or 30-day asthma relapses [19 (6.48%) vs 26 (5.21%) p=.46], respectively. The dexamethasone group had a significantly shorter LOS [1.0 day (0.8-1.4) vs 1.2 days (0.8-1.6) p<.001].

CONCLUSIONS:
Relapse and readmission rates for asthma care in an inpatient setting are similar for children treated with dexamethasone as compared to prednisone. LOS appears shorter in the dexamethasone group, however we cannot determine whether this is a result of confounding by severity due to patients with less-severe episodes being treated with dexamethasone. Dexamethasone minimizes barriers to filling oral steroids post-discharge and should be considered as an alternative to prednisone for children hospitalized with acute asthma exacerbations.
Unexpected Effects of Antibiotic Timing in Pediatric Musculoskeletal Infection

Michael Benvenuti, Thomas An, John Schoenecker

OBJECTIVES:
Musculoskeletal infection (MSKI) is a common cause of morbidity and hospital resource utilization in the pediatric population. However, there are no widely used guidelines for the timing of antibiotic initiation for these infections. Many physicians prefer to withhold antibiotics until tissue cultures can be taken in an effort to improve culture yields. However, there is little evidence that this practice improves culture results or outcomes in pediatric MSKI. Therefore, investigating the effects of antibiotic timing on culture sensitivity and outcomes may lead to improved clinical practice guidelines for treating children with MSKI.

METHODS:
An IRB-approved retrospective review was conducted to identify patients aged 0-18 who presented to the pediatric emergency room at a tertiary care children’s hospital with MSKI over a five-year period (2008-2013). Demographic data, culture results, severity markers, and intervention timing were obtained from the medical record. Logistic regression and Cox survival analysis were performed to determine the relationship of antibiotic timing with culture sensitivity and time to discharge.

RESULTS:
Patients with local infection were more likely to have a positive tissue culture following antibiotic administration (odds ratio 28.3, p<0.05), even after accounting for differences in age and disease severity. Additionally, later administration of antibiotics in this group correlated with a decreased likelihood of discharge (hazard ratio 0.46, p<0.05) after accounting for disease severity with CRP and respiration. In patients with disseminated infection, antibiotic administration was not shown to correlate with any difference in culture results (odds ratio 1.67) or time to discharge (hazard ratio 0.98).

CONCLUSION:
The authors were surprised to find that tissue culture sensitivities were not decreased by antibiotic administration in either local or disseminated MSKI. This result suggests that antibiotic administration should not be delayed in order to obtain tissue cultures. The correlation of earlier antibiotic administration with shorter length of stay in children with local MSKI lead the authors to conclude that antibiotics should be initiated as quickly as possible to prevent dissemination in children with suspected local infection. Further study with a larger patient population and randomized treatment groups are necessary to confirm these findings and establish clinical practice guidelines.
A Clinical Prediction Algorithm to Stratify Pediatric Musculoskeletal Infection by Severity and Dissemination

Thomas An and Michael Benvenuti, Jonathan Shoenecker, Derek Williams, Isaac Thomsen

OBJECTIVE:
There is wide variability in the clinical presentation and severity of pediatric musculoskeletal infection. Early stratification of infection severity would help maximize resource utilization and improve patient care. However, there are currently no widely applicable clinical prediction algorithms to stratify pediatric musculoskeletal infection by severity in the emergency department.

METHODS:
An IRB-approved retrospective review was conducted to identify patients aged 0-18 who presented to the pediatric emergency room at a tertiary care children’s hospital with concern for MSKI over a five-year period (2008-2013). 191 pediatric patients met inclusion criteria and were stratified retrospectively into a three-tiered severity stratification system. This system has previously been shown to correlate with hospital outcomes in this patient population. An ordinal logistic regression model to predict infection severity stratification was performed using STATA 14. Variables included in the regression included WBC, CRP, respiratory rate, pulse, and temperature at admission.

RESULTS:
Multiple multivariate models that incorporated different predictive factors were generated. The most effective model for predicting infection severity incorporated CRP, temperature, and pulse. The Harrell’s C statistic, an analog of the area under the receiver operator characteristic, was 0.827 for this model, demonstrating effective predictive ability. Presentation CRP was the most important variable in the predictive model, with an odds ratio of 1.027 (p<0.001).

CONCLUSIONS:
Clinical and laboratory data obtained in the emergency department may be used to accurately stratify pediatric musculoskeletal disease severity. This early stratification has the potential to improve triage of patients and direct hospital resources towards patients with more severe, disseminated disease. Prospective studies are necessary to validate the efficacy of the predictive model detailed in this study.
Similar Clinical Severity and Outcomes for MRSA and MSSA Pediatric Musculoskeletal Infection

Thomas An, Michael Benvenuti, Megan Mignemi MD, Issac Thomsen MD, Jonathan Schoenecker MD Ph.D.

OBJECTIVES:
Studies on pediatric musculoskeletal infection have suggested that methicillin resistant Staph. aureus (MRSA) causes worse hospital outcomes than methicillin susceptible Staph. aureus (MSSA). Based on these results, clinical prediction algorithms have been developed to differentiate between MRSA and MSSA early in a patient’s clinical course. This study compares hospital outcomes for pediatric patients with MRSA and MSSA musculoskeletal infection presenting to the emergency department at Vanderbilt. The authors hypothesized that there would be no significant differences in in the severity of infections caused by MRSA and MSSA.

METHODS:
An IRB-approved retrospective study was conducted to identify pediatric patients with S. aureus musculoskeletal infection over a 5-year period (2008-2013). The patient population was identified through sequential review of the pediatric orthopedic consult list. Demographic information, laboratory values, and clinical outcomes were obtained from the electronic medical record. Statistical analysis performed with GraphPad Prism 6 (La Jolla, Ca) and STATA 14 (College Station, TX).

RESULTS:
Of the 92 identified cases of S. aureus pediatric musculoskeletal infection, there were 49 cases of MRSA (53%) and 43 cases of MSSA (47%). There were no significant differences between MRSA and MSSA infections in median hospital length of stay (4.8 vs. 5.7 days, p=0.50), febrile days (0.0 vs. 1.5 days, p=0.10), and peak CRP (117 vs. 103 ug/ml, p=0.52). However, a higher proportion of MRSA infections required operative intervention compared to MSSA infections (85% vs. 62%, p=0.015*). A predictive logistic regression model based on CRP, temperature, WBC, pulse and respiratory rate at presentation demonstrated poor ability to differentiate between MRSA and MSSA infection, with an area under the receiver operator characteristic of 0.676.

CONCLUSIONS:
The results demonstrated no significant difference in most hospital outcomes between MSSA and MRSA musculoskeletal infection. In addition, a predictive model based on severity markers obtained at presentation was unable to effectively differentiate between MRSA and MSSA infection. Therefore, the clinical utility and capacity for early differentiation between MRSA and MSSA depends on regional virulence patterns that may be specific for each institution. Given the changing trends in S. aureus virulence and resistance patterns, algorithms to differentiate between strains will need to be updated regularly with clinical data.
Peak D-Dimer is Predictive of Hospital Outcomes for Staph. aureus MSK Infection

Thomas An, Michael Benvenuti, Megan Mignemi MD, Jonathan Schoenecker MD Ph.D

OBJECTIVES:

S. aureus expresses virulence factors that utilize the host coagulation system to facilitate abscess formation and hematogenous dissemination. During the initial stages of infection, S. aureus virulence factors coagulase and von Willebrand binding protein (vWbp) activate the coagulation system and promote fibrin deposition to form an abscess. Later expression of staphylokinase (SAK) leads to hematogenous dissemination by acting as a plasminogen activator to promote abscess rupture. Given these mechanisms of S. aureus dissemination, the authors tested the hypothesis that elevated fibrin breakdown products (D-dimer) in pediatric patients would be predictive of degree of infection dissemination and hospital outcomes.

METHODS:

An IRB approved retrospective study of children evaluated for S. aureus musculoskeletal infection (MSKI) was conducted over 5 years (2008-2013). Patients with D-dimer measurements were included in the study. Standard laboratory values and relevant clinical outcomes were collected. Infection severity was defined according to operational definitions based on degree of infection dissemination.

RESULTS:

Peak D-Dimer for S. aureus MSKI correlated significantly with hospital outcomes (length of stay (LOS), number of operative procedures, ICU LOS, days with fever > 101.5, p<0.01 for all variables). The median initial and peak D-Dimers for disseminated infections were higher than those of local infections (1.7 vs. 1.1 ug/ml and 3.5 vs. 16 ug/ml, respectively), but this difference was not statistically significant. A cut-off D-dimer value of 1.2 ug/ml significantly differentiated disseminated infections from local infections with a sensitivity of 86% and a specificity of 50%.

CONCLUSIONS:

Peak D-dimer levels were predictive of hospital outcomes for pediatric patients with S. aureus MSKI. Initial and peak D-dimer in disseminated infection were higher than in local infection, but the difference was not statistically significant. The difference in D-dimer between local and disseminated infection correlates with the pathophysiology of Staph. aureus dissemination through abscess rupture.
Pericranial Autograft Closure and Perioperative EVD Placement Reduces Need for Definitive CSF Diversion in Pediatric Brain Tumor Patients Undergoing Posterior Fossa Resection

Ritwik Bhatia, Michael C. Dewan, Andrew Hale, Stephen Gannon, Chevis N. Shannon, Robert P. Naftel, John C. Wellons

OBJECTIVE:
Determine if pericranial autograft dural closure and/or perioperative EVD (extraventricular drain) placement reduces need for definitive CSF (cerebrospinal fluid) diversion.

METHODS:
This was a retrospective cohort study incorporating pediatric brain tumor patients (age 0-17) undergoing posterior fossa tumor resection from January 2000 to January 2015 at VUMC. Patient health information was collected and stored in RedCap. Our primary outcome measure was need for definitive CSF diversion (defined as ventriculoperitoneal shunt or endoscopic third ventriculostomy).

We used 2x2 contingency tables and Fisher’s exact test to evaluate the association of the variables identified on outcomes. We conducted statistical analysis using GraphPad and R. Statistical significance was set a priori at p<0.05.

RESULTS:
151 patients met inclusion criteria. Among 131 patients not receiving pericranial autograft closure, 32% required definitive CSF diversion. Of the 20 patients receiving pericranial graft, 10% required definitive CSF diversion. Of the 34 patients that received EVD, 53% required definitive CSF diversion. Of the 117 patients that did not receive EVD, 21% required definitive CSF diversion. Using Fisher’s exact test, we determined patients receiving pericranial autograft closure trend towards reduced need for definitive CSF diversion (p=0.173), while those receiving perioperative EVD placement alone experience increased need for definitive CSF diversion (p=0.011).

Of the 13 patients who received pericranial autograft and perioperative EVD, 8% required definitive CSF diversion. Of the 21 patients who received other methods of dural closure and perioperative EVD, 81% required definitive CSF diversion. Using Fisher’s exact test in this cohort, we determined that patients receiving both pericranial autograft closure and perioperative EVD experience reduced need for definitive CSF diversion (p=0.019).

CONCLUSIONS:
Pediatric brain tumor patients receiving pericranial autograft closure and perioperative EVD experience reduced need for definitive CSF diversion compared to patients receiving other methods of dural closure and perioperative EVD for posterior fossa resection. This difference is driven primarily by the choice of pericranial autograft for dural closure rather than decision to perioperatively place EVD. More studies and statistical analyses are needed to evaluate additional clinical predictors.
Significant Reduction in Preoperative Testing at a Preoperative Evaluation Clinic is Not Associated with Increase in Day of Surgery Testing or Case Cancellations

Han Shi, Maxim Terekhov, MS, Jesse M. Ehrenfeld, MD, MPH, Jonathan P. Wanderer, MD, MPhil

OBJECTIVES:
Unnecessary preoperative testing has been scrutinized for rising healthcare costs in the United States. Vanderbilt’s Preoperative Evaluation Clinic (PEC) and similar centers around the country evaluate risk for surgical patients and coordinate preoperative testing. Protocol changes at Vanderbilt have been adopted with the intention of reducing unnecessary preoperative testing, and we sought to evaluate their impact on downstream care.

METHODS:
Our group reviewed clinical workup revisions made in Vanderbilt’s PEC from 2010 to 2015 and identified a key interval of change leading to a significant reduction in preoperative testing. We then queried the Perioperative Data Warehouse for preoperative chemistry tests, complete blood counts, electrocardiograms, and chest x-rays before and after the key interval. Chi-square tests were then used to determine the effect of the reduction in preoperative testing on tests performed on the day of surgery and case cancellations.

RESULTS:
We analyzed 100,496 anesthetic cases with PEC evaluations performed between January 2010 and October 2015. There was an overall downward trend in all preoperative tests and labs performed: electrocardiograms (62.9% to 32.7%, p<0.01), coagulation blood draws (71.4% to 51.4%, p<0.01), blood cell counts (71.38% to 51.42%, p<0.01) and basic metabolic panels (70.6% to 51.3%, p<0.01) after the protocol change without a change in tests ordered on the day of surgery. This was not associated with a significant increase in case cancellation.

CONCLUSION:
A reduction in preoperative testing was seen at our PEC from 2012-2015 due to clinical protocol changes. This was not associated with a respective increase in day of surgery laboratory tests and imaging ordered or an increase in case cancellation rates.
Improved Access to Healthcare Amongst Residents - A Health and Wellness Initiative

Amanda Harris, Atul Kapila, Ryan Brown, Ryan Kindle, Meera Wright, Natalie Nesmith, Brittany Waterman, Jennifer Green

OBJECTIVES:
Data presented at the American Psychiatric Association (APA) 2015 Annual Meeting revealed that residency burnout is a serious concern. A study conducted by the University of North Carolina found that 79% of internal medicine residents exhibited evidence of burnout. A Lancet study in 2009 found that physicians who have a poor personal health profile are less likely than are those who are healthy to perform evidence-based screening and counseling for a healthy lifestyle to their patients. Our program aimed to improve access to healthcare amongst residents by creating allocated time away from work for personal health maintenance, including primary care, dental care, mental health and obstetrics/gynecology.

METHODS:
A pre-intervention survey was used to evaluate residents’ self-perception of being up-to-date on routine health maintenance. Each interested resident was then provided a “Health and Wellness Day” during a future clinic rotation to schedule healthcare appointments. We also provided an up-to-date list of primary care physicians, obstetricians/gynecologists as well as mental health providers for residents to reference. We sent a survey evaluating residents’ self-perception of health six months after the intervention to determine its efficacy.

RESULTS:
Our intervention increased the percentage of residents with a primary care provider from 40% to 64% and increased the percentage of residents with an obstetrician/gynecologist from 33% to 61%. The percentage of residents who have seen a primary care provider within six months more than doubled. Self-perception of being up-to-date on routine health maintenance by residents increased from 46% to 70%. More residents reported formal screening for alcohol abuse, hypertension, cervical cancer, and HIV. Lastly, the percentage of residents with a perceived mental health concern who desired and obtained mental health care increased from 35% to 75%.

CONCLUSION:
Resident access to healthcare can be improved. Our intervention of enacting a biannual “Health and Wellness Day” increased resident self-perception of health maintenance and access to healthcare providers. Due to the efficacy of this intervention, the “Resident Health and Wellness” initiative continues. This has also influenced the creation of a resident-run committee to identify other areas of improvement in resident well-being.
Metabolic Complications Precede Alloreactivity and are Characterized by Changes in ST2 signaling

Romany A N Johnpulle, MD, Sophie Paczesny, MD, PhD, Dae Kwang Jung, BS, Etienne Daguindau, MD, Madan H. Jagasia, MD, MBBS, MS, Bipin N. Savani, MD, Wichai Chinratanalab, MD, Robert F. Cornell, MD, Stacey Goodman, MD, John P. Greer, MD, Adetola A. Kassim, MD, MS, Salyka Sengsayadeth, MD, Brian G. Engelhardt, MD, MSCI

New-onset post-transplant diabetes mellitus (PTDM) is a common complication that can precede acute graft-versus-host disease (aGVHD) and is associated with inferior survival after allogeneic hematopoietic cell transplantation (HCT). Glucose homeostasis and aGVHD are affected by IL-33 binding to its receptor, suppression of tumorigenicity 2 (ST2). Soluble ST2 (sST2) modulates the IL-33/ST2 axis and is a biomarker for aGVHD and non-relapse mortality (NRM). We hypothesize that PTDM and NRM are related to IL-33/ST2 signaling and that sST2 will predict PTDM diagnosis.

Serum sST2 levels were measured by ELISA at engraftment and Day+30 in 36 euglycemic HCT patients (pts) followed prospectively for PTDM (defined as weekly fasting blood glucose ≥126 mg/dL or random blood glucose ≥200 mg/dL from day 0 to day+100). Results were confirmed in a validation cohort consisting of 26 pts without pre-existing diabetes retrospectively analyzed for PTDM (defined as random blood glucose ≥200 mg/dl from day 0 to day+100). Pts with established diabetes were analyzed separately (N=12).

New-onset PTDM was diagnosed in 24 (67%) and 15 (58%) pts from cohorts 1 and 2, respectively. In cohorts 1 and 2, PTDM preceded grade 2-4 aGVHD in 12 and 8 individuals, respectively. When compared to recipients without PTDM, pts developing PTDM in cohort 1 had elevated sST2 levels at engraftment (39.5 ng/mL vs. 20 ng/mL; P=0.02) and at day+30 (102 ng/mL vs. 22 ng/mL; P<0.01). Higher sST2 levels were associated with aGVHD severity [103 ng/mL vs. 24 ng/mL at engraftment; P<0.01 and 175 ng/mL vs. 40 ng/mL at day+30; P=0.02 (grade 3-4 vs. grade 0-2 aGVHD, respectively)]. The validation cohort confirmed that PTDM pts had elevated engraftment sST2 when compared to individuals maintaining euglycemia (21 ng/mL vs. 13 ng/mL; P=0.01). Engraftment sST2 levels were similar between pts with pre-existing diabetes before HCT (N=12) and those developing new-onset PTDM after transplant from cohort 2 (P=0.48). Multivariate analysis of cohorts 1 and 2 showed high engraftment sST2 predicted increased PTDM and NRM risk independent of conditioning and grade 3-4 aGVHD.

SST2 was elevated in PTDM indicating a relationship between glucose homeostasis and the IL-33/ST2 axis. Correction of metabolic complications may improve HCT outcomes. Future biomarker analysis will need to account for potential baseline differences in sST2 levels due to metabolic abnormalities.
SLEEP PATTERNS IN PEDIATRIC CROHN’S DISEASE: AN INTERIM ANALYSIS

Gabriel Winberry, MD, Sari Acra, MD, MPH, Beth Malow, MD, MS, Maciej S. Buchowski, PHD

OBJECTIVES:

Self-reported sleep disturbances are common in adults with IBD and adversely affect quality of life, however, no objective sleep data exists in adult or pediatric IBD populations. The purpose of this study is to demonstrate feasibility of the use of actigraphy as an objective measure of sleep in pediatric Crohn’s Disease (CD, as well as characterize sleep patterns in children with CD. We hypothesize that both subjective and objective measures of sleep in children with CD will negatively correlate with Pediatric CD Activity (PCDAI) score.

METHODS:

Children with CD age 12-18 years were invited to participate. Exclusion criteria included sleep disorders and systemic steroid therapy. Subjective sleep assessment was done using the validated Adolescent Sleep-Wake Scale. Sleep patterns were objectively assessed using a triaxial accelerometer worn on the non-dominant wrist for 7 consecutive days (24 h/day). Total sleep time (TST) and sleep efficiency (SE; total sleep time/time in bed x100) were calculated. Demographic, anthropometric, and clinical data were used to calculate PCDAI scores. Descriptive statistics and Pearson correlation coefficients comparing subjective and objective markers of sleep and disease activity were calculated. P-values of <0.05 were considered significant.

RESULTS:

At interim analysis, 23 out of 28 subjects (82%) approached were consented, 18 (78%) participants had completed clinical questionnaires, and 11 (48%) had completed actigraphy (remaining subjects are currently undergoing actigraphy). 11 (100%) had valid actigraphy data. The median PCDAI was 12.5 (2.5-20). The mean TST in those completing actigraphy was 466±62 minutes per night, similar to reported ranges of TST for healthy adolescents (476± 56). No significant correlations between subjective sleep quality or objective measures of sleep and disease activity were identified. All subjects reported no issues with compliance with the actigraph.

CONCLUSIONS: Actigraphy is a feasible tool for examining sleep patterns in pediatric IBD. Interim analysis has not identified a correlation between disease activity and either subjective or actigraphic measures of sleep, possibly due to small sample size and homogeneity in population (only mild-moderately active patients). These findings are being further explored in a larger number of subjects, including subjects with moderate-severe disease activity (recruitment ongoing).
PrimeMD, a symptom management smartphone application for head and neck cancer patients

Jeffrey Friedman, Ryan Ber, Mary Dietrich, Sheila Ridner

The medical industry has been inundated with smartphone applications (apps) that can be utilized as clinical tools. Despite the large numbers, there remains a need for novel apps to streamline patient treatment and patient communication, and to increase physician productivity. There are currently no validated, available and supported mobile apps for patient engagement, communication or symptom monitoring in the field of Radiation Oncology. The objective of this study was, through the use of a mobile app in clinical practice, to determine if patients will use a symptom management smartphone app that has the ability to manage and improve care delivered by radiation oncologists.

Adults with head and neck cancer whom were undergoing radiation therapy at Vanderbilt University Medical Center were recruited in person to participate in the study. A simple, user-friendly app with an alert system and provider dashboard, termed PrimeMD, was installed onto the patient’s smartphone. Four times per day, patients were reminded via an alarm, to enter their pain levels, whether or not they had taken their medication, and whether their pain affected their ability to eat and drink. This report was sent to a dashboard that could be viewed by a healthcare provider. Upon concluding the study, patients completed an exit survey containing five sections including general satisfaction, usability of the app and whether they would recommend the app to another patient. How frequently patients entered data to the app was correlated to their exit survey rating for general satisfaction.

Of the 24 individuals who participated in the study, 45% were female, 8% were African American, 50% had at least some college, and the mean age was 58.4 years (SD 9.09) (Range 41-82). When patients were asked to rate their general satisfaction with the app, the median score was 90 out of 100. When asked to rate the usability of the app, the median score was 95 out of 100. When patients were asked whether they would recommend the pain management smartphone application to other head and neck cancer patients, the median score was 100 out of 100.

Within the field of Radiation Oncology there is a need for novel apps that allow for patient engagement and communication with the physician. The use of PrimeMD in a population of head and neck cancer patients demonstrated that there is a need and desire by patients for a novel app that can allow for better patient management, communication, and earlier interventions.
Postoperative Care using a Secure Online Patient Portal: Changing the (inter) Face of General Surgery

Kristy Kummerow Broman, Omobolanle Oyefule, Sharon Phillips, Rebecca Baucom, Michael Holzman, Ken Sharp, Richard Pierce, William Nealon, Benjamin Poulose

OBJECTIVES:
While many patients seek greater accessibility to care providers, surgeons face increasing time constraints due to workforce shortages and elevated performance demands. Online postoperative care may improve patient access while increasing surgeon efficiency. We aimed to evaluate the feasibility and acceptability of online visits for follow-up after low risk general surgical operations.

METHODS:
A prospective pilot study within an academic general surgery service compared online and in-person postoperative visits from May-November 2014. Online visits included a secure symptom survey, surgeon review of wound pictures taken by patients, and correspondence using a secure online patient portal. Included patients underwent elective laparoscopic cholecystectomy, umbilical hernia repair, or inguinal hernia repair by one of five surgeons. The primary outcome was patient acceptance of online visits in lieu of in-person clinic visits. Secondary outcomes included detection of complications via online visits, provider-reported effectiveness, and visit times.

RESULTS:
Fifty patients completed both online and in-person visits. Online visits were acceptable to most patients (76%) as their only follow-up, and were preferred by 34%, while 34% had no preference and 32% preferred clinic visits. For 68% of patients, surgeons reported that both visit types were equally effective, while the clinic visit was more effective in 24% and the online visit in 8%. No complications were missed via online visits, which took significantly less time for patients and providers.

CONCLUSIONS:
In this population, online postoperative visits were accepted by patients and surgeons, took less time, and effectively identified patients who required further care.
Induced Differentiation Inhibits Sphere Formation In Neuroblastoma

Brian T. Craig, Eric J. Rellinger, Alexandra L. Alvarez, Jingbo Qiao, Yan Guo, Dai H. Chung

OBJECTIVES:
Neuroblastoma arises from neural crest precursor cells, and differentiation status is a key factor used for clinical decision-making. Metastatic relapse in bone marrow is the leading cause of mortality in children with this devastating disease, and the differentiating agent 13-cis-retinoic acid is used as post-therapy maintenance to decrease the risk of relapse. Neuroblastoma tumor-initiating cells have been isolated from the bone marrow of patients in remission using sphere culture, which also promotes growth of neural crest stem cells. Sphere culture may therefore enrich for a cancer stem cell phenotype in neuroblastoma. We sought to test whether sphere formation depends on differentiation status and to elucidate the molecular mechanisms responsible for the sphere-forming phenotype.

METHODS:
Four human neuroblastoma cell lines were cultured in low attachment, serum-free media with EGF (20 ng/ml) and bFGF (40 ng/ml) and tested for sphere-forming frequency by limiting dilution analysis. Cellular differentiation was induced by treatment with 13-cis-retinoic acid (5 mM). Gene expression profiling of sphere-cultured cells was performed by paired-end RNA sequencing and validated by RT-qPCR. ANOVA and Student’s t test were used for multiple and two-group comparisons, respectively.

RESULTS:
MYCN-amplified LAN-1 (6.1%) and BE2C (4.9%) had much higher sphere-forming frequency than non-MYCN--amplified SK-N-SH (1.7%) or SK-N-AS (0.7%) (p<0.001). Inducing differentiation inhibited sphere formation in BE2C and LAN1 to the level of the non-MYCN-amplified cells. Gene expression profiling was used to contrast the high sphere-forming BE2C to the low sphere-forming SK-N-SH cells to identify potentially novel regulators of sphere formation. Interestingly, the hematopoietic progenitor cell marker CD34 and the TGF-b family member GDF15, important in glioblastoma and multiple other cancers, were the two most highly differentially expressed transcripts.

CONCLUSIONS:
Sphere culture in neuroblastoma correlates with MYCN amplification, depends on the cellular differentiation state and is associated with increased expression of progenitor cell markers. Taken together, these data suggest that frequent sphere formation may represent a cancer stem cell phenotype in neuroblastoma, and that this in vitro model system could shed light on the critical mechanisms that lead to metastatic bone marrow relapse after therapy.
Sciatic Nerve Magnetic Transfer MRI is a Stronger Predictor of Disability in Charcot-Marie-Tooth Diseases than Downstream Measures in Skeletal Muscle

Weston Langdon, Lauren Brooks, Jun Li, Richard Dortch

OBJECTIVES:
To compare MRI measures of nerve (magnetization transfer ratio, MTR) and muscle (atrophy scores and muscle MTRs) as biomarkers of disability in Charcot-Marie-Tooth (CMT) diseases.

METHODS:
MRI was performed at 3.0T from the mid-thigh to the knee in the following cohorts: CMT1A (n=10), CMT2A (n=3), HNPP (n=3), and age-matched controls (n=21). MTR was measured in the SN and surrounding skeletal muscle from fat-suppressed MT-weighted volumes (resolution = 0.8x0.8x6 mm3); and a trained radiologist graded atrophy/fat replacement from axial proton-density weighted volumes using the Goutallier classification system (0-4, higher values=increased atrophy).

RESULTS:
SN MTRs exhibited the strongest relationship with LNS (r²=0.49, p<0.01). For skeletal muscles, only the posterior compartment MTRs (innervated by the sciatic nerve) were significantly related to LNS (r²=0.33, p<0.03). For atrophy grades, posterior compartment muscle showed the highest atrophy grades; however, the relationship between these grades and LNS was not significant (r²=0.34, p=0.18).

CONCLUSIONS:
Direct measures of myelin/axon pathologies in the SN are a stronger predictor of leg disability than downstream measures in skeletal muscles. Additionally, posterior compartment muscles, which are innervated by the SN, are more severely affected than other muscle compartments in CMT. As a result, MTR measures of the SN may be a promising outcome measure for future clinical trials.
Investigating apparent coronary artery calcium regression

Alexandra Ritts

OBJECTIVES:
Coronary artery calcium (CAC) is an established independent predictor of cardiovascular disease events. Once present, CAC is thought to progress, but is highly variable between individuals as well as with different observed rates in various studies. Measurement variability for low levels of CAC is significant and differentiating between measurement error and true calcified plaque regression is problematic. Few studies have serial scans in the same individuals across the many years that demonstration of regression might require. We evaluated CAC change over 10 years in the Coronary Artery Risk Development in Young Adults (CARDIA) study to determine if CAC regression occurred in any of the 2,158 participants.

METHODS:
The CARDIA study measured CAC using non-contrast, cardiac CT at 5-year intervals in 2000-01, 2005-6, and 2010-11 in 2,158 participants (56% female, 42% African American). Agatston scores (AU) were calculated for each scan year. Participants ranged in age from 33-45 years-old at the first scan (2000-01). CAC stability was analyzed using previously suggested formulas for significant CAC change.

RESULTS:
On initial CT scan in 2000-01, 1,945 participants had no detectable CAC (0 AU score) and 213 had measurable CAC present (median score 18 AU, range 1-3978). Participants with CAC on the initial scan were more likely to be older, white, male, a smoker, to have high cholesterol and blood pressure, and to have diabetes (all p<0.05). After 10 years, 22% of those with no CAC at baseline had developed CAC (424/1945). For participants with measurable CAC on initial scan, 6.1% (13/213) had a measured decrease in CAC score over 10 years with a median decrease of 2.9 AU (-4.5 to -2.0 interquartile range). Only a single participant had an apparent decrease in score >10 AU over the 10-year follow-up. Thus, using a cut-point of only 1 AU/year change in CAC over 10 years, >99.9% of participants would be considered stable or progressing.

CONCLUSIONS:
We found that true regression of CAC is unlikely to occur in middle-aged adults followed for 10 years. Measurement limitations and associated measurement variability at low Agatston scores may contribute to scores with apparent decreases less than 10 AU noted. These data suggest that any amount of detectable CAC is likely to remain stable or increase over a decade at mid-life. Clinical decisions should not be made relative to apparent declines in CAC scores because these are likely measurement errors.
Stress-Induced Hyperglycemia and Mortality in Critically Injured Trauma Patients

Jaime de la Fuente, Brian K O’Hara, MD, Justin E Richards, MD, Addison K May, MD, FACS

Hyperglycemia in the critically ill leads to increased morbidity and mortality. Studies have confirmed an increased risk of mortality in hyperglycemic, non-diabetic patients, known as stress induced hyperglycemia (SIH), when compared to those with hyperglycemic diabetes mellitus. The purpose of this study was to evaluate the impact of stress induced versus occult diabetic hyperglycemia on mortality in critically ill trauma patients while also identifying predictors of occult diabetes mellitus (ODM).

A retrospective, single-center investigation at a level-1 academic trauma center collected Hemoglobin A1C (HgA1C) data and glucose values on patients admitted to the trauma intensive care unit. Patients were identified as previously undiagnosed diabetics (ODM) or non-diabetics by HgA1C data. The primary outcome of the study was inpatient mortality. The calculated hyperglycemic index (HGI), a validated tool to evaluate long-term glucose control using averages above a set normoglycemic limit (108 mg/dl), was used to follow blood glucose concentrations during the hospital stay. An HGI >2.3, correlating to a glucose value over 150 mg/dl, defined hyperglycemia. A multivariate regression analysis was used, controlling for injury severity score (ISS), age, days on inotropic support and Glasgow Coma Scale (GCS), to determine the impact of hyperglycemia on mortality.

Five hundred and eighty seven patients admitted to the trauma intensive care unit were included in the study. 24% of patients were identified as having ODM and 24% of the patients had persistent hyperglycemia during the hospital stay as determined by HGI indices. There were 127 mortalities in the studied patient population. HGI was higher in the ODM patient cohort (p=0.0001). Non-diabetic, hyperglycemic patients had a mortality rate of 40%, compared to 22% of occult diabetic patients with hyperglycemia (p=0.001).

This study suggests persistent SIH in non-diabetic patients leads to a statistically significant higher risk of mortality when compared to normoglycemic and hyperglycemic ODM patients. In the setting of acute illness or surgery, continued hyperglycemia in those without diabetes serves as a valuable marker of injury severity. SIH that continues throughout the hospital course potentiates the altered physiology seen in trauma patients and contributes to an increased risk of mortality. The impact of non-diabetic hyperglycemia seen in this study may guide further investigations towards management of acute hyperglycemia given its association with poor outcomes.
True Aneurysms of the Pancreaticoduodenal Arcade: Is repair of the associated celiac artery stenosis necessary?

Julia Boll, R. James Valentine, Kenneth W. Sharp, John A. Curci, Thomas C. Naslund, Clifford L. Garrard

OBJECTIVES:
True aneurysms of the gastroduodenal (GDA) and pancreaticoduodenal (PDA) arteries have been attributed to increased collateral flow due to tandem celiac artery stenosis or occlusion. While GDA/PDA aneurysm exclusion is recommended because of the high reported risk of rupture, it remains uncertain whether simultaneous celiac artery reconstruction is necessary to preserve end-organ flow.

METHODS:
A retrospective analysis of consecutive patients admitted 1996-2015 with true aneurysms of the GDA or PDA.

RESULTS:
Twenty subjects with true aneurysms of the PDA (n=16) or GDA (n=4) were identified. The mean age was 61.5 years (range 35-85 y) and 11 (55%) were women. Nine (45%) presented with rupture, 8 (40%) presented with pain, and three (15%) were asymptomatic. Aneurysm size was discernible in 15 cases: the mean size of aneurysms was 16 mm (range 3-25 mm) in subjects with rupture, 19 mm in symptomatic subjects, and 16 mm in asymptomatic subjects. Eight of the 9 subjects who presented with rupture had contained retroperitoneal hematomas, while one had free rupture into the peritoneal cavity. 16 (80%) had an associated celiac artery > 60% stenosis or occlusion, one (5%) had a > 80% SMA stenosis, and one (5%) had both celiac and SMA stenoses. Two (10%) subjects had other aneurysms (hepatic, renal arteries). 13 (65%) subjects underwent successful endovascular coiling, only one of whom had a prophylactic celiac artery bypass. Three (15%) subjects underwent open aneurysm exclusion and celiac bypass, while four (20%) others were observed (including one deemed not a surgical candidate). There were no aneurysm-related deaths in this series, and no subject who underwent coiling without celiac revascularization developed hepatic ischemia or other mesenteric morbidity during a median follow-up of 6 months (maximum 200 months). None of the three asymptomatic patients who were observed experienced rupture during follow up of 12, 60, and 72 months, respectively.

CONCLUSIONS:
While some GDA and PDA aneurysms may be appropriate to observe in asymptomatic patients, these data suggest that the most common presentation is pain or bleeding. However, the bleeding is most often self-contained. Maximal diameter is not a predictor of presentation. Aneurysm exclusion is safely and effectively achieved with endovascular coiling. Although associated celiac artery stenosis is found in the majority of cases, celiac revascularization is not necessary.
Using Genetic Biomarkers to Predict the Likelihood of Brain Metastasis

Brian Bingham, Chike Abana, Tatsuki Koyama, Anuradha Bapsi Chakravarthy, Fen Xia

BACKGROUND:
Metastasis is a complex process and the cause of 90% of cancer deaths. Unfortunately, the features currently used to predict metastatic risk cannot be used at the level of an individual patient. We hypothesize that a patient’s genetic background contributes to metastatic risk. Therefore, genetic variations associated with metastasis could function as prognostic biomarkers. A pilot case control study found the TT allele at SNP rs4506565 and the GG allele at SNP rs1800795—within genes transcription factor 7 like 2 (TCF7L2) and interleukin 6, respectively—to be significantly associated with metastasis to any site. Further analyses also suggested an association between these alleles and brain metastasis which trended toward significance.

OBJECTIVE:
We will compare the prevalence of the TT allele at SNP rs4506565 and the GG allele at SNP rs1800795 in adult patients with primary malignant neoplasms of the lung, breast, colon/rectum and melanoma of the skin who develop brain metastases to matched control patients without metastases.

METHODS:
Case patients were selected from the Synthetic Derivative/BioVU, a de-identified database of patient information from Vanderbilt’s EMR that can be linked to genetic information—using ICD-9 and Tumor Registry codes for the primary malignancies of interest. Due to variations and repetitions in ICD-9 entries to suggest/confirm a specific diagnosis, we conducted an exhaustive review of all case patient charts to ensure high data integrity. Each case will be matched to two controls based on primary cancer site, follow-up time, age, gender, and race. Both groups will be genotyped to determine their allelic variations at rs4506565 and rs1800795 and calculate allelic incidence rates and odds ratios. The significance of our observations will be analyzed with a Chi-squared test.

RESULTS:
A case population of 874 patients was reviewed and is being used to generate a control patient population with a target size of 1,748 patients. Further results are forthcoming pending genetic analysis in early 2016.

CONCLUSIONS:
Identifying host genetic variations associated with a higher likelihood of brain metastasis would allow physicians to tailor treatment decisions to individual patients. If this study confirms a relationship between rs4506565 and rs1800795 alleles and brain metastasis from primary malignant breast, lung, and colorectal neoplasms as well as melanoma of the skin, we will confirm these findings using prospectively collected patient data.
NOVEL METHOD UTILIZING CONTRASTED CT SCAN AS SURROGATE TO NUCLEAR MEDICINE IMAGING FOR DETERMINING DIFFERENTIAL RENAL FUNCTION IN URETEROPELVIC JUNCTION OBSTRUCTION

Jacob Ark, S. Duke Herrell

OBJECTIVES:
Ureteropelvic junction obstruction (UPJO) can deteriorate the function of the affected kidney. Operative intervention for symptomatic UPJO is dichotomously based: if the kidney is functional, relieve the obstruction (i.e. pyeloplasty); if the kidney is nonfunctional, remove it (i.e. nephrectomy). Nuclear medicine renogram (RG) is the gold standard in determining differential renal function. However, RG does not offer detailed anatomic information, so CT scans are also obtained preoperatively, making it a natural surrogate candidate to RG in estimating renal function. We predict that basic measurements taken from a contrasted CT scan can be used to reliably determine whether a kidney with UPJO is definitively functional or nonfunctional, thus obviating the need for a RG in many cases.

METHODS:
This is a single institution, retrospective cohort of patients with UPJO who either underwent pyeloplasty or nephrectomy between December 2004 and December 2014. Included patients had both a preoperative contrasted CT and a RG within 180 days of each other. A single observer performed renal measurements on contrasted CT scans to predict the results obtained from RGs.

RESULTS:
56 patients were included in the study. Renal measurements calculating the average cortical area and Hounsfield units were used to produce a strong correlation between differential CT measurements and differential renal function on RG (Pearson’s r = 0.92, p < 0.00001). Using an equation generated by linear regression, CT measurements predicting >39% and <10% function correlated with RG values of >30% (100% specificity) and <10% (100% specificity), respectively, on ROC analysis. Using these cut-off values, over half (30/56) of the RGs would be considered unnecessary for determination of differential renal function.

CONCLUSIONS:
Contrasted CT in UPJO patients may be utilized to identify definitively functional or definitively nonfunctional kidneys, negating the need for RG prior to appropriate operative intervention in many cases. Our study is the largest homogenous UPJO cohort to evaluate the correlation between CT and RG, does not require additional imaging software, and maintains 100% specificity for determining clearly functional and nonfunctional kidneys when using appropriate cut-offs. The study design favors real-world application, and these findings show great potential in reducing medical cost and time to treatment without sacrificing quality or confidence in medical care.
eHealth Literacy is Associated with Self-Monitoring of Blood Glucose among Patients with Type 2 Diabetes

Taylor Coston, Andrea Lagotte, Chandra Osborn

Self-monitoring of blood glucose (SMBG) facilitates glycemic control, but adherence rates are low. Health literacy and numeracy skills reflect the ability to understand and apply health information and numbers, respectively, and when limited are associated with being less adherent to recommended self-care behaviors, with mixed relations with SMBG. Electronic health (eHealth) literacy is the ability to understand and apply health information from electronic sources and may also be associated with SMBG. Therefore, we examined the relationship between health literacy, numeracy, and eHealth literacy and SMBG, and explored potential moderation by insulin status.

We analyzed cross-sectional data from adults with T2DM recruited for a medication adherence promotion randomized trial. At baseline, we administered The Brief Health Literacy Screen (BHLS), Subjective Numeracy Scale (SNS), and Electronic Health Literacy Scale (eHEALS), and Summary of Diabetes Self-care Activities (SDSCA) SMBG subscale. Regression models assessed the unadjusted and adjusted relationships between the BHLS, SNS, eHEALS and SDSCA-SMBG subscale.

Participants (n=104) were on average 55.6±10.5 years old; 59% female; 72% White; with 15.3±1.9 years of education, and 26% with incomes <$40K; 45% prescribed insulin and the average A1c was 8.2±1.5%. The BHLS and SNS were not associated with SMBG, whereas eHEALS was significantly associated with SMBG in unadjusted (β=.28, p=.00) and fully adjusted models (β=.37, p=.004). While a moderating effect of insulin on the eHealth literacy-SMBG relationship was not significant, there was a differential effect of eHealth literacy on SMBG based on insulin status (non-insulin treated: effect=.22, p=.001; insulin treated: effect=.08, p=.26).

Higher eHealth literacy scores were associated with more frequent SMBG, particularly for patients not prescribed insulin. Future intervention work to promote SMBG should consider accommodating patients with limited eHealth literacy.
Implementation of Clinical Care Pathways is associated with a Generalized Increase in the Use of Multimodal Analgesia

Han Shi, Maxim Terekhov, MS, Jesse M. Ehrenfeld, MD, MPH, Matthew D. McEvoy, MD, Adam B. King, MD, Jonathan P. Wanderer, MD, MPhil

OBJECTIVES:
Enhanced recovery after surgery (ERAS) pathways provide the opportunity to reduce surgical costs and complications, yet they have not been widely adopted in the United States. Our institution established a Perioperative Consult Service (PCS) to implement ERAS pathways. This study examines the adoption of multimodal analgesia both inside and outside of ERAS pathways and factors influencing the utilization of multimodal analgesia.

METHODS:
Surgical cases between January 2013 and October 2015 were retrieved using our Perioperative Data Warehouse. We compared surgical cases before and after ERAS implementation (June 2014), and examined cases outside of ERAS pathways. Outcomes included provider, patient, and procedural factors associated with utilization of multimodal analgesia.

RESULTS:
We studied 62,595 surgical cases, including 59,300 cases outside of ERAS pathways. Cases utilizing any multimodal analgesia increased from 26.11% to 39.77% (p<0.001) before and after the initial ERAS pathway implementation. Factors influencing this adoption included patient-specific factors such as lower American Society of Anesthesiologists Physical Status Class, younger age, and Caucasian race. Provider-specific factors included number of prior ERAS pathway cases for attendings and anesthesia providers, resident and trainees (vs. certified registered nurse anesthetists). Procedure-specific factors included laparoscopy and specific surgical services (gynecology, neurosurgery, orthopedics).

CONCLUSIONS:
An increase in multimodal analgesia usage was seen at our institution from 2013 to 2015 outside of the ERAS pathway implementations. This approach tended to be used more by trainees, providers with more ERAS pathway experience, with patients who were younger, heathier, female, Caucasian race and specific surgical services.
Med Talks: Creating a Video Database to Increase Medical Student Knowledge About Institutional Research

Brian Bingham, Eszter Szentirmai, Alexandra Foxx, Anderson Spickard, MD

OBJECTIVES:

Early medical school research experience is associated with increased motivation of medical students to pursue research later in their careers. At Vanderbilt Medical School, students learn of available research projects through a required research course, a text database, lectures, research forums, or institutional publications. However, students’ familiarity with the research occurring at their institution or the selection of research projects has not been studied. TED Talks is a popular conference of video talks. Applying the TED Talks model to create a video database of local research has the potential to increase medical student knowledge about and involvement in institutional research projects.

METHODS:

For this project, we surveyed students regarding their involvement in and knowledge of research as well as their opinion about a video database of research. There were 56 respondents to the baseline survey.

RESULTS:

All medical students surveyed had participated in research, and 69.6% of students planned to incorporate research into their careers. Despite this, students had limited knowledge of research at their institution: 19.6% didn’t know about any specific projects going on at Vanderbilt, and 50% knew of only a few specific projects. To familiarize themselves with the research at Vanderbilt, medical students most frequently reported looking into projects in their chosen specialty (62.5%) followed by hearing of research through in-person talks, the medical school research course, institution-based publications, the text research database, and research forums. The majority of students noted that they would access a database of “TED Talk”-like videos about institutional research (80.4%), citing length <20 minutes (98.2%) and good speaker quality (94.6%) as the most important factors that would increase their chances of watching these talks.

CONCLUSIONS:

We conclude that medical student knowledge of institutional research is lacking and establishing a “TED Talk”-like video database for dissemination of institutional research information would likely be well received. We have created such a database, which exists on an online web portal where students can search and view videos of interest. We are currently studying the success of this database by collecting feedback from students about the features of effective videos and its impact on medical students’ research project choices and motivation to pursue research in their careers.
The Use of Natural Language Processing to Determine Prostate Cancer Clinical Risk Strata

Justin R. Gregg, Max Lang, Lucy Wang, Jeremy Warner, Daniel Barocas

OBJECTIVES:
In the clinical setting, risk stratification informs prognostication and treatment decisions. It also underlies system-wide efforts to promote the delivery of appropriate cancer care, such as risk-stratum-specific use of bone scan in localized prostate cancer. Thus, determining risk stratum is a prerequisite for payor-driven quality incentives and penalties, physician-led quality improvement, and decision-support tools. While the elements of risk stratum are available in the electronic medical record (EMR), manual data collection is resource intensive, limiting the scalability of these activities. Therefore, we investigated the accuracy of an automated data extraction method, natural language processing (NLP), for extraction of D’Amico risk stratum elements.

METHODS:
Manually collected clinical stage, biopsy Gleason score, and preoperative PSA values from our prospective institutional prostatectomy database were used to categorize patients as low, intermediate or high-risk. NLP algorithms were developed to automate the extraction of the same data points from the EMR, and risk stratum was calculated based on NLP. The ability of NLP to identify the elements of risk stratum (recall) was calculated, and the accuracy of NLP was compared to the manually collected data using the weighted Kappa statistic (K); standard error (SE) is reported.

RESULTS:
Of the 2353 patients treated from 2010-2015, NLP identified all 3 elements in 1945 (recall = 82.7%). Among patients with all 3 elements, NLP had a 91.9% raw agreement with manual risk stratification (K=0.78, SE = 0.02). The K for clinical T stage, Gleason score and PSA extraction by NLP was 0.89, 0.89 and 0.87, respectively. 83.3% of extracted PSA values were within 1.0 ng/mL of the manually collected PSA level.

CONCLUSIONS:
NLP can achieve greater than 90% accuracy on D’Amico risk stratification of localized prostate cancer, with recall of greater than 80%. These figures are comparable to other NLP tasks and illustrate the known tradeoff between recall and accuracy. Automating the collection of risk characteristics could be used to power real-time decision support tools and to scale up quality measurement in cancer care.
Association of T cell and Macrophage Activation with Vascular Health in HIV


OBJECTIVES:
Delineating the relationships between vascular health, inflammation, and immune activation is important to the study of cardiovascular disease (CVD) risk in HIV-infected persons on long-term antiretroviral therapy (ART). We assessed associations between T cell and macrophage activation, brachial artery flow mediated dilation (FMD; a functional measure of arterial smooth muscle response to ischemia), and circulating intercellular adhesion molecule 1 (ICAM-1) and vascular cell adhesion molecule 1 (VCAM-1; two markers of endothelial cell activation).

METHODS
We enrolled 70 HIV-infected adults on Atripla with sustained virologic suppression for >2 years, a CD4+ count >350 cells/µl, no known diabetes or CVD, and no statin use, and measured FMD, ICAM-1, and VCAM-1. Activated (CD38+), senescent (CD57+PD1+), and memory (CD45RO+) CD4+ and CD8+ T cells were measured by flow cytometry. Soluble markers of macrophage activation (sCD14, sCD163, and macrophage inflammatory protein-1α [MIP-1α]) were measured by ELISA and cytometric bead array. The relationships between immunologic and vascular parameters were assessed using regression models adjusted for age, sex, smoking, duration of ART, and body mass index.

RESULTS
Median age was 45 years (IQR 39, 50), median CD4+ count 701 cells/µl (IQR 540, 954), 43% were female and 54% non-white. Lower brachial artery FMD was associated with high CD8+ T cell activation (p<0.01), but FMD was not associated with other T cell subsets or macrophage markers. In contrast, higher ICAM-1 was associated with higher sCD14, sCD163, and MIP-1α (p<0.01 for all), and higher VCAM-1 with sCD163 and MIP-1α (p<0.01 for both). Furthermore, low CD4+ activation and high CD4+ memory cells were associated with high VCAM-1 (p=0.01 for both).

CONCLUSIONS
In HIV-infected adults with virologic suppression, cytotoxic CD8+ activation was associated with impaired brachial artery smooth muscle relaxation. In contrast, increased soluble inflammatory markers, possibly shed by vascular macrophages, were associated with endothelial cell activation. This suggests T cell and macrophage activation adversely affect vascular health via differing mechanisms, and CVD studies in HIV patients should utilize both functional and biomarker vascular assessments. A possible link between a robust CD4+ memory cell expansion on ART and endothelial activation should be investigated further.
Reducing Overuse of Cardiac Telemetry Monitoring: An Initiative to Implement Choosing Wisely Recommendations on General Medicine Services

Rohini Chakravarthy, David Leverenz, Pierce Trumbo, Wade Iams, Meghan Kapp, Kathryn Goggins, Sunil Kripalani

OBJECTIVES:
Choosing Wisely ® is a national campaign aimed at promoting high-value care. The Choosing Wisely Steering Committee at Vanderbilt University Medical Center (VUMC) implements select Choosing Wisely (CW) recommendations at the institution. The Society of Hospital Medicine discourages the “use of continuous telemetry outside of the Intensive Care Unit (ICU) without using a protocol that governs continuation.” Per this recommendation, we aimed to reduce inappropriate telemetry use on general medicine services. The inappropriate use of telemetry increases the cost of care, prolongs hospital stays, produces false positives that interrupt patient care, and increase the risk of falls.

METHODS:
Utilization metrics per general medicine service included the proportion of patients on telemetry for greater than 48 hours, the mean duration of telemetry (in days) for patients on telemetry, and the overall proportion of patients on telemetry. An overarching goal of this trainee-led committee activities is to train a generation of leaders in high value care implementation.

RESULTS:
Pre-implementation data collected during one week in November 2014 demonstrated: 9-21% (mean: 15%) of patients on teaching general medicine services received telemetry monitoring for greater than 48 hours, and the mean duration of continuous telemetry use was 1.8-3.6 days (mean: 2.7 days). Over one year post-implementation, data collected over one week in January 2016 these rates were: 6-22% (mean: 11%) and 0.75-4.8 days (mean: 2.6 days) respectively. These values provide a snapshot of telemetry use over the course of the intervention.

CONCLUSION:
The current initiative has demonstrated the role of complex clinical decision-making in telemetry ordering, competing institutional and patient-centered priorities, the value of stakeholder engagement and peer champions, and the benefits of real-time data feedback. The next step in reducing unnecessary telemetry utilization is implementation of an automatic discontinuation protocol to empower nursing staff to guide appropriate utilization when certain safety criteria are met. By sequentially implementing Choosing Wisely initiatives, we are gaining a deeper understanding of nuanced barriers and keys to success when seeking to reduce instances of medical overuse.
Evaluation of Diabetes Mellitus as a Risk Factor for Major Complications in Patients Undergoing Aesthetic Surgery

Ravinder Bamba MD, Varun Gupta MD, R. Bruce Shack MD, James Grotting MD, K. Kye Higdon

OBJECTIVES:
Diabetes mellitus has been linked with a variety of perioperative adverse events. The purpose of this study was to compare complications between diabetic and non-diabetic patients undergoing various aesthetic surgical procedures, to identify specific procedures where diabetes significantly increases risk of complications, and to study diabetes as an independent risk factor for major complications following aesthetic surgery.

METHODS:
A cohort of patients who prospectively enrolled in the CosmetAssure insurance program and underwent cosmetic surgical procedures between May 2008 and May 2013 was reviewed. Major complications were compared between the diabetic and non-diabetic patients. Stratified analysis was performed across different procedures and Body Mass Index categories. Univariate and multivariate regressions analyses was performed to evaluate diabetes as an independent risk factor for major complications.

RESULTS:
From May 2008 to May 2013, a total of 183,914 cosmetic surgery procedures were performed on 129,007 patients enrolled in the CosmetAssure program. Pre-existing diabetes was recorded in 2,368 (1.8%) of patients, forming the exposure group of our cohort. Sixty-five percent of the diabetic patients were overweight or obese (BMI ≥ 25) compared to 35.7% of the non-diabetic patients (p<0.01). Overall, 2,506 patients (1.9%) had a major complication. Diabetics had significantly more complications compared to non-diabetics (3.1% vs 1.9%, p<0.01). In univariate analysis, infectious (1.1% vs 0.5%, p<0.01) and pulmonary (0.3% vs 0.1%, p<0.01) complications were significantly higher among diabetics. Complication rates were even higher in those with a BMI over 30 and diabetes (Figure 5,6,7) Notably, diabetics had higher risks of complication in body cases (4.3% vs 2.6%, p<0.01) and specifically abdominoplasty (6.1% vs 3.0%, p<0.01).

In multivariate analysis, diabetes was found to be an independent risk factor of any complication (relative risk 1.31, p=0.03) and infection (relative risk 1.70, p<0.01).

CONCLUSION:
Diabetes is associated with increased major complications in body procedures, particularly abdominoplasty. Our analysis highlights outcomes of diabetic patients undergoing cosmetic surgery, and specifically reveals that diabetes is an independent risk factor for major complications, most notably infection.
Outcomes of Primary versus Complex Closure in Intrauterine Myelomeningocele Repair

Diana G. Douleh, Ashly C. Westrick, Mary A. Carroll, Stephane A. Braun, Ray L. Paschall, Ann L. Kavanaugh-McHugh, Kelly A. Bennett, John C. Wellons III, Chevis N. Shannon

OBJECTIVES:
Intrauterine myelomeningocele repair (IUMR) has been previously validated for selected patients by the Management of Myelomeningocele Study as offering better neurologic outcomes, decreased need for shunting by age 12 months, and improved motor development compared to standard postnatal repair. IUMR is a technically difficult procedure, presenting the neurosurgeon with the time-constrained, intraoperative demand to determine the method of closure: primary closure with local surrounding skin or complex closure with bilateral vertical incisions parallel to the defect and advancement of the resultant flaps. The purpose of this study was to determine the effects of complex closure, as performed at Vanderbilt University Medical Center (VUMC), on defect closure outcome at birth and hydrocephalus development.

METHODS:
A retrospective review complemented with the maternal fetal medicine surgery clinical database was performed on all patients having undergone IUMR repair at VUMC from March 2011 to September 2015. Maternal demographics, neonatal data, clinical, and follow-up outcomes were collected. We assumed our cohort followed a normal distribution, therefore parametric statistics were run using SAS 9.2. Statistical significance was set a priori at p <.05.

RESULTS:
We identified 60 patients having undergone IUMR at VUMC from March 2011 to September 2015. Primary closure was performed in 51 patients (85%) and complex closure was performed in 9 patients (15%). As Vanderbilt serves as a referral center for fetal surgery, data were not available for children followed up outside of the VUMC system. Neonatal baseline data was available for 29 patients. Of these, 22 were closed primarily and 7 required complex closure. Those with complex closure were less likely to require additional closure for wound dehiscence following birth (0% vs. 9.09%). Although not found to be statistically significant, CSF diversion for the treatment of hydrocephalus was required less frequently in those receiving complex closure versus those closed primarily, 28.57% vs. 48.0%. Closure type, complex versus simple, had no effect on preterm delivery (85.7% vs. 80.0%, respectively, p=1.0).

CONCLUSIONS:
Patients with complex closure were found to have a greater instance of closure at delivery and decreased need for a CSF diversion procedure within 12 months of birth. Although not statistically significant, the results indicate a potential protective effect of complex closure on wound dehiscence and hydrocephalus development.
A novel association between high density lipoprotein levels and the risk of acute kidney injury after cardiac surgery

Loren E Smith, Derek K Smith, DDS, MacRae F Linton, MD, Frederic T Billings IV, MD, MSc

OBJECTIVES:
Acute kidney injury (AKI) after cardiac surgery occurs in up to 30% of patients and is an independent predictor of death. HDL may attenuate mechanisms of AKI. We hypothesized that a high preoperative HDL cholesterol concentration is protective against postoperative AKI.

METHODS:
We analyzed data from a prospective, 393-subject trial of perioperative atorvastatin to prevent post-cardiac surgery AKI. Statin-using patients were randomized to placebo or 80mg atorvastatin the morning of surgery and 40mg on postoperative day 1. Stain-naïve patients were randomized to placebo or 80mg the day prior to surgery and 40mg daily thereafter during hospitalization. The association between HDL level and maximum serum creatinine change from baseline in the first 48 postoperative hours was assessed using a two-component latent variable mixture model and AKI risk factors. Regression analyses assessed the interaction chronic statin use, perioperative atorvastatin treatment, and HDL level on AKI risk.

RESULTS:
Postoperative AKI occurred in 99 patients (25.2%). Median (10th, 90th percentile) preoperative HDL was 37.6 (25.0, 54.0) mg/dl and postoperative creatinine change 0.09 (-0.11, 0.59) mg/dl. Lower HDL levels were independently associated with increased creatinine rise (p=0.02). Regression analysis showed this association was present in statin-using but not statin-naïve patients (p=0.008). The protective effect of high HDL in chronic statin users was enhanced with perioperative atorvastatin treatment (p=0.004) and with increasing chronic statin dosage (p=0.003). Similar analyses using LDL found no association with postoperative AKI risk (p=0.51).

CONCLUSIONS:
Increasing HDL levels are associated with smaller creatinine change among patients receiving chronic statin therapy with larger decreases observed in those on increased dosage of chronic statin. This effect is potentiated by receiving perioperative statin therapy.
Association Between Parent Health Literacy and Infant Immunization Status

Edward Iglesia, Lee M Sanders, MD, MPH, Andrea B Bronaugh, BA, Eliana M Perrin, MD, MPH, H Shonna Yin, MD, MS, Alan M Delamater, PhD, Russell L Rothman, MD, MPP

BACKGROUND:
Low parent health literacy is associated with poor child health outcomes and preventive care behaviors. Childhood immunization is a Healthy People 2020 leading health indicator and targets a rate of 80%. The relationship between health literacy and immunization status is under-explored.

OBJECTIVE:
To examine the relationship between parent health literacy and infant immunization status.

DESIGN/METHODS:
Cohort analysis was performed on data from Greenlight, a cluster RCT of a low-literacy intervention to prevent early childhood obesity. The primary predictor variable was parent health literacy (Short Test of Functional Health Literacy in Adults; adequate ≥ 23, low < 23). Outcomes included up-to-date status (yes/no) of all recommended CDC/ACIP immunizations at milestone ages of 3, 5, and 7 months, as well as receipt of at least one seasonal influenza immunization by 12 months of age. Immunization records were abstracted from participants' health records. Unadjusted associations were performed using Pearson chi-square test. Multivariate logistic regression was performed adjusting for child gender, out-of-home childcare, WIC program status, caregiver age and relationship, country of birth, race/ethnicity, household language, number of adults/children in the home, household income, parent education level, child clinic attendance show rate, and study site.

RESULTS:
Eight-hundred forty-three parent-child dyads enrolled at 2 months of age and completed the STOF-HLA. At 3, 5, and 7 months of age, 86%, 68%, and 51% of infants were up-to-date with their immunizations, respectively. Fifty-four percent received at least one influenza immunization by 12 months of age. Immunization records were abstracted from participants' health records. Unadjusted associations were performed using Pearson chi-square test. Multivariate logistic regression was performed adjusting for child gender, out-of-home childcare, WIC program status, caregiver age and relationship, country of birth, race/ethnicity, household language, number of adults/children in the home, household income, parent education level, child clinic attendance show rate, and study site.

CONCLUSIONS:
Low parent health literacy is associated with nonreceipt of influenza immunization in infants, but not with other routine immunizations. There may be misperceptions about the benefits of influenza immunization that are influenced by low literacy. A low-literacy approach should be used to increase influenza immunization rates.
Cost Analysis of Cerebrospinal Fluid Leaks and Cerebrospinal Fluid Leak Prevention in Patients Undergoing Cerebellopontine Angle Surgery

*Alexander Chern BS, Jacob B Hunter MD, Marc L Bennett MD*

**OBJECTIVE:**
To determine if cranioplasty techniques following translabyrinthine approaches to the cerebellopontine angle (CPA) are cost-effective

**Study Design:** Retrospective case series

**Patients:** One hundred and eighty patients with available financial data who underwent translabyrinthine approaches at a single academic referral center between 2005 and 2015

**Intervention:** Cranioplasty with a dural substitute, layered fat graft and a resorbable mesh plate secured with screws

**Main Outcome Measures:** Billing data was obtained for each patient’s hospital course for translabyrinthine approaches and postoperative cerebrospinal fluid (CSF) leaks

**RESULTS:**
One hundred and nineteen patients underwent translabyrinthine approaches with an abdominal fat graft (AFG) closure, with a median cost of $25,759.89 (range $15,885.65-$136,433.07). Sixty-one patients underwent translabyrinthine approaches with a dural substitute, AFG, and a resorbable mesh for closure, with a median cost of $29,314.97 (range $17,674.28-$111,404.55). The median cost of a CSF leak was $50,401.25 (range $0-$384,761.71). The additional cost of a CSF leak when shared by all patients who underwent translabyrinthine approaches is $6,048.15. The addition of a dural substitute and a resorbable mesh plate following translabyrinthine approaches reduced the CSF leak from 12% to 1.9%, an 84.2% reduction, and a median savings per patient of $2,932.23. Applying our cohort’s billing data to previously published cranioplasty techniques, costs, and leak rate improvements following translabyrinthine approaches, all techniques were found to be cost-effective.

**CONCLUSIONS:**
Resorbable mesh cranioplasty is cost-effective at reducing CSF leaks following translabyrinthine approaches. Per our billing data and achieving the same CSF leak reduction, cranioplasty costs exceeding $5,080.32 are not cost-effective.

Define Professional Practice Gap & Educational Need: Minimal literature has discussed costs associated with post-operative CSF leaks. It is imperative for physicians to appreciate such costs as the American healthcare system shifts towards a bundled payment system.

Learning Objective: To describe costs associated with CSF leaks and cranioplasty techniques used to reduce postoperative CSF leak formation.

Desired Result: Attendees will appreciate costs of postoperative CSF leaks and cranioplasty techniques that can drastically reduce both the incidence and costs of postoperative CSF leaks.
Thank You for your participation and attendance at the 34th Annual Research Forum