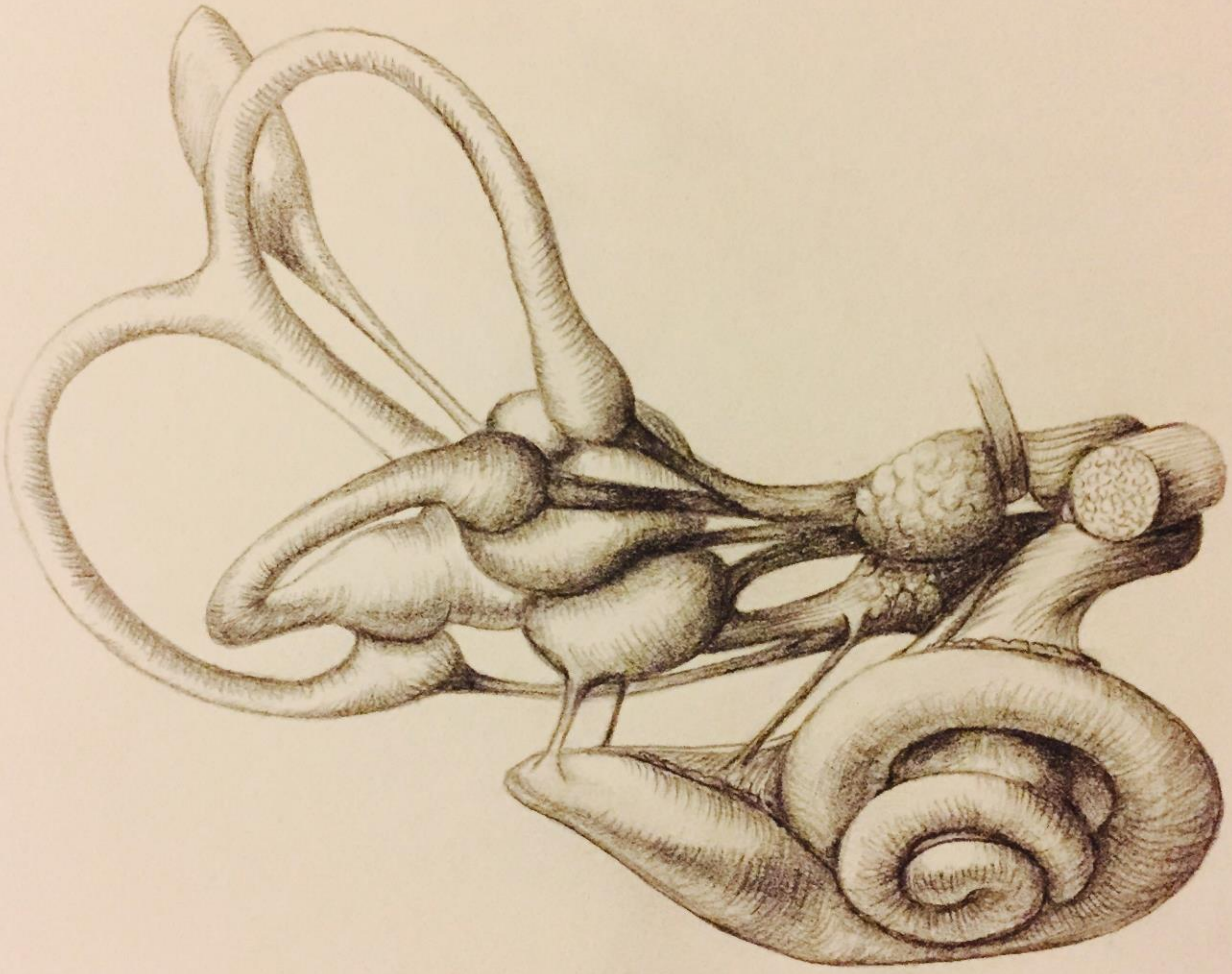
7th Annual
Medical Student Research Day



February 6, 2015

Johns Hopkins University School of Medicine
Armstrong Medical Education Building

Cover image courtesy of

Alice He, MS2

The inner ear is one of the most fascinating parts of the human body. The inner ear is a sophisticated structure that combines complex biophysics with intricate beauty. It is one of the smallest structures in the body, but its detailed anatomy also makes it one of the most beautiful structures. Its complex design allows for two important functions: balance and sound detection. Balance of the entire human body is dictated by the tiny amount of fluid contained within the tubes, and sound detection occurs through a carefully coordinated mechanism involving inner hair cells contained within the cochlea. This pencil sketch showcases the beautiful anatomy of the inner ear: semicircular canals, cochlea, utricle, and saccule.

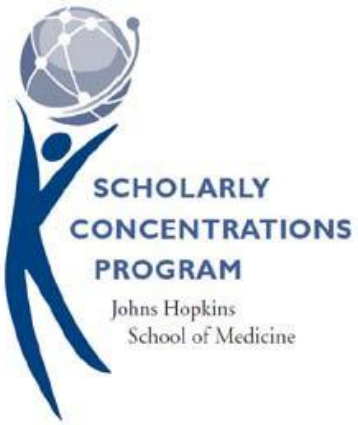
TABLE OF CONTENTS

Medical Student Research Day 2015

We are pleased to have you join us for the 7th annual Medical Student Research Day of the Johns Hopkins University School of Medicine. As clinicians in training, we are fortunate to work among faculty who conduct a broad range of investigation that yields advances in the knowledge of human health. For the past five years, we have been privileged to have an event that presents the extensive endeavors that students take to advance this mission at the school.

The mission of the Johns Hopkins University School of Medicine is to educate medical students, graduate students, and postdoctoral fellows in accordance with the highest professional standards; to prepare clinicians to practice patient-centered medicine of the highest standard; and to identify and answer fundamental questions in the mechanisms, prevention and treatment of disease, in health care delivery and in the basic sciences.

Medical Student Research Day is a forum for medical students at Johns Hopkins to present their own research to the greater Hopkins community. It is an opportunity for students to participate in the exchange of intellectual ideas in a professional format and meet faculty who relish the pursuit of better science and more effective medicine. Our mission is for Medical Student Research Day to foster the development of young researchers who will aid in the advancement of scientific medicine for years to come.



The Scholarly Concentration (SC) program is a faculty-mentored scholarly experience for medical students. This program provides the infrastructure and mentoring necessary for students to produce a scholarly project in an area of individual interest, and encourages the acquisition of attitudes and skills for lifelong learning and scholarship. The SC program offers the following five areas of study:

Basic Science	Sarah Wheelan, MD, PhD
Clinical Research	Kelly Gebo, MD, MPH Jennifer Haythornthwaite, PhD Steve Sozio, MD, MHS Megan Reller, MD, MPH
History of Medicine	Randall Packard, PhD Graham Mooney, PhD
Medical Humanities Bioethics and The Healing Arts	Joe Carrese, MD, MPH Gail Geller, ScD, MHS
Public Health and Community Service	Eric Bass, MD, MPH David Friedman, MD, PhD

The overall goals of the SC program are to promote intellectual curiosity, appreciation of scholarly inquiry, flexibility, passion for discovery, openness to new ideas, and the ability to work both independently and collaboratively.

PROGRAM SCHEDULE

12:00 – 12:30 PM	**Registration/Lunch** *AMEB Main Lobby*
12:30-2:15 PM	**Podium Presentations** *AMEB Lecture Hall*
2:15-3:45 PM	**Poster Session** *AMEB 2nd Floor*
3:45-4:45 PM	**Concurrent Oral Presentations** *RM 320, 326, 341, 342, 343, 344, 345, 370*
4:45-5:30 PM	**Keynote speaker, *Dr. Dorry Segev*** **MSRD Award Ceremony** *AMEB Lecture Hall*

KEYNOTE SPEAKER

Dorry Segev, M.D., Ph.D.

Associate Professor of Surgery and Epidemiology at the Johns Hopkins University School of Medicine

Dr. Dorry Segev is a pioneer in abdominal transplant surgery who has made numerous critical contributions to the field of transplantation through his work in complex statistical analyses for mathematical modeling of transplantation allocation and outcomes and simulation of medical data. He specializes in innovative strategies for incompatible organ transplantation, minimally invasive live donor surgery, and disparities in access to transplantation. His many accomplishments include developing a mathematical model to facilitate a nationwide Kidney Paired donation program in both the United States and Canada, for which he received the American Society of Transplant Surgeons 2006 Vanguard Prize and was featured in the TIME magazine “Innovators” issue.

Dr. Segev received his undergraduate degree in computer science before receiving his medical school, general surgery, and multi-visceral abdominal transplant surgery training at Johns Hopkins. Since then, he has authored more than 150 peer-reviewed research articles in journals including New England Journal of Medicine, JAMA, American Journal of Transplantation, Annals of Surgery, and Journal of the American Society of Nephrology. He is an NIH Clinical Research Scholar, American Geriatrics Society Dennis Jahnigen Scholar, National Institute of Aging Paul Beeson Scholar, senior investigator for the Scientific Registry for Transplant Recipients, and Doris Duke Clinical Scientist Development Award recipient.

In addition to his many achievements in transplant surgery, Dr. Segev has also received multiple awards in Lindy Hop and swing dancing including placing multiple times in the American Lindy Hop Championships and winning the 2002 UK Championship with his wife and research partner Sommer Gentry.

Dr. Segev is an Associate Editor for the American Journal of Transplantation, American Journal of Kidney Diseases and Liver Transplantation. His work has been regularly featured in TIME magazine, the Discovery Channel, US News & World Report, the New York Times, and other prominent media outlets.

Faculty Judges

Eric Bass, MD, MPH
Professor of Medicine

Jamil Bayram, MD, MPH
Assistant Professor of Emergency Medicine

Mary Catherine Beach, MD, MPH
Associate Professor of Medicine

Diane M. Becker, ScD, MPH
Professor of Medicine
Director of Center for Health Promotion

Wendy Bennett, MD, MPH
Assistant Professor of Medicine

Kathleen Burns, MD, PhD
Assistant Professor of Pathology, Pathobiology Graduate Program, and Oncology

Joseph Carrese, MD, MPH
Associate Professor of Medicine

Margaret Chisolm, MD
Associate Professor
Director of Education at Johns Hopkins Bayview Department of Psychiatry

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Assistant Professor of Biostatistics and Bioinformatics

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Assistant Professor of Infectious Disease Epidemiology

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Professor of History of Medicine

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Professor of Ophthalmology

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Assistant Professor of Pediatric Oncology

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Professor of Oncology

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John J. Strouse, MD, PhD
Assistant Professor of Hematology

Daniel Todes, PhD
Professor of History of Medicine

Sarah Wheelan, MD, PhD
Assistant Professor of Oncology
Biostatistics and Bioinformatics

Schedule of Podium Presentations

12:30 pm	Allen Feng	*Deconstructing The Total Laryngectomy Neck Incision: A Clinical Review and Finite Element Analysis*
12:40 pm	Anirudh Arun	*Immunomodulation of T cells in inflammatory environments: a novel mechanism for pathogenesis of autoimmunity*
12:50 pm	Meera Chappidi	*Arthroscopic Transosseous Rotator Cuff Repair is Cost-Effective Compared to Anchored Technique*
1:00 pm	Seema Kacker	*Financial Implications of RHD Genotyping of Pregnant Women with a Serologic Weak D Phenotype*
1:10 pm	Seva Khambadkone	*Impact of a specific dietary intervention on the microbiome-gut-brain axis and risk for neuropsychiatric disorder*
1:20 pm	Rebeccah McKibben	*Hepatitis C Virus Infection Is Associated with Subclinical Coronary Atherosclerosis in the Multicenter AIDS Cohort Study (MACS)*
1:30 pm	Leah Medrano	*The lupus patient and the advent of corticosteroid therapy*
1:40 pm	Maria Phillis	*The Importance of Facial Lesion Reconstruction for Normalizing Affect Display*
1:50 pm	Ryan Shields	*Risks and Benefits of Routine Collection of Sexual Orientation and Gender Identity Information in Healthcare: The Patient Perspective*
2:00 pm	Daren Simkin	*Working with Gore Vidal: A Memoir of Caregiving and Aging*

Schedule of Concurrent Oral Presentations

1. Basic Science: Room 320

3:45-3:55 pm	Devin Miller	*The Impact and Mechanisms of Antibody-Mediated Rejection in Vascularized Composite Allotransplantation*
3:55-4:05 pm	Maimon Hubbi	*An Essential Role for Lysosomal Function in Cancer Cell Proliferation*
4:05-4:15 pm	Sarah Scotland	*Metformin targets human acute myeloid leukemia cells through upregulation of the ATF4/DDIT3/4 stress response pathway*
4:15-4:25 pm	Georgia C. Yalanis	*An Electrospun Fiber-Hydrogel Composite with Interfacial Bonding for Soft Tissue Regeneration in vivo*
4:25-4:35 pm	Shekhar Gadkaree	*Cyclic Dinucleotide induced Regression of Tumor in a Squamous Cell Carcinoma Mouse Model*

2. Basic Science and Clinical Research: Room 326

3:45-3:55 pm	David Gullotti	*Assessment of repetitive mild traumatic brain injury by retinal imaging with optical coherence tomography*
3:55-4:05 pm	Ridwan Alam	*Active Surveillance: When Can Patients Stop Worrying?*
4:05-4:15 pm	Ridwan Alam	*Using the Manual Muscle Test to Predict C5 Palsy Resolution*
4:15-4:25 pm	Katie Hsih	*Attachment style is a predictor for the effects of oxytocin on social cognition*
4:25-4:35 pm	Malgorzata Dymerska	*Predictive Value of Size of Port-Wine Stains in Sturge-Weber Syndrome*

3. Clinical Research: Room 341

3:45-3:55 pm	Alim Ramji	*Cannulated Lag Screw Fixation of Displaced Lateral Humeral Condyle Fractures is Associated with Lower Rates of Open Reduction and Infection than Pin Fixation*
3:55-4:05 pm	Stanley Guillaume	*Anchored versus Anchorless Rotator Cuff Repair: A Biomechanical Analysis*
4:05-4:15 pm	Akachimere Uzosike	*Duration of drain indwelling following instrumented posterolateral fusion of the lumbar spine predicts surgical site infection requiring reoperation*
4:15-4:25 pm	William Plum	*Predictors of Early and Late Mortality Following Valve Operations for Infective Endocarditis*
4:25-4:35 pm	Allen Young	*Long Term Outcomes of Aortic Root Operations for Marfan Syndrome: A Comparison of Bentall versus Aortic Valve-Sparing Procedures*

4. Clinical Research and Public Health: Room 342

3:45-3:55 pm	Alex Harding	*Changes In Care Continuity And Outcomes After The 2011 Resident Duty Hours Restrictions: Data From An Academic Medical Center's Department Of Medicine*
3:55-4:05 pm	Sydur Rahman	*Disparities in Patient Satisfaction between Races in Inpatient Pediatrics*
4:05-4:15 pm	Robin Megill	*The "July Effect" in Thoracic Surgery: A NSQIP Analysis*
4:15-4:25 pm	Jacob Cox	*Comparative Analysis of the French and American Trauma Systems Using Patient Outcomes*
4:25-4:35 pm	Caleb Fan	*Safety Culture and Surgical Site Infection Outcomes Following Colorectal Surgery*

5. Clinical Research: Room 343

3:45-3:55 pm	Wynne Callon	*Features of the Lesch-Nyhan Phenotype Correlate More Closely with Guanine than Hypoxanthine Phosphoribosyltransferase Enzyme Activity*
3:55-4:05 pm	Aaron Parzuchowski	*Frequency of Protocol Deviations in Pediatric versus Adolescent and Young Adult Populations with Hodgkin's Lymphoma and its Impact on Clinical Outcomes*
4:05-4:15 pm	Katie Holroyd	*Deep brain stimulation targeting the fornix for mild Alzheimer's Dementia: baseline population description and design of the ADvance trial*
4:15-4:25 pm	Regina de Luna	*Can Patients Read What They Are Signing? A test of consent form readability among ophthalmic patients*
4:25-4:35 pm	Sbaa Syeda	*Preoperative motor strength and time to surgery are the most important predictors of improvement in foot drop due to degenerative lumbar disease.*

6. Bioethics and Public Health: Room 344

3:45-3:55 pm	Stephanie Wang	*Talking about "Burden" in the Clinic: Caring for Older Patients with Multimorbidity*
3:55-4:05 pm	Katherine Marcus	*Systems of Communication and Decision-making for Chronically Critically Ill Infants: Identifying "Red Flags" to Prompt Discussion about Goals of Care*
4:05-4:15 pm	Sminu Bose	*Developing a Best Practices Advisory Tool in Epic To Address the Palliative Care Needs of Oncology Patients*
4:15-4:25 pm	Phoebe Bacon	*Enhancing autonomy in biobank decisions: Too much of a good thing?*
4:25-4:35 pm	Carolyn Arnold	*Urban Children with Poorly Controlled Asthma Disagree with Caregivers and Clinicians on Reasons for Not Using Controllers*

7. History of Medicine and Public Health: Room 345

3:45-3:55 pm	Mark Iscoe	*Can You Do It in Silicon? The Quest to Create a Computer-Based Medical Expert in the 1970s*
3:55-4:05 pm	Sze Yan Janelle Ho	*History of Smokeless Tobacco 1960s-1990s: Evasion of Governmental Regulation and the Creation of Scientific Ignorance in Smokeless Products*
4:05-4:15 pm	Kamini Kuchinad	*A qualitative study of barriers and facilitators to engaging in the HIV care continuum among individuals with substance use/misuse*
4:15-4:25 pm	Ekene Obi-Okoye	*Provider Knowledge and Perceptions of Current Breastfeeding Support During Prenatal Care*

8. Public Health: Room 370

3:45-3:55 pm	Manoj Maddali	*Economic and epidemiologic impact of early antiretroviral therapy initiation on HIV care continuum in India*
3:55-4:05 pm	Rosa Miller Polan	*Susceptibility weighted imaging in pediatric arterial ischemic stroke: a valuable alternative for the non-invasive evaluation of altered cerebral hemodynamics*
4:05-4:15 pm	Joshua Lupton	*The association between serum homocysteine and an atherosclerotic lipid profile*
4:15-4:25 pm	Ian Yarett	*TSH level as a predictor of weight loss magnitude in Johns Hopkins Weight Management Center patients*
4:25-4:35 pm	Aparna Krishnan	*Barriers to colorectal cancer screening as determined by the knowledge, attitudes, and practices of patients at Orange Blossom Family Health*

POSTER PRESENTERS

AMEB 2nd Floor

Listed Alphabetically by Research Category

BASIC SCIENCE

#	Name	Title
1	Somya Abubucker	Evaluation of the Combination of Histone Deacetylase Inhibitors with Mebendazole in Meningioma
2	Julio DeJesus	Clinical and surgical outcomes of gliosarcomas: the Johns Hopkins Hospital experience
3	Shekhar Gadkaree	Cyclic Dinucleotide induced Regression of Tumor in a Squamous Cell Carcinoma Mouse Model
4	Ilona Juan	Yeast Augmented Network Analysis (YANA) to Identify a Therapeutic Target for Parkinson's Disease
5	Rabia Karani	The proteome of normal human retrobulbar optic nerve
6	Lyonell Kone	Screening for GBM specific pro-inflammatory cytokines in murine macrophages
7	Andrew Luksik	The role of haptoglobin in vasospasm following subarachnoid hemorrhage.
8	Emily Murphy	Molecular profiling of murine nucleus accumbens inputs using recombinant Rabies virus
9	Powell Perng	Therapeutic Effect of local and Systemic Carmustine on Anti-PD-1 Immunotherapy in a Murine Brain Glioma Model
10	Cole Sterling	Assessing intracranial delivery of carboplatin and dichloroacetate for the treatment of glioblastoma multiforme in rodents
11	Sharif Vakili	Electrocorticographic Correlates of Metaphysics and Cognitive Dissonance

12	Frances Wang	Elucidating mechanism of skin type regulation for the prevention and treatment of stump site dermatosis in amputees
13	Adela Wu	In vivo study assessing the migratory capacity of mesenchymal stem cells

CLINICAL RESEARCH

#	Name	Title
14	Jarred Bressner	Orthopaedic management of the spine in patients with Loeys Dietz Syndrome
15	Nicholas Calotta	Severe Carpal Tunnel Syndrome: Does Endoscopic Release Compare Favorably to Open Release for these Patients?
16	Sophia Chen	Risk Factors and Implications of Post-Discharge Complications after Bariatric Surgery: a NSQIP Analysis
17	Chris Cottrell	Effect of Smartphone App Usage on Adherence to 10,000 Steps Program
18	Kristin Darwin	Depressive symptoms are associated with poorer antiretroviral adherence and less viral suppression among hazardously drinking HIV-infected women
19	Judy Doong	Impaired Recognition of Musical Sound Quality Deterioration in Cochlear Implant Users: Sample Rate and Comb-Filtering
20	Ankur Doshi	Implementing a Clinical iPad Application to Detect Sleep Disorders is Feasible Across Multiple Non-Sleep Outpatient Clinics
21	Megan Gornet	Does Size Matter? A Comparison of Preoperative MRI in Adolescent Idiopathic Scoliosis (AIS) Patients With Curves <80 vs ≥80°
22	Alexis Graham	Increasing Protein Intake during Overfeeding Increases Energy Expenditure, Satiety, and Urinary Cortisol
23	Alice He	Cochlear Implant Users Require Exaggerated Pitch Contours to Identify Mandarin Tones
24	Alice Hung	Differences in Functional Outcome Across Subtypes within Spetzler-Martin Grade II Arteriovenous Malformations (AVMs)

25	Dvone Jackson	The Feasibility of Radiation Dose De-Escalation for the Treatment of Very-Low Risk Prostate Carcinoma
26	Nicole Jiam	Feasibility of Flat-Panel CT Imaging for Individualized Pitch Mapping in Cochlear Implant Users
27	Sarah Joo	Hepcidin as a Mediator of Cardiovascular Risk in Children with Systemic Lupus Erythematosus and Lupus Nephritis
28	Maria Kryatova	Nasal Infantile Hemangiomas: Characteristics, Complications, and Outcomes
29	Ishaq Lachin	Alternative Medical Practices in Post-Operative Pain Management
30	Katherine Levandoski	Favorable Long-Term Outcomes in Pediatric Patients with Atypical Spitz Tumors Treated with Wide Excision
31	Jacob Light	Novel Subretinal Findings in Stargardt Disease Using Spectral Domain-Optical Coherence Tomography (SD-OCT)
32	Melanie Major	The Effect of Timing on Breast Reconstruction Outcomes in Diabetic Women: A Comparison of NSQIP and Johns Hopkins Patient Data
33	Madeleine G. Manka	Does Use of a Second Cuff Improve Artificial Sphincter Effectiveness? Evaluation Using a Comparative Cadaver Model
34	Rouzbeh Mashayekhi	Does microRNA 146b-5p expression level predict central lymph node metastasis of papillary thyroid cancer?
35	Russell Maxwell	A Retrospective Analysis of Progression to Brain Metastasis According to BRAF-V600 Mutational Status
36	Jessica Moore	Complex Esophageal Reconstruction Procedures Have Similar Outcomes to Routine Esophagectomy
37	Ankur Narain	Examination of Peri- and Post-operative Complications in Patients With Implantable Cardiac Devices After Total Shoulder Arthroplasty
38	Suresh Kevin Nayar	Multidisciplinary Rehabilitation of Hip Fractures: Bridging the Gap between Orthopaedics and Physical Therapy
39	Mohamud Qadi	Effect of prior ophthalmic surgery on open globe injuries
40	Nick Rosculet	The Neutrophil To Lymphocyte Ratio Is A Prognostic Indicator For Head And Neck Squamous Cell Carcinoma

41	Anthony Serritella	An Analysis of VTE Prophylaxis Practice in Oncology Patients after Implementation of a Standardized Mandatory Computerized Clinical Decision Support Tool
42	Harita Shah	Healthcare Activation and Health Literacy in Low-Income Spanish- and English-Speaking Parents of Young Children
43	Liyang Tang	Does Emotional Intelligence Affect Cochlear Implant Outcomes in Older Adults?
44	Trinh Trang	Multicenter Retrospective Cohort Study of Topical Timolol for Treatment of Infantile Hemangiomas
45	Kevin Yuqi Wang	Tract-specific Diffusion Tensor Imaging in Cervical Spondylotic Myelopathy After Decompressive Spinal Surgery
46	Ophelia Yin	Polycystic Ovary Syndrome Does Not Appear to Affect Menopausal Transition Symptoms

HISTORY OF MEDICINE

47	Ambar Mehta	A Historical Analysis of New York City's Tuberculosis Epidemic
48	Ayresleigh Rowland	Mind, Matter, and Motherhood: Shifting Paradigms of Puerperal Insanity in the Early 20th Century
49	Mary Smith	The East Baltimore Medical Plan: A look at the realtionship between JHMI and the East Baltimore Community
50	Alex Stone	Crowded: The Development of Emergency Medicine at the Johns Hopkins Hospital
51	Crystal Wang	Investigating the etiology of dengue hemorrhagic fever in Thailand from 1950-1967

MEDICAL HUMANITIES, BIOETHICS, and the HEALING ARTS

#	Name	Title
52	Christopher Bailey	Automated social media for learning: Facebook push notifications for Radiology correlation and education during Gross Anatomy
53	Zachary Obinna Enumah	Healing Systems, Attitudes and Perceptions in Nyarugusu Refugee Camp, Kigoma, Tanzania
54	Niyati Mamtora	Catching Waves: The Perspectives of Physicians Who Surf
55	Maxine Norcross	LiveWell in a Learning Community: A Student-Driven Curriculum Supporting Self-Care
56	John Schimek	Helping Hands: Peer advice for parents of pediatric oncology patients

PUBLIC HEALTH and COMMUNITY SERVICE

#	Name	Title
57	Laura Anzaldi	Tracking Purpose in Life of Those Affected by Multiple Sclerosis Who Are Members of an Online Support Network
58	Karun Arora	Providing High-Volume, High-Quality, Low-Cost Cataract Surgery in Sub-Saharan Africa
59	Marcelo Cerullo	Assessing the association between insurance and management of pediatric blunt splenic injuries
60	Cody Cichowitz	Assessing Continuity of Care from Hospital to Community in South Africa
61	Pujan Dave	Ability of Bottle Cap Color to Facilitate Accurate Glaucoma Patient-Physician Communication Regarding Medication Identity
62	Timothee Fruhauf	Predictors of Contraceptive Use Among Youth Ages 15-24 in Ghana

63	Jasmine Holmes	Project Perfect Fit: Quality Improvement Initiative of the Lose Dat Program
64	Seema Kacker	Socioeconomic Correlates of Trauma: An Analysis of Emergency Ward Patients in Yaoundé, Cameroon
65	Sunaina Kapoor	Cost-effectiveness of Isoniazid Preventative Therapy for HIV-infected pregnant women in India
66	David J. Lee	Disparities in Patient Satisfaction based on Race, Gender, Education, and Payer Satatus
67	Erina Lie	Propanolol Use in the Management of Infantile Hemangiomas
68	Sandra Lopez	Impact of Conflict of Interest in Plastic Surgery: An Analysis of Research Outcomes
69	Sally Mahmoud	Assessing Minneapolis efforts to treat refugee, immigrant, and US Born patients for Latent Tuberculosis: a retrospective cohort study
70	Andres Mallipudi	Caregiver Administration of Non-Prescription Antibiotics to Children in Baltimore's Latino Population
71	Anita Ram	Predictors of Cigarette Smoking Reduction among Pregnant, Drug Dependent Women
72	Anu Ramachandran	Evaluating the Cost Effectiveness of Implementing CRAG-LFA as a Screening Tool for Cryptococcal Meningitis among HIV patients in Uganda
73	Samantha Roman	Attitudes and Experiences of Internal Medicine Residents in Managing Comorbid Medical and Psychiatric Disorders
74	John Schulz	Medicare Accountable Care Organizations' Public Reporting and Composition of Shared Savings Plans
75	Arnav Srivastava	Exploring Health Care Provider Perspectives on Pain Management in the Emergency Department
76	Sharif Vakili	A Comparison of Systems to Measure Patient Flow through Ambulatory Clinics
77	Tim Xu	The Surgical Unit-based Safety Program (SUSP) to Reduce Surgical-Site Infections
78	Tracy Yang	Process Evaluation Findings of B'More Healthy Communities for Kids: A Multi-Level, Multi-Component Obesity Prevention Program

2014 MSRD Podium Presentations

Nicole Jiam	*Sorting nexin 27: A fundamental mediator of AMPA receptor trafficking and synaptic plasticity*
Sharon Weeks	*A modified Kampala Trauma Score (KTS) outperforms the Injury Severity Score (ISS) in trauma mortality prediction*
Dinah Lewis	*Unintended sexual consequences of drinking among women attending an urban STI clinic*
Marcelo Cerullo	*Faster is Better: Enhanced Enrollment in Public Insurance Programs Reduces Pediatric Mortality following Traumatic Brain Injury*
Jonathan Yeh	*Using a Question-Prompt List as a Communication Aid for Advanced Cancer Care*
Diane Kuhn	*The Rise of Leishmaniasis in Rio de Janeiro in the Context of Political Decentralization*
Sepehr Tehrani	*Selectively Permeable Nanofiber Constructs To Prevent Inflammatory Scarring And Enhance Nerve Regeneration in Peripheral Nerve Injury*
Kevin Curtiss	*A comparison of minimally invasive approaches to partial nephrectomy: a multi-surgeon analysis from a large tertiary care center*
Alexandra Robison	*Incorporating Discussions of Spirituality and Religiosity into NICU Family Meetings*
Tina Munjal	*Use of the Phantom Electrode Strategy to Improve Bass Frequency Perception For Music Listening in Cochlear Implant User*

Acknowledgements

The MSRD Organizing Committee would like to thank the following people for their support putting this event together. Without their help, this day would not have been possible.

Faculty Judges

The Office of Student Affairs

Doug Hughes

Victor Raspa

John Steele

Mark Dodd

The Scholarly Concentrations Faculty

2015 MSRD Organizing Committee

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Michele Massa

Dr. Mary Catherine Beach

Dr. Thomas Koenig

PODIUM PRESENTATION ABSTRACTS

Listed Alphabetically

Anirudh Arun, MS2
Basic Science

Mentor: Giorgio Raimondi, PhD

Immunomodulation of T cells in inflammatory environments: a novel mechanism for pathogenesis of autoimmunity

Background: Type I Diabetes (T1D, diabetes mellitus type 1) is an autoimmune disease characterized by T cell-mediated destruction of insulin-producing beta cells of the pancreatic islets. The "fertile field" hypothesis of T1D, in which localized, pre-existing insulitis brought on by a preceding viral infection, can create an inflammatory environment that predisposes the organ to autoimmune attack, has been supported by recent studies demonstrating elevated levels of Type I Interferons (TI-IFNs) in the pancreas of deceased T1D patients and mouse models of the disease (NOD mice). In this study, we seek to determine whether TI-IFNs can create a "fertile field" by altering immunoregulatory cytokine signaling in mouse T cells, specifically the IL-10 (immunosuppressive) pathway compared to the pro-inflammatory IL-6 pathway, thereby predisposing those cells to aberrant immunosuppression and autoimmune attack.

Methods: By using fluorescent antibodies specific for phosphorylated STAT3, a critical intermediate in both IL-10 and IL-6 signaling pathways, we determined the effect of TI-IFN pre-exposure on IL-10/IL-6 activity using flow cytometry. We also utilized a novel technology, the Quantigene FlowRNA assay, as well as microarray analysis, to detect expression of SOCS (Suppressor of Cytokine Signaling) homologs SOCS1 and SOCS3. These homologs are hypothesized to mediate cross-talk between cytokine signaling pathways, as both are upregulated in inflammatory cells by cytokine exposure and, in turn, suppress JAK/STAT signaling.

Results: We demonstrate that IL-10 signaling, but not IL-6 signaling, is significantly suppressed in CD4+ CD44+ memory T cells following exposure to TI-IFNs for 48 hours. However, this down-regulation of the response was not associated with SOCS1 or SOCS3 upregulation in response to TI-IFN exposure, as measured by Quantigene FlowRNA and microarray assays.

Conclusion: Selective IL-10 signaling suppression by prolonged TI-IFN exposure can predispose CD4+ CD44+ memory T cells to lose sensitivity to immunosuppressive signals, shedding light on a novel, non-SOCS-mediated mechanism for pathogenesis of autoimmunity in T1D.

Meera Chappidi, MS3 Mentor: Uma Srikumaran, MD

Clinical Research

Arthroscopic Transosseous Rotator Cuff Repair is Cost-Effective Compared to Anchored Technique

Background: Arthroscopic rotator cuff repair has focused on restoration of and compression across the natural anatomic footprint, which historically reflects the repair achieved with the traditional, open transosseous technique. Recent instrumentation advances have accommodated an arthroscopic, anchorless transosseous repair, which reproduces the gold standard of open transosseous repair. Currently, no published literature exists comparing outcomes from arthroscopic, anchorless, transosseous repair to standard arthroscopic anchored repair.

Methods: A retrospective case-control analysis of 60 arthroscopic rotator cuff repairs performed by a single surgeon with minimum 1-year follow-up was conducted. Control patients underwent anchored repair, and experimental group patients underwent transosseous anchorless repair. Intraoperative data on the tear size, number of tendons involved, and degree of retraction was recorded. Visual analog pain (VAS), subjective shoulder value (SSV), American Shoulder and Elbow Surgeons (ASES) scores, and range of motion were collected pre and post-operatively. Statistical and cost analysis was performed.

Results: There were 29 patients in the control and 31 patients in the experimental group. Baseline demographic data for age ($p=0.06$) and sex ($p=0.76$) did not differ between groups. The experimental group had significantly larger tears ($p<0.001$). At 1-year follow-up, there was significant ($p<.001$) postoperative improvement in both groups SSV, VAS, and ASES scores compared to preoperative scores. There was no difference post-operatively between the two groups with respect to SSV ($p=0.66$), pain score ($p=0.46$), ASES score ($p=.24$) or range of motion in abduction, forward elevation, and external rotation ($p=0.95$, 0.71, 0.48). Cost analysis showed 30-80% implant savings per case for the anchorless, transosseous group depending on tear size.

Conclusion: Arthroscopic anchorless, transosseous repair achieves similar clinical and patient reported outcomes with 30-81% reduction in implant costs, compared to traditional arthroscopic anchored repair. Further investigation through a randomized-controlled clinical trial is warranted to confirm the clinical equivalence and cost-effectiveness of the arthroscopic, anchorless transosseous repair.

Allen Feng, MS4 Mentor: Jeremy Richmon, MD

Clinical Research

Deconstructing The Total Laryngectomy Neck Incision: A Clinical Review and Finite Element Analysis

Background: Post-operative complications can be attributed to technical aspects of surgery, yet no studies have investigated the mechanics behind commonly used incisions for total laryngectomies (TL). We sought to investigate the impact of neck incision location on post-operative complications for total laryngectomy (TL) using finite element analysis (FEA) and clinical data.

Methods: Mathematical and clinical analyses of two commonly utilized neck incisions for TL were conducted: 1) a low-neck apron (LNA) incision with incorporated tracheostoma and, 2) a mid-neck apron (MNA) incision with separate tracheostoma. Nonlinear hyperelastic finite element models were created to simulate each type of neck incision under different loading conditions. A retrospective analysis of all patients undergoing TL with pharyngectomy and flap closure at JHMI between August 2005 and February 2013 was then performed. The effect of neck incision location on post-operative wound complications was analyzed and compared to finite element models.

Results: For a constant displacement of 40mm, the magnitude of stress seen in the LNA model is up to 11 times larger than that of the MNA model and is concentrated at the junction of the incision and fixed tracheostomal edges. These findings correlated with our clinical analysis of 49 patients who underwent TL with pharyngectomy and flap closure. 48% (15/31) of LNA patients experienced incisional wound dehiscence compared to 11% (2/18) of MNA patients ($p<0.01$). Generalized linear regression models also demonstrated significantly increased odds of wound dehiscence for patients with a LNA incision (OR 29.8, CI 1.4 – 631.5, $p = 0.029$).

Conclusion: Both FEA and clinical analysis demonstrate a significantly greater concentration of stress at the junction of the LNA neck incision and tracheostoma, manifesting as a significantly higher wound dehiscence rate. In tandem, the numerical and clinical data present strong evidence for using the MNA incision to reduce mechanical loading on the neck and improve post-operative outcomes.

Seema Kacker, MD/PhD or Student in Residence Mentor: Aaron Tobian, MD PhD

Public Health and Community Service

Financial Implications of RHD Genotyping of Pregnant Women with a Serologic Weak D Phenotype

Background: Hemolytic disease of the fetus and newborn (HDFN), classically caused by maternal-fetal incompatibility of the Rh blood group D antigen, can be prevented by Rh immune globulin (RhIg) prophylaxis. While prophylactic practices for pregnant women with serologic weak D phenotypes vary widely, RHD genotyping could provide clear guidance for management. This analysis evaluated the financial implications of using RHD genotyping to guide RhIg prophylaxis among pregnant females.

Methods: A Markov-based model was constructed to evaluate the costs of RHD genotyping for pregnant females with serologic weak D phenotypes to inform RhIg prophylaxis. Using a comparison strategy of managing these women conservatively as RhD-negative, direct medical costs were assessed over 10- and 20-year periods for a simulated population of US women. One-way and probabilistic sensitivity analyses were used to assess the robustness of conclusions.

Results: Using base-case parameters, RHD genotyping for pregnant women with serologic weak D phenotypes is expected to marginally reduce overall costs. RHD genotyping these patients, rather than conservatively managing them as RhD-negative, would be cost-saving when the cost of genotyping is below $256. Genotyping would decrease net costs among non-Hispanic Caucasian females (-$0.17/pregnancy), but would increase costs among non-Hispanic African Americans (+$0.51/pregnancy), non-Hispanic American Indian/Alaskans (+$0.10/pregnancy) and Hispanics (+$0.37/pregnancy). Incorporating RHD genotyping would not significantly impact costs among Asians and Hawaiian/Pacific Islanders.

Conclusion: Using RHD genotyping to guide RhIg prophylaxis among pregnant women with serologic weak D phenotypes may be clinically beneficial without increasing overall costs.

Seva Khambadkone, MS2 Mentor: Timothy Moran, PhD

Basic Science

Impact of a specific dietary intervention on the microbiome-gut-brain axis and risk for neuropsychiatric disorder

Background: The nervous and gastrointestinal (GI) systems communicate by a bidirectional gut-brain axis integrating neurohormonal and immunological signaling. Emerging research implicates the gut microbiome as an overlaying mediator of this communication in a schema recently termed the microbiome-gut-brain axis. The well-observed co-morbidity between psychiatric and GI disorders is associated with gut dysbiosis, with treatment of dysbiosis attenuating both neuropsychiatric and GI symptoms. Because the gut microbiome is sensitive to a variety of environmental factors, including diet and medication, it is an accessible, attractive potential target for both understanding the root mechanisms involved in psychiatric disease and treating such disease. Recent epidemiological data among patients with bipolar disorder showed significant association between ingestion of cured meats, beef jerky cited most frequently, and development of mania (OR 6.0, P<10^-8).

Methods: In this study, we used a rat model to investigate the effects of the consumption of beef jerky on mood-related behavior phenotypes and physiological parameters and to elucidate the potential microbiome-gut-brain mechanisms involved. Adult male Sprague-Dawley rats were given ad libitum access to standard chow (n=12) or standard chow and beef jerky (n=12) for 14 days prior to and throughout behavioral testing. Food intake and body weight were measured every 2 days. Following behavioral testing animals were killed and tissue and fecal samples collected for analysis.

Results: There were no differences in total caloric intake or body weight between the two groups, suggesting that differences in phenotype are due to diet composition and not to caloric consumption. Behavioral testing suggested that consumption of beef jerky was associated with locomotor hyperactivity (P=0.018), sleep cycle disruption (P=0.005), and increased pleasure-seeking behavior (P=0.037), all representing mania-like phenotypes.

Conclusion: Overall, our results reflect the human data, suggesting that beef jerky consumption may potentially increase risk for mania-like behavior. Analysis of potential gut microbiome, epigenetic, metabolic, and inflammatory influence is ongoing.

Rebeccah McKibben, MS4 Mentor: Eric Seaberg, PhD

Clinical Research

Hepatitis C Virus Infection Is Associated with Subclinical Coronary Atherosclerosis in the Multicenter AIDS Cohort Study (MACS)

Background: Hepatitis C virus (HCV) infection may contribute to increased risk for coronary artery disease among HIV-infected individuals. The objective of this study was to determine the contribution of chronic HCV infection to coronary atherosclerosis among men in the Multicenter AIDS Cohort Study (MACS) and assess potential synergistic effects of HIV/HCV-coinfection on coronary artery disease.

Methods: The study population included 994 MACS cohort study participants who were enrolled in the cardiovascular sub-study during 2010-2013. These men (87 with chronic HCV infection) underwent non-contrast cardiac CT scans, and 755 men (56 with chronic HCV infection) also underwent coronary CT angiography. Associations between chronic HCV infection and the prevalence of coronary plaque, stenosis, and plaque extent as measured using non-contrast CT and coronary CT angiography were assessed using Poisson and linear regression methods. Models were adjusted for age, race, education, center, enrollment period (pre- or post-2001), and HIV serostatus, with additional adjustment for coronary artery disease risk factors, injection drug use, and heavy alcohol use.

Results: Chronic HCV-infected men were more likely to be HIV-infected, African-American, current smokers, have lower body mass index, and have a history of intravenous drug use compared to HCV-uninfected men. After adjustment for demographics, HIV serostatus, behavioral factors, and coronary artery disease risk factors, chronic HCV infection was significantly associated with higher prevalence of coronary artery calcium (adjusted prevalence ratio (aPR)=1.29, 95% confidence interval (CI): 1.02-1.64), any plaque (aPR=1.26, 95% CI:1.09-1.45), and noncalcified plaque (aPR=1.42, 95% CI:1.16-1.75), and the highest prevalence was observed among men with HCV RNA ≥2x106 IU/mL. Chronic HCV infection and HIV were not synergistically associated with any plaque outcome.

Conclusion: Persons with chronic HCV infection were more likely to demonstrate coronary atherosclerosis independent of coronary artery disease risk factors and HIV infection. Further study is needed to explore mechanisms by which HCV infection may increase coronary artery disease risk.

Leah Medrano, MS2 Mentor: Daniel Todes, PhD

History of Medicine

The lupus patient and the advent of corticosteroid therapy.

The patient records of Dr. A. McGehee Harvey, a prominent physician at Johns Hopkins Hospital in the early 1950s, provide an opportunity to study the early days of corticosteroid therapy, and, especially, its effects on the experiences of patients with systemic lupus erythematosus (SLE).

SLE is an autoimmune disease characterized by chronic inflammation and multiple organ system involvement. With the advent of corticosteroid therapy, specifically cortisone and ACTH, in the early 1950s, physician and researcher interest in lupus and other inflammatory diseases disseminated across the country. We know little, however, about patient experiences with the early development of this therapy. My research is intended to illuminate the impact of corticosteroid therapy on the patient experience and the doctor-patient relationship, aspects of medicine that are becoming increasingly important in an era of patient-centered care.

Dr. Harvey was a clinician and researcher concerned with SLE during the advent of cortisone therapy. His publications, patient records, and correspondence with lupus patients in the late 1940s-early 1950s reveal the hardships and complexities in living with lupus at this time. Like diabetes after insulin therapy, lupus after cortisone ceased to mean an inevitable early death, and was transformed into a chronic disease. Some aspects of the lupus experience remained unchanged, for example, family involvement, but the nature of patient-physician interactions and the overall patient experience changed profoundly. Corticosteroid therapy brought both benefits and unanticipated consequences. Patients' lives were affected by steroid-induced remissions, complications in managing flares with a sensitive drug, and adverse side effects. It became both the patient's and the physician's task to confer about and manage the many aspects of this disease. Aside from the historical significance, my research on the experiences of Harvey's patients, and his relationship with them, also provides an opportunity to reflect about these important dimensions of medicine today.

Maria Phillis, MS2 Mentor: Lisa Ishii, MD

Clinical Research

The Importance of Facial Lesion Reconstruction for Normalizing Affect Display

Background: Affect display is important for non-verbal communication and social engagement. Prior research demonstrated patients with facial lesions suffer significant affect display penalty. We measured the impact of surgically reconstructing facial lesions on restoring affect display.

Methods: 120 observers completed one of four surveys of 20 images of faces in repose. Observers viewed 8 preoperative faces, 8 postoperative faces and 4 faces judged by experts to be "normal." Each survey evenly represented four lesion classes: small peripheral(SP), small central(SC), large peripheral(LP) and large central(LC). Observers rated affect by selecting all terms that applied from the Derogatis Affects Balance Scale, Ekman's emotions and a "neutral" term. Latent class analysis and regression were used to determine the affect classes and significance of covariates: operation status, size and location of lesions. Postoperative were compared with "normal" via bootstrap analysis to determine significant differences in affect display.

Results: Both scales collapsed into three latent classes: positive, neutral and negative. Faces with lesions pre-operatively were significantly more likely to be graded negatively (SP: mean:38.4% (CI:32.5-44.4%), SC:50.5%(43.3-57.7%), LP:58.3%(51.9-64.7%), LC:47.5%(41.2-53.9%)) than "normals" (23.5%(19.0-28.1%)) or post-operatively (SP:14.1%(10.6-17.6%), SC:20.7%(16.0-25.4%), LP:27.2%(21.9-32.5%), LC:18.9%(14.9-22.8%)). Faces with lesions pre-operatively were less likely to be graded positively (SP:21.3%(16.8-25.7%), SC:20.4%(16.4-24.3%), LP:13.0%(9.6-16.4%), LC:21.3%(17.2-25.4%)) than "normals" (45.9%(39.9-51.9%) or post-operatively (SP:38.4%(32.3-44.5%), SC:41.0%(35.0-46.9%), LP:29.8%(24.3-35.4%), LC:41.5%(35.8-47.2%). Post-operatively, faces with SP, SC and LC lesions were restored to similar or improved positive and negative affect as the "normal." Post-operatively, faces with LP lesions were significantly improved in positive and negative affect from pre-operatively, and restored to similar levels of negative affect as "normal" faces, but still significantly different from "normal" faces in positive affect.

Conclusion: Facial reconstructive surgery is effective in restoring affect display in patients with facial lesions. This result provides novel objective data supporting the positive impact of reconstructive surgery on patients' quality of life.

Ryan Shields, MD/PhD or Student in Residence Mentor: Adil Haider, MD, MPH

Medical Humanities

Risks and Benefits of Routine Collection of Sexual Orientation and Gender Identity Information in Healthcare: The Patient Perspective

Background: There has been considerable research into the health disparities of sexual orientation (SO) and gender identity (GI) minorities. However, further research is limited by the lack of routine collection of SO/GI information. Both the Institute of Medicine and the Joint Commission recently recommended SO/GI be included in electronic health records (EHRs), but few institutions have implemented this recommendation. This qualitative study examines the perspectives of patients regarding the routine collection of SO/GI in clinical settings.

Methods: Participants were recruited through local support groups, public flyers, and email listservs. Participants were screened and selected to ensure a diverse population of SO and GI minorities. In-depth, semi-structured interviews were conducted, tape-recorded, and transcribed. Two reviewers independently coded and analyzed the transcripts using a grounded-theory approach.

Results: Fifty-one participants were interviewed (14 heterosexual, 9 lesbian, 12 gay, 11 bisexual, and 5 queer individuals; 14 of whom identified as transgender). Major themes from the data included issues of privacy, medical relevance, identity recognition, and normalization of SO/GI minorities. Storage of SO/GI information in EHRs and who has access to this information was a central concern; many participants worried about disclosure to unwanted parties and the possibility of a homo/transphobic provider subsequently providing worse treatment. Perceived benefits of routine collection of SO/GI included more respectful communication (e.g. using the correct gender pronouns), avoidance of misunderstandings and instances of “forced outing,” and increased awareness of the specific health needs of SO/GI minorities for both patients and providers.

Conclusion: Collection of SO/GI information may soon become standard practice during medical encounters, and it is important to consider the factors that affect patient comfort and willingness to disclose this sensitive information. When SO/GI information is incorporated into EHRs, interventions and policies to minimize risk and address patient concerns will be critical to successful implementation.

Daren Simkin, MS2 Mentor: Wayne Biddle

Medical Humanities

Working with Gore Vidal: A Memoir of Caregiving and Aging

Background: Caring for older members of society is one of today's great challenges and opportunities, yet there is a paucity of first-hand literary accounts that describe the unique provider-elderly patient relationship. The purpose of this project was to illuminate the experiences of aging and caregiving through a book manuscript that chronicles the relationship between Gore Vidal, the late renowned American writer, and the young man who served as his assistant and caregiver.

Methods: The author spent over three years working with Gore Vidal and took copious notes on the experience. To examine the themes of caregiving and aging, the author reviewed these notes and identified particularly illustrative scenes. These he pieced together into a narrative structure, adding context and thematic development as appropriate. The resulting text was written from the author/caregiver's perspective in a relaxed, memoir style.

Results: A book manuscript – 19 chapters, over 66,000 words – was produced. It describes the period (2004-2006) stretching from the day the two men met until the end of the publicity tour for Vidal's book, Point to Point Navigation. The manuscript chronicles the development of their relationship as well as the evolution of the author's role from Vidal's typist, to his full-time assistant, to his caregiver and friend. It also follows the pair as they traveled around the world, through the health care system, and into a series of startlingly candid late-night conversations. An epilogue describes Vidal's 2012 private memorial. Approximately 15 photos with captions accompany the text.

Conclusion: The manuscript sheds light on the challenges of old age (e.g., loneliness, physical debility) as well as those of the caregiver (e.g., burnout, maintaining sense of self). Ultimately, however, it emphasizes the extraordinary intimacy and inspiring potential of the caregiver-older patient relationship. It is hoped, therefore, that the text may offer insights helpful to others in similar relationships.

ORAL PRESENTATION ABSTRACTS

Listed Alphabetically

Ridwan Alam, MS2 Mentor: Ali Bydon, MD

Clinical Research

Using the Manual Muscle Test to Predict C5 Palsy Resolution

Background: Over 80% of patients with postoperative C5 palsy recover spontaneously. However, prognostic factors for this recovery are poorly understood. We evaluated the use of the manual muscle test (MMT) score at condition onset in predicting the time course and likelihood of C5 palsy resolution.

Methods: Over a seven-year period, 44 patients who experienced C5 palsy following a posterior cervical laminectomy and instrumented fusion surgery were evaluated for the primary outcome of resolution from this condition. Resolution was defined as a deltoid MMT score that was at least equal to that of the preoperative condition. The hazards of C5 palsy resolution were calculated using a complementary log-log function in a discrete-time proportional hazards model. Prediction of time to C5 palsy resolution was calculated using a multiple linear regression model.

Results: Thirty-six of the 44 patients (81.8%) with postoperative C5 palsy had full resolution from their condition. The median MMT score at onset for those who resolved was 3–, and Kaplan-Meier analysis showed the median time to recovery was approximately 1 year. The hazards of C5 palsy resolution increased by 18% for every 1-grade increase in MMT score at onset (P = 0.005, HR = 1.18, 95% CI = 1.05-1.33). Males displayed a 73% lower hazard of resolution than females (P = 0.003, HR = 0.27, 95% CI = 0.12-0.64). Finally, a lower MMT score at onset predicted a longer time to resolution (P = 0.009, coefficient = -0.19, 95% CI = -0.32 – -0.05).

Conclusion: Higher MMT scores at C5 palsy onset predicts a higher likelihood of resolution and shorter recovery times. Females display a higher likelihood of resolution compared to males. Most patients with postoperative C5 palsy can be reassured that their condition will spontaneously resolve within 1 year, with greater reassurance given to those with a higher MMT score at onset.

Ridwan Alam, MS2 Mentor: H. Ballentine Carter, MD

Clinical Research

Active Surveillance: When Can Patients Stop Worrying?

Background: Active surveillance is an accepted alternative to immediate intervention for patients with favorable risk prostate cancer. However, there is still concern over the risk of cancer progression or misclassification due to biopsy sampling error. We evaluated the risk of prostate cancer reclassification over time in active surveillance.

Methods: From 1995 to 2014, 808 men (557 very-low-risk and 251 low-risk) on active surveillance who were compliant with prostate biopsies were evaluated for the primary outcome of reclassification to worse disease by grade or extent. Freedom from reclassification was estimated using the Kaplan-Meier approach with adjustment for covariates using a Cox proportional hazards model.

Results: Within the first two years of surveillance, the survival free of reclassification by grade ($P = 0.20$) and extent ($P = 0.25$) were similar between men with very-low-risk and low-risk disease. After two years, men with low-risk disease were 2.4 times more likely to reclassify based on grade when compared to men with very-low-risk disease ($P = 0.002$, HR = 2.4, 95% CI = 1.9-3.5). Beyond two years in surveillance, the risk of lifetime reclassification by grade and extent decreased by 30% ($P < 0.0001$, HR = 0.70, 95% CI = 0.60-0.76) and 35% ($P < 0.0001$, HR = 0.65, 95% CI = 0.57-0.72), respectively, with each non-reclassifying biopsy.

Conclusion: The rate of reclassification during surveillance is not equally distributed across time or risk groups. Due to misclassification at the time of diagnosis, the rates of reclassification between very-low-risk and low-risk groups are similar within the first two years but differ significantly beyond two years. Reclassification risk falls over time with each biopsy that did not show reclassification after two years. Therefore, men in active surveillance who are compliant with their annual biopsies can be reassured that their risk of lifetime reclassification declines with each non-reclassifying biopsy after two years.

Carolyn Arnold, MS2 Mentor: Megan M Tschudy, MD MPH

Public Health and Community Service

Urban Children with Poorly Controlled Asthma Disagree with Caregivers and Clinicians on Reasons for Not Using Controllers

Background: Inadequate use of daily controllers prevents control among urban children with asthma. Influences on adherence have not been examined in a child-caregiver-clinician triad, and this study aims to characterize barriers to controller use among children with poorly controlled asthma from those three perspectives.

Methods: Using mixed-methods, we interviewed publicly insured children with asthma and their caregivers; their primary care clinicians took an online survey. Included children (7-17yr.) had a prescribed daily-inhaled corticosteroid and an ED visit for asthma in the past year. Participants rated given reasons for not using controllers (dichotomized never vs. ever) and reported frequency of missed doses (never, 1-2/week, ≥3/week). McNemar tests compared child to caregiver, child to clinician, and caregiver to clinician. Logistic regressions assessed associations between report of each reason and caregiver-reported non-adherence, controlled for child gender and age.

Results: Fifty child-caregiver dyads participated, with 34 of 50 clinicians replying. Children (40% female; median age 10yr., IQR 6.5) had mostly non-Hispanic Black (90%) caregivers with high-school education or less (68%). More children than caregivers reported medications running out (p=.03) as a reason for non-adherence. Clinicians were more likely than caregivers (p<.001) and children (p=.03) to cite medications running out, than children to cite controllers being a “pain to take” (p=.002), and than caregivers to cite forgetfulness (p=.03). Remarks include: “it seems like it is [embarrassing]” and “with friends she just don’t want to.” Child report of reasons (forgetfulness p=.003, aOR=10.4; side effects p=.04, aOR=3.4) and caregiver report of reasons (forgetfulness p=.003, aOR=14.6; not need med p=.01, aOR=4.7) were associated with non-adherence. Clinician report never predicted non-adherence.

Conclusion: Clinicians overrate the role of forgetfulness, refills, and medications being “a pain to take.” Since caregiver and child, not clinician, reasons for non-adherence predicted lower medication use, emphasis on these barriers may be important for asthma interventions.

Phoebe Bacon, MS2 Mentor: Debra J. Mathews, PhD MA

Medical Humanities

Enhancing autonomy in biobank decisions: Too much of a good thing?

Background: Ethical discourse about the return of individual research results (IRRs) to study participants has taught us that people want results, and are more likely to enroll in biobanks when results are offered. In response, we developed an online "preference-setting" tool for the return of IRRs from a pediatric genomic biobank that allows participants to set filters based on the preventability and severity of a condition, and to opt-out of four categories of IRRs (mental illness, developmental disorders, childhood-onset neurodegenerative disorders, adult-onset conditions). The purpose of this study was to identify factors associated with intent to participate in a biobank among users of this tool.

Methods: As part of a larger study about return of results from a biobank, this project involved a secondary data analysis comparing "intent to participate" with respect to IRR preferences, attitudes about results received, demographics, and other baseline information.

Results: Among 1,026 users, 86.5% responded that they would participate in a biobank that returned IRRs using this tool. In bivariate analysis, "desire to receive all possible IRRs" was among the variables associated with intent to participate, and intent was lower among respondents who were more selective with regard to their preferences ($p<0.0001$). In a multivariate regression model, only non-white race, family health history, comfort level, and lower self-reported anxiety were positively associated with intent to participate ($p<0.05$).

Conclusion: Though many individuals desire to filter the types of IRRs they receive, this study suggests that those participants who set more specific preferences are ultimately less likely to enroll in a biobank than those who are less discerning. Furthermore, participation may be more correlated to personal dispositions and baseline attitudes than to the design of the tool or the ability to filter results. Interestingly, a model designed to offer the greatest degree of autonomy may not be one that maximizes participation.

Sminu Bose, MS2 Mentor: Mark Hughes

Medical Humanities

Developing a Best Practices Advisory Tool in Epic To Address the Palliative Care Needs of Oncology Patients

Background: Recent ASCO guidelines recommend that, upon diagnosis with advanced cancer, palliative care (PC) should be integrated into a patient's standard oncology treatment. Despite demonstrated benefits, oncologists hesitate to consult palliative specialists citing that oncologists already provide PC services. However, recent studies indicate inadequate symptom management and lack of advance care planning by oncologists. One strategy for addressing this is to enhance primary PC provided by oncologists and generalists. This project's purpose was two-fold: 1) to create a primary PC tool which would be triggered as a Best Practices Advisory (BPA) in Epic, a widely used EMR and 2) to develop selection criteria for PC-eligible patients for BPA pilot testing.

Methods: To determine the components of the BPA, we condensed relevant clinical guidelines for addressing various PC needs in oncology patients. An ICD-9-CM code search was conducted to create an accurate selection scheme for PC-eligible patients for whom the BPA would appear.

Results: Patient selection scheme using Epic Problem List:

(≥1 secondary malignancy ICD-9 code(s)) OR (≥1 malignant neoplasm ICD-9 code(s) AND ≥1 complication ICD-9 code(s))

BPA components:

1. Uncontrolled Symptoms: Checklist for pain, nausea, etc. Once a symptom is checked, order sets for management appear.

2. Goals of Care: Link to secondary note to record patient's goals of care.

3. Advance Care Planning: If code status or advance directive is not filed, Smartlink for completing advance directive and/or MOLST appears.

4. Hospice Referral: Ambulatory hospice referral link appears if patient has less than 6 month prognosis.

Conclusion: Creating an accurate selection scheme for all JHH outpatients is complicated due to physicians' varying Epic documentation behaviors. We plan to pilot the BPA in ENT Oncology, focusing first on a subset of patients to validate our tool before expanding. Successful utilization of the BPA may translate to increased patient quality of life, satisfaction, and survival.

Wynne Callon, MS2 Mentor: David Schretlen, PhD

Clinical Research

Features of the Lesch-Nyhan Phenotype Correlate More Closely with Guanine than Hypoxanthine Phosphoribosyltransferase Enzyme Activity

Background: Lesch-Nyhan disease (LND) is a rare, X-linked recessive neurodevelopmental disorder caused by deficiency of hypoxanthine-guanine phosphoribosyltransferase (HGprt), an enzyme in the purine salvage pathway. HGprt recycles two substrates: hypoxanthine and guanine. It is unclear which of these two functions is more relevant for the pathogenesis of LND, with some evidence pointing to hypoxanthine recycling and other evidence to guanine recycling. This study investigated the correlation between Hprt and Gprt enzyme levels and cognitive, motor, and behavioral features of LND to determine if either of these enzyme functions is differentially correlated with the phenotypic characteristics.

Methods: We assayed hypoxanthine (Hprt) and guanine (Gprt) recycling in skin fibroblasts from 17 persons with LND, 11 with an attenuated variant of the disease (LNV), and 19 age-, sex-, and race-matched healthy controls (HC). Validated rating scales were used to measure dystonia, cognition, and behavior. We examined the strength of associations between Hprt and Gprt activity levels and these phenotypic measures.

Results: Both Gprt and Hprt enzyme activity levels were statistically significantly correlated with all but one of the measures of LND phenotype. In addition, Gprt showed a slightly stronger correlation than Hprt for 13 of 14 phenotype measures. The binomial probability of finding that Gprt correlates more highly than Hprt with 13 of 14 phenotype measures, if the null hypothesis is true, is less than 1 in 1,000 (0.00086). While not a statistical significance test, this suggests that Gprt is more strongly associated with many aspects of the LND/LNV phenotype than Hprt.

Conclusion: Gprt showed a slightly stronger correlation than Hprt with 13 of 14 LND phenotype measures. This suggests that loss of guanine recycling might be more closely linked to the LND/LNV phenotype than loss of hypoxanthine recycling. Resolving this controversy is important for guiding further studies of the neurobiology of LND and its potential treatments.

Jacob Cox, MS2 Mentor: Fizan Abdullah, MD

Public Health and Community Service

Comparative Analysis of the French and American Trauma Systems Using Patient Outcomes

Background: The objective of this paper is to compare mortality outcomes between patients treated at a trauma center in France and matched patients in the United States, particularly focusing on differences in outcomes based on the severity of injury. Although trauma systems in France and the United States differ significantly in prehospital and in-hosptial management, there are currently no published analyses of differences in mortality between the systems that account for injury severity.

Methods: Coarsened exact matching identified matching patients between a single center trauma database from Lyon, France, and the National Trauma Data Bank (NTDB) of the United States. Moderate to severely injured [injury severity score (ISS) > 8] adult patients (age > 16) presenting alive to level 1 trauma centers from 2002 to 2005 with blunt or penetrating injuries were included. After matching patients, multivariate regression analyses were performed to determine the difference in mortality between patients in Lyon and the NTDB.

Results: A total of 1043 significantly injured patients were presented to the Lyon center. Matching eligible patients with complete records were sought from 165,833 patients in the NTDB. After 1:1 matching, 829 patient pairs were produced. Amongst the least severely injured patients (TRISS > 90) the mortality odds ratio amongst NTDB patients was 3.04 times higher than that of the Lyon center [95% confidence interval (CI) = 1.56-5.90]. Amongst the most severely injured patients (TRISS < 60) the mortality odds ratio amongst Lyon database patients was 4.55 times that of the NTDB [95% CI = 2.38 - 9.09]. Further subset analyses were run focusing on variables that determine a patients TRISS value (ISS, GCS, SBP). Of these subset analyses, the most severely injured patients according to ISS (40-75) and the most severely injured according to GCS (3-5) had a statistically significantly higher odds of dying in the Lyon dataset as compared to the NTDB. No SBP category was found to have a statistically significant difference in mortality. None of these ISS, GCS, or SBP subsets were found to have a statistically significantly better odds or survival amongst the Lyon dataset as compared to the NTDB dataset.

Conclusion: Trauma patients admitted to a single French trauma center had a significantly better chance of survival if they were in less critically injured (TRISS > 90) as compared to their NTDB counterparts, but stood a statistically significantly worse chance of survival if they were more severely injured (TRISS > 90, ISS 40-75, or GCS 3-5).

Regina de Luna, MS2 Mentor: Ramulu, PR

Clinical Research

Can Patients Read What They Are Signing?

A test of consent form readability among ophthalmic patients

Background: One tenth of recently hospitalized patients in the US suffer from poor visual (distance) acuity. The inability of these patients to read consent forms and healthcare instructions may contribute to worse overall health outcomes. We performed a retrospective study to compare the frequency of poor reading (near) acuity in patients undergoing ophthalmic surgery with that of patients undergoing non–-ophthalmic surgery.

Methods: 138 patients undergoing ophthalmic surgery at the Wilmer Eye Institute and 138 patients undergoing non--ophthalmic surgery at the Johns Hopkins Outpatient Center were enrolled in the study. Near visual acuity and reading speed was measured using the MNRead Visual Acuity test, a continuous text reading-acuity chart. Critical print size (CPS) was defined as the smallest print size that supported a reading speed of at least 50% of the average of the participant's three largest reading speeds.

Results: The average CPS was 1100% larger for Wilmer patients than for JHOC patients [0.37logMAR (sd 0.28) versus 0.03logMAR (sd 0.22)]. The maximum reading speed was 30% slower for Wilmer patients than for JHOC patients [199wpm (sd 77 range 37 - 600wpm) versus 286wpm (sd 119 range 115-1276wpm)]. At the print size of the consent form, (logMAR 0.4), 19% of Wilmer patients (26 subjects) had maximum reading speeds below 100wpm compared to 4% of JHOC of patients (5 subjects). However, all of the aforementioned patients could read above 125wpm when given larger print.

Conclusion: Compared to their non-ophthalmic counterparts, patients undergoing ophthalmic procedures have a larger CPS and read slower. Some patients undergoing ophthalmic procedures had a maximum reading speed less than 125wpm at the size of the consent form. However, when given a larger print size, their reading speed was greater than 125wpm. These results suggest that there are patients who would benefit from larger print consent forms and healthcare instructions in an effort to improve compliance and healthcare outcomes.

Malgorzata Dymerska, MS2 Mentor: Bernard Cohen, MD

Clinical Research

Predictive Value of Size of Port-Wine Stains in Sturge-Weber Syndrome

Background: Sturge-Weber Syndrome (SWS) is typically defined by the presence of a facial port-wine stain accompanied by neurologic involvement and/or glaucoma. The neurologic sequelae of SWS can have the biggest impact on patient's daily function and quality of life. It is currently unknown, however, whether the extent of birthmark is predicative of intracranial involvement and therefore clinical disability. In this study we investigated whether size of facial birthmarks in patients with SWS correlates with the degree of central nervous system involvement by neuroimaging and clinical neurological exam.

Methods: 51 SWS patients (53% male) with facial birthmarks and brain abnormalities documented on MRI were included. A pediatric neurologist prospectively assigned previously validated clinical severity scores based on seizures, hemiparesis, visual field cut and cognitive impairments. Three raters, blinded to clinical scores, independently graded the extent of facial birthmark in each patient (% affected of each hemifacial distribution of the three branches of trigeminal nerve) based on photographs taken before any laser treatments. Their scores were then averaged. A neuroradiologist, blinded to all clinical information, assigned a neuroimaging score based on previously established criteria of intracranial involvement in SWS. Birthmark scores were correlated with the imaging and neurological severity results using nonparametric correlation analysis.

Results: MRI scores for each hemisphere were positively correlated with their respective hemifacial birthmark extent (Spearman's correlation coefficient, left: $\rho=0.54$, $p<0.001$; right: $\rho=0.67$, $p<0.001$). Clinical severity scores were similarly associated with the overall facial extent of port-wine stains in patients over the age of 6 ($n=21$, $\rho=0.46$, $p<0.05$). In particular, the degree of cognitive impairment was significantly correlated with the skin score ($n=21$, $\rho=0.56$, $p<0.01$).

Conclusion: The extent of facial port-wine stains in SWS can serve as a useful predictor of the degree of brain abnormality and clinical severity.

Caleb Fan, MS2 Mentor: Martin Makary, MD

Public Health and Community Service

Safety Culture and Surgical Site Infection Outcomes Following Colorectal Surgery

Background: Hospital workplace culture may impact surgical outcomes; however, this association has not been established. We designed a study to assess the association between safety culture and surgical site infection (SSI) rates following colorectal surgery.

Methods: We measured surgical unit safety culture in 7 Minnesota community hospitals using the Hospital Survey on Patient Safety Culture survey and determined SSI using National Healthcare Safety Network definitions. We calculated Pearson's r for each of 12 dimensions of safety culture and colorectal SSI rate.

Results: Mean survey response rate was 43%. SSI rates ranged from 0-30% and culture scores ranged from 16-92 on a scale of 0-100. Ten dimensions of safety culture were inversely associated with colorectal SSI rates: teamwork across units (r = -0.96; 95% CI [-0.76, -0.99]), continuous improvement (r = -0.95; 95% CI [-0.71, -0.99]), feedback and communication about error (r = -0.92; 95% CI [-0.56, -0.99]), overall perceptions of patient safety (r = -0.90; 95% CI [-0.45, -0.99]), hospital management support for patient safety (r = -0.90; 95% CI [-0.44, -0.98]), teamwork within the surgical unit (r = -0.88; 95% CI [-0.38, -0.98]), communication openness (r = -0.85; 95% CI [-0.26, -0.98]), supervisor expectations and actions promoting safety (r = -0.85; 95% CI [-0.25, -0.98]), non-punitive response to error (r = -0.78; 95% CI [-0.07, -0.97]), and frequency of events reported (r = -0.76; 95% CI [-0.01, -0.96]). After adjusting for surgical volume and pre-op ASA physical status, communication openness and non-punitive response to error were no longer significantly correlated with colorectal SSI.

Conclusion: Our study is limited by restricted access to hospital data, preventing stratification by open versus laparascopic procedures. Overall, eight dimensions of safety culture were associated with colorectal SSI rates. These data suggest a role for positive safety and teamwork culture and engaged hospital management in producing high-quality surgical outcomes.

Shekhar Gadkaree, MD/PhD or Student in Residence Mentor: Young Kim, MD/PhD

Basic Science

Cyclic Dinucleotide induced Regression of Tumor in a Squamous Cell Carcinoma Mouse Model

Background: Cyclic dinucleotides (CDNs), which signal through the STING (Stimulator of Interferon Gene) pathway, are a novel class of adjuvants that have been shown to induce anti-tumor responses in vivo. The in-vivo tumor response to CDNs in a squamous cell head and neck cancer model is not well documented. In this study, we examined the anti-tumor immune responses generated by natural and synthetic CDNs on SCCVII squamous cell tumors in a murine model.

Methods: SCCFVII tumor bearing C3H/HeOUJ mice (n = 5 per group) were treated with synthetic or natural CDN intratumorally to assess their antitumor effect. The mice underwent three injections with either RR-CDG (synthetic cyclic-di-guanine), CDG (natural cyclic-di-guanine), R848 (TLR 7/8 agonist), or phosphate buffered saline (control), and the in vivo tumor growth rate was followed. Splenocytes were analyzed for cytokine profile using flow cytometry. In addition to measuring the anti-tumor immune response, the direct toxicity of the CDNs was measured by performing in vitro dose response cell viability assays.

Results: The RR-CDG and CDG treatment groups showed significantly decreased tumor size when compared to the R848 and PBS treatment groups ($p<0.05$). The splenocytes from the RR-CDG treated mice showed an enhanced TH1 response, as determined by increased expression of IFNγ, when compared to the CDG, R848, and PBS treatment groups. In vitro tumor cell killing assay showed that there was no direct tumor cytotoxicity effect in response to CDNs. CDNs demonstrated an indirect enhanced systemic immunological effect on tumor cells.

Conclusion: Synthetic and natural CDN treated mice had significantly reduced tumor volumes when compared to R848 (TLR7/8 agonist) and control treated mice. Mice treated with synthetic and natural CDNs also showed increased splenocyte secretion of IFNγ and a predominant Th1 response when compared to mice treated with R848 (TLR7/8) agonists or controls, supporting the use of intratumoral injection of CDN into HNSCC patients.

Stanley Guillaume, MS2 Mentor: Uma Srikumaran, MD

Clinical Research

Anchored versus Anchorless Rotator Cuff Repair: A Biomechanical Analysis

Background: Rotator cuff tears are a common cause of shoulder pain and dysfunction, with many requiring surgical repair. The purpose of our study is to evaluate the biomechanical properties of two different arthroscopic techniques; transosseous-equivalent (TOE) repair with anchors versus anchorless arthroscopic transosseous repair (AT).

Methods: In this controlled laboratory study, we conducted biomechanical testing on simulated cadaveric rotator cuff tears in eight paired (sixteen) fresh-frozen, human cadaveric shoulders. Shoulders were randomized to one of two repair groups (eight in each group): TOE versus anchorless AT. After supraspinatus repair, specimens were tested to determine cyclical gap formation and maximum load to failure and stiffness. A linear regression model with random effects for specimens was performed comparing sex, age, repair type, bone mineral density, side and failure load (to cause 5 mm gap).

Results: In the eight matched pairs, the TOE group had a significantly higher tensile load to cause 5mm gap (p=.007). In 7/8 specimens with TOE repair, the site of ultimate failure was at the musculotendinous junction. One of the TOE specimens had suture gapping/breakage as ultimate mechanism of failure. In the AT group, 6/8 specimens had failure of the knot or suture, suture cut out through bone tunnels, or a combination of both. Two specimens in the AT group had failure at the tendon junction.

Conclusion: In a biomechanical comparison, the TOE method of rotator cuff repair was found to have a significantly increased load to failure compared with AT. The most common mechanism of failure in the TOE group was at the musculotendinous junction. In contrast, the AT group most commonly failed as a result of suture cut-out through the bone tunnels, or failure of the suture, leaving the musculotendinous junction intact. This may have clinical implications on potential for clinicians to consider these modes of failure when using these techniques.

David Gullotti, MS2 Mentor: Betty Tyler

Basic Science

Assessment of repetitive mild traumatic brain injury by retinal imaging with optical coherence tomography

Background: Mild traumatic brain injury (mTBI) is a common morbidity in many types of neurotrauma, including military, contact sports, and motor vehicle accidents. Unfortunately, current TBI diagnostic methods are neither sensitive nor prognostic. If the diagnostic power were improved, better suggestions for future care could be given to the patient, such as when to refrain from activities that may risk additional injuries as well as when it may be safe to return to them, and we could study the full time course of the histological, pathological, and clinical effects of these injuries.

Methods: The goal of this experiment is to improve the diagnosis of repetitive, mild traumatic brain injury with a high resolution, non-invasive imaging modality, Optical Coherence Tomagraphy (OCT). Male C57/Black 6 mice were injured using a previously established weight drop model (Marmarou) four times over the course of 7 days. Then, using established murine ocular OCT imaging protocols, we collected images of the retinal layers at various time points following these injuries.

Results: Initial analysis of images from naïve mice suggests only a small variance in retinal layer thickness over the time course of 4 weeks. We anticipate being able to detect the acute effects of TBI on retinal layer thickness and then will undertake further investigation to titrate the resolution to which this modality is able to detect varying severities of injuries.

Conclusion: Previous studies have noted the chronic effects of repetitive TBI at three months post injury. We aim to push the time until detection much earlier so that we can follow the physiological and histological course of the injury. If successful, it could provide fields such as the military with meaningful tools to better care for troops by diagnosing previously elusive levels of brain injury, and could prevent the long-term sequelae of repeated brain injury in athletes

Alex Harding, MS4 Mentor: Kimiyoshi Kobayashi

Clinical Research

Changes In Care Continuity And Outcomes After The 2011 Resident Duty Hours Restrictions: Data From An Academic Medical Center's Department Of Medicine

Background: Restrictions on resident work hours enforced by the ACGME in July 2011 have been controversial. No study has quantified the change in continuity of care following the changes and limited data exist on how the changes affected health outcomes.

Methods: Data were obtained from the Massachusetts General Hospital's Department of Medicine Responding Clinician database. Change in continuity of care from AY 09-10 to AY 12-13 for the intern-staffed services was compared to the change on the PGY-2-staffed Step-Down Unit (SDU), which was expected to be less affected by the rule changes. Association of 30-day readmission/length of stay with continuity of care was examined.

Results: There were a total of 10,755 and 2,309 admissions in AY 09-10, and 9,977 and 2,581 in AY 12-13, from intern-staffed services and SDU, respectively. From AY 09-10 to AY 12-13, the median number of care providers per admission increased from 5 to 6 (20%) on intern services compared to no change in the median of 5 care providers per admission on the SDU ($p < 0.0001$). Median care periods per patient-day increased from 2.0 to 2.8 (40%) on intern-staffed services, while it decreased from 2 to 1.8 (10%) ($p < 0.0001$) on the SDU. On the intern-staffed services, an increase in the number of care providers per admission was strongly correlated with longer length of stay (Spearman $r = 0.80$, $p < 0.0001$), while other metrics for care continuity had weaker relationships with length of stay. None of the measures of care continuity was associated with a large change in odds of 30-day readmission.

Conclusion: Medical patients at an academic medical center experienced decreased care continuity after the ACGME duty hours rule changes. Increased number of care providers per admission was associated with an increased length of stay, suggesting that decreased care continuity may have impacted health outcomes.

Sze Yan Janelle Ho, MS2 Mentor: Jeremy Greene, MD

History of Medicine

History of Smokeless Tobacco 1960s-1990s: Evasion of Governmental Regulation and the Creation of Scientific Ignorance in Smokeless Products

Substantial literature had described the tobacco industry's methods of promoting ignorance using scientific ambiguity and evasion of regulatory or legal loopholes. While it was widely known that the industry had employed those tactics in cigarettes, the fact that the same methods were used in smokeless tobacco products was not previously described. This projects aims to highlight smokeless tobacco as a product that was both similar and different from cigarettes—both in the way it was regulated legally and the strategies the industry employed in response to those regulations. Using systemic searches within the Legacy Foundation archives at UCSF, PubMed, PubMed Health and LexisNexis, for smokeless tobacco, snuff, snus and related products, this project used historical documents to illustrate the development, scientific evaluation and social acceptance of smokeless tobacco from the 1960s to 1990s. Additional correspondences between the FDA and the industry were used from the David Kessler archives. From these materials, it was found that smokeless tobacco was deliberately created by the industry in the late 1960s—just as cigarettes were first regulated. Within the context of intense cigarette regulation, these products were specifically designed to target youth and smoking populations. Conscious efforts were made to ensure that these products would not fall under the jurisdiction of FDA regulation. To maintain the image that these products were "harmless" in health effects, the industry infiltrated itself in the scientific discourse of whether smokeless tobacco caused health outcomes such as oral carcinoma. As a result, the scientific literature surrounding oral carcinoma oscillated between showing positive and negative associations with smokeless products. However, as increasingly strong evidence emerged in the 1980s to support the likelihood of adverse health outcomes from smokeless tobacco, governmental and grass-root movements gathered momentum to close the regulatory loophole that the industry first took advantage of in the 1960s.

Katie Holroyd, MS2 Mentor: Constantine Lyketsos, MD

Clinical Research

Deep brain stimulation targeting the fornix for mild Alzheimer's Dementia: baseline population description and design of the ADvance trial

Background: There are currently few treatments and no cure for Alzheimer's disease (AD). Animal models and one clinical trial have indicated that deep brain stimulation (DBS) of memory circuits may improve symptoms and slow disease progression. The ADvance trial was designed to examine DBS of the fornix as a treatment for mild AD.

Methods: ADvance is a randomized, double-blind, placebo-controlled, clinical trial conducted at 6 sites. Eighty-five subjects were screened for the trial. Of these, 42 subjects who met inclusion/exclusion criteria were implanted with deep brain stimulators adjacent to the fornix bilaterally. They were randomized 1:1 to DBS "off" or DBS "on" groups for the initial 12 months of follow-up. After one year, all subjects will have their devices turned "on." Participants are followed for 13 visits over 48 months for cognitive and psychiatric assessment, brain imaging, and safety monitoring. Primary outcome measures include: Alzheimer's Disease Assessment Scale (ADAS-cog-13), Clinical Dementia Rating sum of boxes (CDR-SB), and cerebral glucose metabolism measured with FDG-PET. Here we report the study methods, baseline characteristics of screened and implanted participants, and test-retest reliability of cognitive outcome measures.

Results: Implanted subjects had a mean age of 68.2, were 55% male, and had mean ADAS-Cog-13 and CDR-SB baseline scores of 28.9 (SD 5.2) and 3.9 (SD 1.6), respectively. There were no differences between screened implanted and screened non-implanted subjects on most demographic or clinical assessments. Implanted subjects had significantly lower (better) mean ADAS-cog-11 and CDR-SB scores than those screened but not implanted, supporting the diagnosis of mild AD in trial participants. Scores on the major outcome measures were consistent at screening and baseline visits measured via both Pearson and Intraclass correlation coefficients.

Conclusion: This project characterizes the study population and validates the primary outcome measures used in the ADvance trial in preparation for later efficacy analyses.

Katie Hsih, MS2 Mentor: Sophia Vinogradov, MD

Clinical Research

Attachment style is a predictor for the effects of oxytocin on social cognition

Background: Individuals with schizophrenia have significant deficits in social cognition that are strongly associated with functional outcomes, yet there are no pharmacologic treatments available to reduce these deficits. The neuropeptide oxytocin has been shown to have prosocial effects when administered intranasally in humans, suggesting therapeutic potential. However, these prosocial effects are not universal. Understanding their variability is critical to targeting the appropriate treatment population. We investigated how individual attachment style modulates the prosocial effects of oxytocin.

Methods: We studied 38 subjects with schizophrenia (32 males) and 31 age-matched, healthy controls (27 males) in two randomized, double-blind, placebo-controlled, cross-over studies of 40 IU of intranasal oxytocin versus saline placebo. The primary outcome was the oxytocin-induced change in social cognition compared to saline, measured using The Awareness of Social Inference Test (TASIT). We examined the modulating effect of attachment style, measured using the Experience in Close Relationships Questionnaire (ECR), using univariate linear regression and Pearson correlation analyses.

Results: We did not find a main effect of oxytocin on social cognition. However, we did find that attachment avoidance predicted the effects of oxytocin on TASIT performance ($R=0.21$, $p<0.05$). High attachment avoidance predicted greater oxytocin-induced gains while low attachment avoidance predicted less gains or even losses. The moderating effects of attachment avoidance were similar among male subjects with schizophrenia ($R=0.24$, $p=0.11$) and healthy controls ($R=0.21$, $p=0.12$). Attachment anxiety did not correlate with the effects of oxytocin on TASIT performance.

Conclusion: Intact social cognitive abilities are associated with better functional outcomes in individuals with schizophrenia. Our data suggest that individuals with high attachment avoidance may experience greater gains in social cognition from intranasal oxytocin compared to individuals with low attachment avoidance. These results support the further exploration of how oxytocin can serve as a potential adjunct treatment to improve social cognition in specific subgroups of patients with schizophrenia.

Maimon Hubbi, MS4 Mentor: Gregg Semenza, MD, PhD

Basic Science

An Essential Role for Lysosomal Function in Cancer Cell Proliferation

Background: Chaperone-mediated autophagy (CMA) is a pathway for selective degradation of proteins through lysosomes. We previously identified a pathway for regulation of the hypoxia-inducible factor-1 (HIF-1) transcription factor via CMA-mediated degradation of its alpha subunit (Hubbi et al., J. Biol. Chem. 2013). In addition to the known role of HIF-1 as a transcription factor mediating hypoxia-responsive gene expression, we identified a role for the HIF-1α subunit as a direct inhibitor of DNA replication and an essential mediator of hypoxia-induced cell cycle arrest (Hubbi et al., Sci. Signaling 2013). Here we tested the hypothesis that lysosomes regulate cell proliferation through the degradation of HIF-1α.

Methods: We examined the effect of pharmacological inhibitors of lysosomal function and genetic targeting of CMA effectors on DNA replication and cancer cell proliferation. We examined the specific role of HIF-1α using genetic and pharmacological approaches to target HIF-1α in a variety of cancer cell lines. Single-cell imaging was used to visualize the relationship between DNA replication, lysosomal function, and HIF-1α levels within the cell cycle.

Results: In a variety of cancer cell lines, pharmacological inhibition of lysosomal function and genetic knockdown of CMA effectors led to upregulation of the HIF-1α subunit, even under non-hypoxic conditions, and subsequent inhibition of DNA replication. Single-cell imaging demonstrated that HIF-1α was targeted for lysosomal degradation at the onset of DNA replication, an effect mediated by the activity of cyclin-dependent kinases. Remarkably, cell proliferation was wholly rescued by genetic knockdown of HIF-1α, demonstrating that the effects of lysosomal function on cell proliferation are mediated through a single protein.

Conclusions: Our results demonstrate that lysosomal function, and in particular the process of chaperone mediated autophagy, are essential for cancer cell proliferation (Hubbi et al, Proc. Natl. Acad. USA 2014). These results lend further credence to the interest in autophagy inhibitors as anti-cancer agents.

Mark Iscoe, MS2 Mentor: Nathaniel Comfort, PhD

History of Medicine

Can You Do It in Silicon? The Quest to Create a Computer-Based Medical Expert in the 1970s

In the 1970s, teams of computer scientists and physicians at several American universities endeavored to create programs that translated patients' medical data into diagnoses and treatment recommendations. Creating these "expert systems" required unprecedented exploration of physicians' thought processes and knowledge bases. And it raised prescient questions about the role of computers in medicine.

Using journal articles, program archives, oral history interviews, and secondary literatures on artificial intelligence and clinical decision-making, I explored the intellectual context of these systems and compared the development, philosophies, and function of three seminal programs: Stanford's MYCIN, Rutgers' CASNET, and PIP, a Tufts/MIT collaboration.

Each took a different epistemological approach. PIP focused on edema and was classified as a "psychological model." Its programmers sought to emulate physicians' reasoning, generating clinical hypotheses from initial patient findings and then re-evaluating them with each additional finding. CASNET also used a psychological model, but grounded it in physiology—it looked at glaucoma through an intricate causal relationship model of the eye. MYCIN, by contrast, was the prototypical "production system," engineered for accurate results, not human-like methods. It used about 500 "if-then" rules to assess bacteremia and meningitis.

The program developers were mainly young, ambitious clinicians and researchers, a close-knit group with varied career trajectories but the shared goals of pushing the boundaries of computer science and improving patient care. They succeeded more on the first front. While each program had some demonstrated efficacy—in a 1978 study, MYCIN outperformed Stanford's infectious disease doctors at diagnosing and recommending treatments for suspected bacterial infections—none saw much clinical use. The primary obstacles were the paucity of good medical data, slow computing speed, physicians' unfamiliarity with computers, the need to continually incorporate new information, and questions of liability. Early expert systems succeeded as intellectual exercises, but were doomed to fail as clinical tools.

Aparna Krishnan, MS2 Mentor: Francoeur Cadet, DO, MPH

Public Health and Community Service

Barriers to colorectal cancer screening as determined by the knowledge, attitudes, and practices of patients at Orange Blossom Family Health

Background: Colorectal cancer (CRC) is a leading cause of cancer-related deaths but preventable with early screening. Orange Blossom Family Health (OBFH), a federally qualified health center, faces low CRC screening rates despite access to free FOBT screening. This study explores patients' knowledge, attitudes and practices regarding CRC and CRC screening to identify specific factors that may contribute to low screening rates.

Methods: Established patients age 50-75 visiting the clinic during a two-week period completed surveys in English, Spanish or Creole on socio-demographics, medical history, knowledge (6 items), attitudes (9 items) and practices (4 items) regarding CRC and CRC screening. We determined associations between survey items in this convenience sample using descriptive statistics, Chi-square tests, Fischer's Exact tests, and logistic regressions.

Results: Survey responders (n=211, RR=84%) included 47% male, 75% minority, 85% uninsured, 55% homeless and 79% English-speaking. Only 36% of patients reported strong self-efficacy to screen for CRC using the FOBT, yet 90% had the intent to screen following PCP recommendation. Racial and ethnic minorities and non-English speakers were more likely than Caucasians and English speakers to be fearful of the FOBT (p=0.032, p=0.001; respectively), but were more likely to screen if they received a PCP recommendation (p=0.003, p=0.017; respectively). Patients who received a PCP recommendation for FOBT screening were more likely to trust their PCP (p=0.042) and report greater self-efficacy to screen (p=0.008). Patients who had previous exposure to cancer screening, scored higher on knowledge questions or reported positive attitudes were significantly more likely to report positive screening practices.

Conclusion: We demonstrate that the health belief model largely influences patients' decisions to screen for CRC at OBFH, particularly for minority patients. The results support the hypothesis that the quality of provider-patient communication and level of health education in a high-risk underserved population are directly related to patients' attitudes and practices of preventive care.

Kamini Kuchinad, MS2 Mentor: Geetanjali Chander, MD MPH

Public Health and Community Service

A qualitative study of barriers and facilitators to engaging in the HIV care continuum among individuals with substance use/misuse

Background: HIV infected individuals with substance use/misuse experience significant barriers to engagement in HIV care at every step of the HIV care continuum including: 1) HIV testing and diagnosis 2) Linkage to clinical care 3) Retention in care pre-antiretroviral therapy (ART) 4) ART initiation 5) Viral suppression. Using qualitative interviewing, we explored the facilitators and barriers to participation in the HIV care continuum among HIV-infected individuals with illegal drug use.

Methods: We performed semi-structured in-depth interviews with 34 male and female HIV infected individuals with recent drug use. The transcripts were analyzed in an iterative process using an editing style analysis. Interviews were conducted until thematic saturation was achieved.

Results: Individuals with a history of substance use faced many barriers and facilitators to care that were similar to those without such a history. Themes that emerged fell into three main domains: linkage to care, retention in care and reengagement in care. Factors that prevented linkage to care included 1) denial and increased drug use at the time of diagnosis, 2) feelings about the inevitability of death leading to increased drug use. In contrast, experiencing negative symptoms due to uncontrolled HIV infection motivated individuals to enroll in care. Barriers to retention in care included forgetting to adhere to medications and appointments because of drug use, prioritizing drug use over HIV treatment and adverse side effects associated with medications. Themes that facilitated retention and reengagement in care included increased sense of self-esteem, sickness and ritual. Many individuals reported that a regular ritual allowed for effective medication adherence even during periods of drug use.

Conclusion: Understanding the barriers and facilitators to care among HIV positive individuals who use drugs can help inform interventions focused on increasing participation in the care continuum and thus reduce the high morbidity and mortality experienced by this population.

Joshua Lupton, MS2 Mentor: Steven Jones, MD

Public Health and Community Service

The association between serum homocysteine and an atherosclerotic lipid profile

Background: High serum homocysteine has been implicated in literature as an independent risk factor for cardiovascular disease, but the mechanism for this risk remains unclear. Mouse models have indicated that hyperhomocysteinemia promotes atherosclerosis through the reduction of high-density lipoprotein cholesterol (HDL-C). However, the limited studies examining the association between hyperhomocysteinemia and reduced HDL-C in humans have had mixed conclusions. The purpose of this study was to examine the relationship between homocysteine and HDL-C, non-HDL-C, and total cholesterol (TC) to HDL-C ratio.

Methods: We used the Very Large Database of Lipids (VLDL), a database collected from U.S. adults referred for vertical Auto Profile analysis of their lipid profile from 2009 to 2011. There were 58,249 subjects that had the measurement of homocysteine. There are also subsets of subjects that had measurements for sex, age, hemoglobin A1c, insulin, blood urea nitrogen (BUN), and creatinine. Subjects were split into quartiles based on homocysteine and the lowest (2.9-8.3 µmol/L) and highest (13.1-108.6 µmol/L) quartile groups were compared using multivariate linear regression.

Results: After adjusting for age and gender in multivariate analysis (n=29,176), being in the highest quartile of homocysteine compared to the lowest quartile was associated with 4.3% lower HDL-C (95% CI -5.1%, -3.6%), 0.9% lower non-HDL-C (95% CI -1.7%, 0%), and 2.9% higher TC:HDL-C ratio (95% CI 2.0%, 3.8%). Adding creatinine, hemoglobin A1c, BUN, and insulin to the regression (n=9,392) eliminated the association between homocysteine quartiles and HDL-C (-0.3%; 95% CI -1.7%, 1.0%), non-HDL-C (-1.4%; 95% CI -3.0%, 0.2%), and TC:HDL-C ratio (-0.4%; 95% CI -1.9%, 1.2%).

Conclusion: While hyperhomocysteinemia is associated with atherosclerotic changes when controlling for only age and sex, these associations are eliminated when additionally controlling for creatinine, hemoglobin A1c, BUN, and insulin. These results do not support the hypothesis that hyperhomocysteinemia directly results in a more atherosclerotic lipid profile.

Manoj Maddali, MS2 Mentor: Maunank Shah, MD PhD

Public Health and Community Service

Economic and epidemiologic impact of early antiretroviral therapy initiation on HIV care continuum in India

Background: India is a resource-constrained setting with significant burden of HIV disease. Recent WHO guidance advocates early ART initiation at higher CD4 counts (≤500 cells/mm3) among people living with HIV (PLWH) to improve survival and reduce transmission, but may be costly. We assessed the epidemiological and economic impact of implementing guidelines for early ART initiation in India.

Methods: We constructed an economic-epidemic model of HIV transmission and disease progression among Indian adults (15-64), incorporating the continuum of HIV care from screening through virological suppression. Our primary outcomes were PLWH, incident cases, quality-adjusted-life-years (QALYs), and costs over a 20-year time-horizon from a health-systems perspective, comparing current practice (ART initiation at CD4 ≤350 cells/mm3) with an intervention implementing recommendations for early ART initiation at higher CD4 thresholds.

Results: Compared to current practice, early ART initiation would avert 254,000 new HIV infections (15.7% reduction) and prevent 158,000 AIDS deaths (10.8% reduction) over two decades, at an incremental (discounted) cost of US$435 million. Early ART initiation was highly cost-effective at $398/QALY-gained, but population level impact was compromised by attrition in the HIV continuum of care. With earlier ART initiation, we projected that 18% of PLWH would on average require second-line therapies. In sensitivity-analysis, yearly screening and retention rates were important determinants of epidemiological impact; an early ART intervention could avert as many as 446,000 new HIV infections (27.5% reduction) and 382,000 AIDS deaths (26.3% reduction) if current rates of PLWH retained in care annually were increased by 50%.

Conclusion: Early ART initiation for PLWH is highly cost-effective, but has modest absolute benefits in reducing new HIV infections and averting AIDS mortality if current rates of screening and retention persist. Sustained economic investments and improved strategies to strengthen the HIV continuum of care will be required to realize the full potential of early ART initiation.

Katherine Marcus, MS2 Mentor: Renee Boss, MD

Medical Humanities

Systems of Communication and Decision-making for Chronically Critically Ill Infants: Identifying "Red Flags" to Prompt Discussion about Goals of Care

Background: Advances in neonatology have created a growing population of infants who survive the acute phase of complex congenital conditions yet remain chronically critically ill, facing months in intensive care, dependence on life-sustaining therapies, and poor outcomes. Systems of medical decision-making have not evolved to reflect the longitudinal care these infants need. Day-to-day decision-making is fragmented, with only sporadic reflections about long-term goals of care. As part of an effort to create a prospective model for longitudinal communication about goals of care, we sought to identify risk factors for fractured communication and decision-making.

Methods: We conducted in-depth retrospective chart reviews of 11 infants born 2013-2014 with congenital heart disease (CHD), a prominent contributor to chronic critical illness. We selected infants with complex clinical courses of care and reviewed medical record documentation from pre-natal care through first hospital discharge or death. An interdisciplinary team developed a medical record data extraction process targeting patient, family, clinician, and system factors associated with coordination and flow of communication and decision-making. We performed a content analysis of the extracted data and identified common risk factors, or “red flags”, associated with fractured communication and decision-making.

Results: Five common “red flags” emerged: 1) multiple extra-cardiac anomalies, which involve many specialists and thus challenge team coordination, 2) cardiac lesions identified by clinicians as “complicated”, indicating management is not straightforward, 3) exceptions to usual care, such as prolonged ECMO, 4) neurodevelopmental risk, which complicates prognostication, 5) significant social vulnerabilities that limit a family’s resources in caring for a medically-complex child.

Conclusion: Preliminary analysis of complex cases of CHD identified “red flags” that could prospectively identify situations at risk of fractured communication and decision-making. These “red flags” will inform the development of a prospective model to track medical record communication for at-risk patients, with the ultimate goal of longitudinal communication interventions.

Robin Megill, MS1 Mentor: Stephen Yang

Clinical Research

The "July Effect" in Thoracic Surgery: A NSQIP Analysis

Background: The “July effect” is a proposed phenomenon that attributes a potential increase in adverse events to be associated with the training of new surgical interns and residents during the first portion of the medical academic year. Previous studies have been conducted in other fields and have demonstrated varying results in terms of the significance of having new physicians within the workforce. The purpose of our study was to test for the existence of the "July effect" within thoracic surgery.

Methods: A retrospective cohort study design was used with the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database from 2005-2011. Multivariate logistic regression was used to conduct statistical analyses.

Results: Operations included in the study surgeries for lung cancer. A total of 11,174 cases met inclusion criteria and were included in the analysis. Of these, 29.2% occurred in the first academic quarter and 37.8% had resident involvement. The rate of serious adverse events (SAE) and adverse events (AE) were 2.32 times higher and 1.91 times higher, respectively, among cases with resident involvement than among those without ($P < 0.05$). However, among cases both with and without resident involvement, the rates of SAE and any AE did not differ by academic quarter ($P = 0.542$, $P = 0.719$).

Conclusion: There was no evidence that the influx of new interns and residents is associated with an increase in the complications of thoracic surgery. Safety measures have been put in place to ensure patient safety during physician training and their effectiveness is demonstrated by the results. Although adverse events were more common among cases with resident involvement than among cases without resident involvement, there is a confounding variable that must be taken into account as residents more often participate is riskier cases in order to learn, rather than routine procedures.

Devin Miller, MD/PhD or Student in Residence Mentor: Gerald Brandacher, MD

Basic Science

The Impact and Mechanisms of Antibody-Mediated Rejection in Vascularized Composite Allotransplantation

Background: The immediate clinical management for patients suffering from devastating tissue injuries often requires multiple blood transfusions and/or skin grafts as life-saving interventions. However, the consequent formation of alloantibodies after these procedures is a barrier facing patients wishing to receive definitive treatment in the form of reconstructive transplantation. This is because sensitization currently stands as a major contraindication for vascularized composite allotransplantation (VCA). Unfortunately, the role of donor-specific antibodies (DSA) and mechanisms of antibody-mediated rejection (AMR) in VCA are still largely unknown.

Methods: Major histocompatibility-mismatched Dark Agouti (DA) donors and Lewis recipients were utilized to examine the effect that sensitization to donor antigens has on the rejection scheme of VCA. Lewis rats were sensitized with full-thickness skin grafts from DA donors and after 30 days received orthotopic hind-limb transplantation. Serum antibody titers, tissue biopsies, and clinical observations were obtained and analyzed.

Results: Serum antibody titers peaked in sensitized recipients 10 and 14 days after skin graft sensitization for IgM and IgG respectively. Sensitized rats receiving no immunosuppression rejected hind limb grafts 4-5 days after transplantation, while non-sensitized rats rejected grafts at 9-10 days ($p<0.05$). Treatment of non-sensitized recipients with tacrolimus (0.5 mg/kg) resulted in rejection-free long-term graft survival (>30 days), whereas the same treatment regimen in sensitized recipients resulted in accelerated rejection around POD 10. IgG and C4d deposition occurred in the epidermis, dermis, and capillaries in hind limb allografts from sensitized rats 3 days after transplantation. In contrast, non-sensitized rats showed minimal IgG or C4d dermal staining at 3 days postoperatively.

Conclusion: Sensitized recipients reject VCA in an accelerated manner as compared to non-sensitized recipients. Additionally, antibody-specific markers of rejection such as IgG and C4d deposition appear at earlier time points in sensitized recipients as compared with non-sensitized controls. Treatment with standard immunosuppressive agents proves to be insufficient at stifling DSA mediated rejection.

Ekene Obi-Okoye, MS2 Mentor: Azadeh Farzin, MD

Public Health and Community Service

Provider Knowledge and Perceptions of Current Breastfeeding Support During Prenatal Care

Abstract: Despite ongoing efforts to increase breastfeeding rates in the U.S. in accordance with the American Academy of Pediatrics recommendations, rates of breastfeeding initiation and duration among African American women continue to lag behind compared to other races. Prenatal period is a critical juncture to develop breastfeeding intention. This study sought to elucidate the perceptions of obstetric providers on breastfeeding support for African American patients during prenatal care.

Methods: From July 2014 to October 2014, a qualitative research study using semi-structured interviews of obstetric providers was conducted at Johns Hopkins Hospital, which serves a significant African-American, low-income community. Subjects were asked to discuss their perspective on the breastfeeding counseling and support for their patients during prenatal care. Interview sessions were recorded, transcribed, and analyzed using an open-coding technique, in which codes were generated by what arose in the interviews as opposed to concepts pre-determined by the researchers. Codes were categorized into major themes.

Results: While a variety of themes emerged, one major finding of this study was that providers were not given practice guidelines to govern their breastfeeding counseling; thus, the timing and the content of breastfeeding discussions varied across providers. In addition, providers also mentioned that they had difficulty addressing their patients' barriers to breastfeeding due to time, lack of continuity in their clinic schedule, lack of education about practical resources, and racial/ethnic disparities between patients and providers. One recommendation for addressing some of these barriers included having a staff member who was more integrated into the East Baltimore community be the ambassador for breastfeeding thereby helping patients feel more comfortable and willing to try breastfeeding.

Discussion: Some limitations of the study include the small sample size that was not shown to reach saturation, lack of follow-up with participants, and analysis being performed by only one research team member.

Aaron Parzuchowski, MS2 Mentor: Stephanie Terezakis

Clinical Research

Frequency of Protocol Deviations in Pediatric versus Adolescent and Young Adult Populations with Hodgkin's Lymphoma and its Impact on Clinical Outcomes

Background: AHOD0031 was designed to determine whether response based therapy improves outcomes in intermediate-risk pediatric Hodgkin lymphoma. The study mandated real-time central review of involved-field-radiotherapy (IFRT) and imaging records by the Quality Assurance Review Center (QARC) to maximize protocol compliance. We examined patterns of radiation protocol deviation and relapse between the pediatric (<15) and adolescent and young adult (AYA) (15-21) patient cohorts.

Methods: QARC review of simulation and port films, photographs, and dosimetry records was required both before treatment and after treatment completion. Records were reviewed by study-affiliated or QARC-affiliated radiation oncologists to identify dose and volume deviations based on concordance of treatment on final review. A 6-10% deviation from protocol-specified dose was scored as "minor"; >10% was "major". A volume deviation was scored as "minor" if margins were less than specified, or "major" if fields transected disease-bearing areas. Proportions with dose deviation and with volume deviation in pediatric and AYA groups were compared. Additionally, the association between protocol deviation and relapse was assessed.

Results: Of the 1712 patients enrolled, 1173 (68.5%) underwent IFRT, of which 212 (18.1%) deviated. Overall, minor and major deviations were found in 12% and 6% of patients, respectively, and deviations were more common in AYAs than pediatrics (19% (135/698) vs. 16% (77/475). Minor volume deviations were most common type in both pediatric patients and AYAs (56% (43/77) and 59% (80/135), respectively. Deviations for both cohorts are overwhelmingly undertreatments, accounting for 75% (58/77) of the pediatric deviations and 77% (104/135)) of the AYA deviations. With regard to relapses, 15% (12/77) of the pediatric deviations were associated with relapse compared to 13% (18/135) of the AYA deviations.

Conclusion: A greater proportion of AYAs had protocol deviations. However, the pediatric population experienced more relapses than the AYAs. Further study is needed to investigate the relationship between relapse, protocol deviations and clinical outcomes.

William Plum, MS2 Mentor: Ashish Shah, MD

Clinical Research

Predictors of Early and Late Mortality Following Valve Operations for Infective Endocarditis

Background: We sought to identify patient-specific characteristics, intraoperative variables and perioperative outcomes that confer an increased risk of both early and late mortality following surgical intervention for infective endocarditis (IE).

Methods: We performed a retrospective cohort study of all adult patients (>18 years) undergoing valve surgery for IE at our institution from 2002-2012. Univariate predictors of 30-day (early) and 1-year (late) mortality were examined using Cox proportional hazards regression and a multivariable model including preoperative factors, intraoperative variables, and postoperative outcomes was constructed. Kaplan-Meier estimates were utilized to compare survival between groups.

Results: Of the 265 patients that met criteria for inclusion, 41% (109), 30% (80) and 29% (76) underwent isolated mitral, isolated aortic, and combined procedures, respectively. The median age was 53 years [range 42-63] and 66% (176) were male. Survival in the entire cohort was 88% at 30-days and 80% at 1-year. Patients with STS-endocarditis risk scores in the highest 25th percentile (≥ 50) experienced statistically worse 30-day survival (73% vs. 93%, $p<0.001$). The strongest predictors of early and late mortality were pre-existing renal failure requiring dialysis (HR=5.89, $p<0.001$), prolonged cross-clamp time (HR=1.01, $p<0.002$), and the development of postoperative pneumonia (HR=8.90, $p<0.004$). In cases of isolated aortic valve endocarditis with annular extension (55), there was no difference in 1-year survival between those managed with debridement and valve replacement versus those undergoing aortic replacement with a homograft (71% vs. 68%, respectively; $p=0.83$). Similarly, in isolated mitral pathology (80), 1-year survival was comparable following repair (92%) and replacement (83%) ($p=0.49$).

Conclusion: In one of the largest studies of surgical patients undergoing valve operations for IE, we identified several clinically relevant predictors of early and late mortality. Patients with existing renal failure undergoing surgical intervention for IE and those who develop postoperative pneumonia require particularly close attention in the perioperative period.

Rosa Miller Polan, MS2 Mentor: Thangamadhan Bosemani, MD

Public Health and Community Service

Susceptibility weighted imaging in pediatric arterial ischemic stroke: a valuable alternative for the non-invasive evaluation of altered cerebral hemodynamics

Background: Background and purpose: SWI provides information about blood oxygenation levels in intracranial vessels. Prior reports have shown that SWI focusing on venous drainage can provide non-invasive information about the degree of brain perfusion in pediatric arterial ischemic stroke. We aimed to evaluate the influence of SWI venous signal pattern in predicting 1) stroke evolution and 2) development of malignant edema in a large cohort of children with arterial ischemic stroke.

Methods: Materials and methods: A semi-quantitative analysis of venous signal intensity on SWI and diffusion characteristics on DTI was performed in 16 vascular territories. The mismatch between areas with SWI-hypointense venous signal and restricted diffusion was correlated with stroke progression on follow-up. SWI-hyperintense signal was correlated with the development of malignant edema.

Results: Results: We included 24 children with a confirmed diagnosis of pediatric arterial ischemic stroke. Follow-up images were available for 14/24 children. MCA stroke progression on follow-up was observed in 5/6 children with and 2/8 children without mismatch between areas of initial SWI hypointense venous signal and areas of restricted diffusion on DTI. This mismatch showed statistically significant association (p=0.03) for infarct progression. Post-ischemic malignant edema developed in 2/10 children with and 0/14 children without SWI-hyperintense venous signal on initial SWI (p=0.07).

Conclusion: Conclusions: SWI-DTI mismatch predicts stroke progression in pediatric arterial ischemic stroke. SWI-hyperintense signal is not useful to predict the development of malignant edema. SWI should be routinely added to the neuroimaging diagnostic protocol of pediatric arterial ischemic stroke.

Sydur Rahman, MS2 Mentor: Emily Boss, MD

Clinical Research

Disparities in Patient Satisfaction between Races in Inpatient Pediatrics

Background: Healthcare quality is increasingly being measured by patient satisfaction scores. This report gauges disparities in patient satisfaction between races in inpatient pediatric specialties at a tertiary care center.

Methods: 904 Press Ganey inpatient pediatric surveys (completed by parents in 2013) were grouped by race (white or non-white). The survey contains 46 Likert-scaled items, which comprise 10 service domains. The survey responses were dichotomized, with 5 as the "top score" and 1-4 as "low scores." Odds ratios between scores were measured by multivariate logistic regression analysis in Stata, controlling for: age, race, sex, insurance type, surgical service, and income bracket.

Results: For the item nurses' promptness in responding to the call button, non-white respondents gave lower scores (OR=0.696, p=0.049). For the item nurses' amount of attention paid to special or personal needs, non-white respondents gave lower scores (OR=0.668, p=0.040). For the item degree to which nurses kept parent informed using understandable language, non-white respondents gave lower scores (OR=0.644, p=0.030). For the item skill of the nurses, non-white respondents gave lower scores (OR=0.495, p=0.001). For the item how friendly and caring the physician was toward child, non-white respondents gave lower scores (OR=0.675, p=0.021). For the item degree to which parent/guardian felt ready to have child discharged, non-white respondents gave lower scores (OR=0.660, p=0.013). For the item speed of discharge process after parent/guardian was told child could go home, non-white respondents gave lower scores (OR=0.694, p=0.021).

Conclusion: Compared to white children, satisfaction is lower for non-white children in the domains of nursing, treatments, visitors, physician,and discharge. Tertiary care centers may improve patient satisfaction in inpatient pediatrics mainly by improving communication between nurses and parents, and by changing discharge procedures.

Alim Ramji, MS3 Mentor: Paul Sponseller, MD

Clinical Research

Cannulated Lag Screw Fixation of Displaced Lateral Humeral Condyle Fractures is Associated with Lower Rates of Open Reduction and Infection than Pin Fixation

Background: Open reduction/internal fixation remains the most common way to surgically stabilize displaced pediatric lateral humeral condyle fractures, but closed reduction/internal fixation is being increasingly used. Our goal was to compare the clinical and functional results of treating displaced pediatric lateral humeral condylar fractures with traditional smooth or threaded pin fixation vs. single cannulated screw fixation.

Methods: From 1998 through 2012, the lateral humeral condyle fractures of forty-eight patients were treated with pin (twenty-two, until 2006) or cannulated, partially threaded screw (twenty-six patients, 2006 onward) fixation. In each, closed reduction with percutaneous fixation was attempted first, followed by open reduction if anatomic reduction was not achieved. For the pin and screw groups, preoperative maximum radiographic displacement averaged 8.4 mm (range, 3.8 to 18.4 mm) and 6.3 mm (range, 2.2 to 15.5 mm), respectively; follow-up averaged 4.3 months (range, 1.5 to twenty months) and 10.3 months (range, two to thirty months), respectively.

We reviewed preoperative and postoperative images and all follow-up clinical examination findings; serially assessed initial displacement, Baumann and carrying angles, range of motion limitations, and clinical alignment; evaluated functional results via the Hardacre et al. system; and investigated all complications.

Results: Open reduction was required in 73% (16/22) and 15% (4/26) of the pin and screw groups, respectively ($p < 0.001$). All fractures were reduced to <1 mm postoperative displacement. Postoperative immobilization averaged 5.9 weeks and 4 for the pin and screw groups, respectively. The only significant difference in complications was the infection rate: five (one deep) and none in the pin and screw groups, respectively ($p < 0.05$).

Conclusion: Closed reduction and percutaneous 4.5-mm lag screw fixation of displaced pediatric lateral humeral condyle fractures is safe and reliable, providing a higher rate of closed reduction, significantly lower infection rate, and earlier mobilization than traditional pin fixation.

Sarah Scotland, MS2 Mentor: Jean-Emmanuel Sarry, PhD

Basic Science

Metformin targets human acute myeloid leukemia cells through upregulation of the ATF4/DDIT3/4 stress response pathway

Background: Metformin, a normoglycemic agent for type 2 diabetics, decreases the risk of cancer in these patients compared to the diabetic population and inhibits growth of various cancers. This occurs primarily through inhibition of electron transport chain complex I (ETC1) and activation of energy sensing protein, AMP-activated protein kinase (AMPK). We previously demonstrated in human acute myeloid leukemia (AML) cells that metformin blocks cell cycle, decreases cell proliferation and colony formation and induces caspase-3-dependent apoptosis in vitro and in vivo in an AMPK-independent manner.

Methods: To further elucidate metformin's mechanism of action and identify RNA biomarkers for the response in vivo, we performed an Affymetrix microarray analysis of RNA expression in 4 AML cell lines following in vitro treatment with metformin.

Results: The results showed that metformin induced anti-cancer stress response genes downstream of activating transcription factor 4 (ATF4), whose upregulation can increase apoptosis, decrease translation, block cell cycle and respond to amino acid deprivation. In fact, the metformin-induced expression profile is similar to that observed in HCT116 colon cancer cells depleted in ATF4 negative regulator, eukaryotic peptide chain release factor subunit 3a (eRF3a), and profiles following amino acid deprivation and inhibition of mammalian target of rapamycin c1 (mTORc1) in various cancer cell types. Specifically, we observed significantly increased expression of ATF4 targets, DNA damage-inducible transcripts 3 and 4 (DDIT3/4). Increased DDIT4 expression appears functional as we observe decreased protein expression of mTORc1, a DDIT4 target and regulator of protein translation. DDIT3 may also play a functional role as we observe increased expression in numerous downstream targets, including cation transport regulator-like protein 1 (CHAC1), a novel pro-apoptotic protein.

Conclusion: Altogether, our work suggests a novel mechanism by which metformin targets AML cells through activation of the ATF4-DDIT3/4 stress response pathway and may provide biomarkers for the response to metformin in vivo.

Sbaa Syeda, MS2 Mentor: Ali Bydon, MD

Clinical Research

Preoperative motor strength and time to surgery are the most important predictors of improvement in foot drop due to degenerative lumbar disease.

Background: Palsy of dorsiflexion, or foot drop, may be due to degenerative lumbar disease and amenable to posterior spinal decompression. The objective of this study is to measure prognostic factors of and time to foot drop improvement after posterior lumbar decompression.

Methods: We performed a retrospective cohort study of 71 consecutive patients at a single institution undergoing first-time, posterior lumbar decompression for foot drop due to degenerative spinal disease. Patient sex, age, comorbidities (Charlson Comorbidity Index), preoperative anterior tibialis strength (manual muscle testing, MMT), and duration of foot drop were ascertained from clinical notes. Prognostic factors affecting foot drop improvement were calculated with a discrete-time proportional hazards model, in which follow-up times and outcome measures were binned into six time intervals: 1 week, 6 weeks, 3 months, 6 months, 1 year, and ≥1 year.

Results: Of the 71 patients, the mean age was 54.6 years, and 66.2% were males. The mean Charlson Comorbidity Index was 2.42. During a mean follow-up of 30.4 months, dorsiflexion function improved postoperatively in 73.2% of patients. The median time to surgery from onset of foot drop was within 6 weeks, and the median preoperative MMT strength of patients with foot drop improvement was 3. Following a discrete-time proportional hazards model, duration of anterior tibialis palsy (HR [95%CI]=0.67 [0.51-0.88], p=0.004) and preoperative muscle strength (HR [95%CI]=1.10 [1.02-1.18], p=0.010) were significant predictors of foot drop improvement. In adjusted Kaplan-Meier analysis, the median time to foot drop improvement was within 6 weeks of surgical intervention.

Conclusion: In the present study, we adopted a discrete-time proportional hazards model to describe dorsiflexion improvement in 71 patients who underwent posterior lumbar decompression for foot drop. Preoperative muscle strength and palsy duration were statistically significant predictors of foot drop improvement. Furthermore, the median time to improvement was 6 weeks.

Akachimere Uzosike, MS2 Mentor: Ali Bydon, MD

Clinical Research

Duration of drain indwelling following instrumented posterolateral fusion of the lumbar spine predicts surgical site infection requiring reoperation

Background: Drains are often placed in the surgical wound to prevent fluid accumulation following instrumented posterolateral fusion (PLF) of the lumbar spine. While some studies have shown that the mere use of drains does not alter the risk of surgical site infection (SSI), there is limited data examining the effect of drain duration on SSI risk. The purpose of this study is to examine the impact of drain duration on the risk of SSI following PLF of the lumbar spine.

Methods: A retrospective review was performed to identify all adult neurosurgical patients undergoing first-time lumbar PLF for degenerative spine disease at two Johns Hopkins institutions between 2007 and 2014. All patients underwent laminectomy and instrumented fusion, with or without interbody devices. The primary outcome measure was reoperation for SSI. A multivariable logistic regression was performed to calculate the adjusted odds ratio of SSI development with increasing drain duration (measured in days). All analyses were adjusted for age, sex, diabetes, depression, current smoking, drain output volume, site of drain removal (inpatient versus outpatient), number of spinal levels fused, and duration of inpatient IV antibiotic infusion.

Results: A total of 215 patients were identified. The mean age was 58.6±12.4 years, and 115 (53.5%) were female. Sixteen patients (7.4%) acquired SSI requiring reoperation. The average drain duration was significantly greater in the SSI subgroup (8.00±1.03 days) than in the non-SSI subgroup (5.92±2.95 days, P=0.009). In a multivariable logistic regression, drain duration (OR=1.21, 95% CI, 1.04-1.40) and current smoking (OR=8.01, 95% CI, 2.08-30.78) were independent risk factors for SSI. Duration of antibiotic infusion and site of drain removal were not significantly associated with SSI development.

Conclusion: The findings of this study suggest that increasing drain duration and smoking are independent risk factors for SSI development following lumbar PLF. Future prospective studies are needed to corroborate these findings.

Judith Vick, MS2 Mentor: Mary Fissell

History of Medicine

The construction of womanhood in antebellum America: a study of cases

In the twenty-first century, we often use genetic explanations to explain what makes a woman a woman and a man a man. Two X's – female; an X and a Y – male. In the nineteenth century, this explanatory framework did not exist, but other explanations certainly did. This project explores the question: How did nineteenth century American medical practitioners construct womanhood and understand sex differences, as evidenced by the case histories published in American journals? In the narratives of patients with anatomical ambiguity such as a woman's lack of a uterus or external genitalia, many 19th century medical men evinced an understanding of the ovary as the feature that made a woman a woman, akin to the double X chromosome today. These writers connected qualities they understand as being feminine, such as a sexual appetite, a feminine expression or countenance, or the "catamenial effort," to be derived from the presence of the ovaries. There was not uniform agreement on this matter, however, and other authors expressed other beliefs or did not consider the ovary at all. While historians such as Alice Dreger have discussed the creation of a nascent medical science of sex difference in Europe (naming the end of the 19th century the "age of the gonads"), I explore how individual American practitioners negotiated sex difference at the bedside. As historian Steve Stowe has demonstrated, case histories are a rich source for examining the deployment of medical knowledge – and antebellum American journals are replete with such narratives. By reading such cases closely, I hope to reveal how doctors struggled with extraordinary patients who did not look like their textbooks predicted, gain some insight into the nature of the patient-practitioner relationship, and even glean some understanding of the the patients' perspectives.

Stephanie Wang, MS2 Mentor: Danelle Cayea, MD

Medical Humanities

Talking about "Burden" in the Clinic: Caring for Older Patients with Multimorbidity

Background: Multimorbidity, or the co-occurrence of multiple chronic medical conditions within one person, is associated with increased patient "burden." Although some studies have explored patients' perspectives on this topic, little is known about the way older patients with multimorbidity discuss and define "burden" in the clinic. The aim of this study was to characterize how older patients with multimorbidity and their physicians talk about "burden" during primary care clinic visits and to identify the types of burdens described.

Methods: As part of a larger study, 30 clinic encounters between internal medicine residents and patients (≥65 years old with ≥2 chronic conditions) were audio-recorded. Open coding of the transcripts resulted in the identification of multiple aspects of the topic of "burden." One-third of the transcripts were independently coded and compared.

Results: On average, patients in the study were 73.6 years of age, had 3.7 comorbidities, and were on 12.6 medications. Types of patient burden discussed fell into three major domains: "Symptom Burden," "Treatment Burden," and "Chronic Behavioral Burden." Major subthemes included chronic disease flare and uncertainty of symptom cause ("Symptom Burden") as well as scheduling, monetary and testing burden and perceived ineffectiveness of medication ("Treatment Burden").

Additionally, patients tended to repeat their concerns if they felt their burdens were unacknowledged. Physicians did not always provide a medical solution to patients' burdens, but through listening and acknowledging patients' concerns, they were often able to conclude the conversation and shift to a different topic. Notably, while older patients with multiple chronic diseases often expressed specific symptom burdens during the clinic visit, eliciting treatment burdens often required physician probing.

Conclusion: It is important for physicians to address patients' perceptions of burden. These results could inform future resident training on how to approach and discuss older patient burden in the clinic.

Georgia C. Yalanis, MD/PhD or Student in Residence Mentor: Justin M Sacks, MD

Basic Science

An Electrospun Fiber-Hydrogel Composite with Interfacial Bonding for Soft Tissue Regeneration in vivo

Background: Reconstructive procedures for surgical defects cause donor site morbidity, infection, failure, and fibrosis. A superior approach using the body's regenerative capacity and a synthetic scaffold allows restoration of form permitting native tissue regeneration. We developed a novel fiber-hydrogel composite using FDA-approved materials to promote soft tissue regeneration in vivo.

Methods: Electrospun poly-ε-caprolactone (PCL) fibers grafted with poly-acrylic acid (PAA) and surface-modified with maleimide were dispersed inside a hyaluronic acid (HA) hydrogel to create a fiber-hydrogel composite with interfacial bonding. GFP labeled adipose-derived stem cells (ASCs) were seeded inside the composite evaluating ASC migration in vitro. Implanting composites under the inguinal fat pad of Lewis rats assessed biocompatibility in vivo. HA hydrogels alone were implanted as controls. Composites and HA controls were explanted en bloc. Samples were fixed and stained using H&E and Masson Trichrome.

Results: Morphology of the composite mimicked ECM with a high porosity. Migrated ASCs were increased in the composite compared to controls as composite nanofibers become a guide similar to the native cytoskeleton permitting cellular migration. Prior to explant, the composite revealed no evidence of infection or fibrosis, demonstrating incorporation into native fat. Histology after 4 weeks demonstrated no inflammatory response above a surgical site response. Staining demonstrated cellular infiltration by native fat through the composite, capillary formation, and regeneration of native fat. Controls lacked cellular infiltration, revealed inflammation above a surgical site response, foreign body reaction, and fibrosis.

Conclusion: We developed a novel fiber-hydrogel composite with optimal porosity and crosslinking density that promotes cellular migration in vitro, and maintains 3-dimensional structure in vivo while promoting cellular infiltration, angiogenesis, adipogenesis, and regeneration of native soft tissue without a foreign body response or fibrosis. Use of this material has significant implications for reconstituting soft tissue defects without the negative sequelae associated with autologous reconstruction or implant-based devices.

Ian Yarett, MS2 Mentor: Lawrence Cheskin, MD

Public Health and Community Service

TSH level as a predictor of weight loss magnitude in Johns Hopkins Weight Management Center patients

Background: It would be of clinical utility and help target obesity interventions if we could identify specific patient characteristics that are predictive of successful short-term weight loss. Thyroid stimulating hormone (TSH) levels have been shown to be positively associated with overweight/obesity (BMI>25), but any association between TSH and short-term weight loss efficacy has yet to be explored. The purpose of our study was to assess whether a patient's baseline TSH level may be predictive of their ability to lose weight through a multidisciplinary, team-based weight loss program.

Methods: We conducted a chart review of 398 present and former patients of the Johns Hopkins Weight Management Center (JHWMC) with BMI>25 who completed their initial assessments and at least 1 follow-up visit within the first month. This sample was 69.6% female and 30.4% male, with a mean age of 47.2 and mean BMI of 39.5 at enrollment. 83.4% of the patients were white, 10.1% African American, 2.3% Asian, and 1.3% Hispanic. We used descriptive and regression analysis to assess the association between initial TSH level and short-term weight loss efficacy.

Results: For both normothyroid (n=123) and hypothyroid patients (n=32) who remained in the program for at least 6 months, there was no significant association between baseline TSH level and percent weight loss at peak (R2=0.003 and R2=0.018, respectively).

Conclusion: Despite the known positive association between TSH level and BMI, we found that starting TSH level was not a significant predictor of short-term weight loss efficacy. This may be useful information to convey to obese patients when conducting initial assessments, or when patients question their metabolism level as a factor in weight control. These results reflect the patient population present at the JHWMC. Further study in other settings is needed to determine whether these findings can be applied more broadly.

Allen Young, MS2 Mentor: Joel Price, MD

Clinical Research

Long Term Outcomes of Aortic Root Operations for Marfan Syndrome: A Comparison of Bentall versus Aortic Valve-Sparing Procedures

Background: Prophylactic aortic root replacement improves survival in Marfan syndrome (MFS) patients with aortic root aneurysms, but the optimal procedure (Bentall vs. valve-sparing aortic root replacement (VSRR)) and long-term outcomes remain undefined.

Methods: MFS patients who had Bentall or VSRR procedures at our institution between 1997 and 2013 were identified. Comprehensive follow-up information was obtained from hospital charts and telephone contact. Kaplan-Meier, Cox and propensity score analyses were performed for the outcomes of mortality, composite thromboembolic/hemorrhagic events, reoperation on the aortic valve/root, and endocarditis.

Results: 165 adult MFS patients had either Bentall (n=67) or VSRR (n=98) procedures. Bentall patients were older (median 37 vs. 36 years, p=0.03), had larger preoperative sinus diameter (5.5cm vs. 5.0cm, p=0.003), more aortic dissections (25.4% vs. 4.1%, p<0.001), higher incidence of moderate/severe aortic insufficiency (49.3% vs. 14.4%, p<0.001) and more urgent/emergent operations (24.6% vs. 3.3%, p<0.001). There were no hospital deaths and nine late deaths in over 17 years of follow-up. By Kaplan-Meier analysis, ten-year survival was 90.5% in Bentall patients and 96.3% in VSRR patients (p=0.10). Nineteen patients had composite thromboembolic/hemorrhagic events (15 Bentall pts vs. 4 VSRR pts, log rank P<0.001); eight patients required aortic valve/root reoperations (4 Bentall pts vs. 4 of VSRR pts, log rank P=0.52) and four developed endocarditis (3 Bentall pts vs. 1 VSRR pt, log rank P=0.14). Multivariable Cox proportional hazards analysis controlling for baseline characteristics revealed that VSRR was associated with fewer composite thromboembolic/hemorrhagic events (HR 0.12, [0.03-0.46], p=0.002), which was confirmed by a propensity score-adjusted regression analysis (HR 0.16, [0.03-0.85], p=0.03).

Conclusion: After prophylactic root replacement in MFS, Bentall and VSRR have similar late survival, freedom from root reoperation, and freedom from endocarditis. However, VSRR result in significantly fewer thromboembolic/hemorrhagic events. These results support continued use of VSRR in MFS.

BASIC SCIENCE

POSTER ABSTRACTS

Listed Alphabetically

Somya Abubucker, MS2 Mentor: Gregory Riggins, MD

Basic Science

Evaluation of the Combination of Histone Deacetylase Inhibitors with Mebendazole in Meningioma

Meningioma is the most common extra-axial brain tumor, and almost half of these neoplasms arise from inactivation or epigenetic modification of the tumor suppressor NF2 gene. When NF2 is dysfunctional, the YAP1 oncogene that is downstream in its pathway translocates to the nucleus and leads to cell proliferation and anti-apoptosis. Our lab had previously identified three drugs (the histone deacetylase inhibitors (HDACIs) vorinostat and panobinostat, and the microtubule synthesis inhibitor mebendazole) as showing some efficacy against meningioma cells. The overall goal of this experiment was to explore the possibility of combining the drugs to create more effective therapy in the setting of NF2-deficient cells or YAP1-overexpressing cells. Although we did demonstrate marked cytotoxicity for all three drugs as monotherapies, we did not identify any synergistic combinations. More intriguing, however, was the finding that the NF2-deficient cells—although still more susceptible to the monotherapies—were more susceptible to the cytotoxic effects of almost all the combinations attempted, suggesting that the mechanism of action of the HDACIs may be the re-activation of the upstream NF2 tumor suppressor rather than stimulation of the downstream YAP1 oncogene. Directly reversing a critical step in tumorigenesis could revert cancer cells to a state in which they are more susceptible to currently used therapies. We will explore the genetic mechanism and clinical ramifications of this unexpected and promising finding.

Tamara Ashvetiya, MS4 Mentor: Peter Johnston, MD

Basic Science

Age-Related Differences in Paracrine-Mediated Angiogenesis

Background: My project focuses on the development of an "implantable bioreactor" for delivery of stem cell-derived cytokines to the post-infarct heart. The aim of stem cell therapy is to regenerate damaged myocardium and to restore function following an infarction. Growing evidence suggests that beneficial effects of stem cell therapy are mediated largely by paracrine action. The elderly stand most to benefit from such therapy, but little is known about age-related differences in paracrine-mediated tissue regeneration. We compared angiogenesis stimulated by young and old mesenchymal stem cells (MSCs) contained in semi-permeable "bioreactors" that allow free exchange of paracrine factors (PFs), but not the MSCs themselves.

Methods: MSCs isolated from young (6 wk) and old (18-24 mo) mice were grown in bioreactors at standard conditions or at hypoxia (5% O2). Bioreactors were exposed to human vascular endothelial cells (HUVECs) and resultant tubule formation (TF) was imaged at 18h. Bioreactors were implanted in pigs for six weeks, and subsequently explanted to assess MSC survival and cytokine production.

Results: At normoxia, PFs from young MSCs induced greater TF than old MSCs ($p=0.0015$). After exposure to hypoxia, more TF was induced by both young and old MSCs, but there was no longer a significant difference between young and old ($p=0.11$). ELISAs measured significant production of VEGF, FGF, SDF-1, IL-8, and HGF. Explanted bioreactors from pigs were found to contain viable MSCs. The cytokine production profiles of explanted bioreactors differed from comparable bioreactors that had never been implanted in pigs, suggesting that MSCs housed within bioreactors respond to environmental conditions by modifying PF production.

Conclusion: Bioreactors implanted in pigs can sustain MSC viability for up to six weeks. Young MSCs show superior paracrine-mediated angiogenesis in vitro compared to old MSCs at normoxia. The bioreactors used here will allow for further comparison of paracrine-mediated age effects in vivo.

Julio DeJesus, MS2 Mentor: Alfredo Quinones-Hinojosa, MD

Basic Science

Clinical and surgical outcomes of gliosarcomas: the Johns Hopkins Hospital experience

Glioblastoma multiforme (GBM) is the most common and aggressive primary tumor of the central nervous system with an incidence of 4-5 per 100,000. Despite radical surgical resection, chemo- and radio-therapy, glioblastoma patients have a dismal prognosis with a median survival of 13.4 months. Gliosarcoma, a variant of GBM characterized by a composition of both gliomatous and sarcomatous elements, is quite rare comprising approximately 2% of GBMs. Gliosarcoma has been traditionally thought to behave similarly to all glioblastomas in terms of disease progression and prognosis and has therefore continued to be managed with the same therapies. Nevertheless, since mostly case series and small institutional experiences are available to date, the behavior, prognosis, and treatment outcomes of gliosarcomas remain controversial and poorly understood. We explored the medical records of 64 patients treated for gliosarcoma at Johns Hopkins Hospital between 1984-2014 in order to gain a better understanding of the natural behavior and treatment response of this malignancy to the currently accepted treatment protocols. Likewise, we assess the clinical and surgical variables that may be associated with increased survival of gliosarcoma patients. Overall, we aimed to understand whether the gliosarcomas represent a unique GBM malignancy and whether their history and treatment provide an opportunity to improve current therapies. We found that 92% of patients ultimately received surgical resection with 36% subsequently receiving radiation treatment. Gross total resection was reported in 59% of these cases with another 10% of cases reporting near total gross resection. However, despite aggressive therapy, median survival was 4.1 months with only 4% surviving above the median (14.6 months) of GBMs. These findings suggest that gliosarcomas have a worse prognosis and treatment response than GBMs to conventional therapies and reveal a need for considering unique treatments such that improvements in survival do not continue to lag behind.

Shekhar Gadkaree, MD/PhD or Student in Residence Mentor: Young Kim, MD/PhD

Basic Science

Cyclic Dinucleotide induced Regression of Tumor in a Squamous Cell Carcinoma Mouse Model

Background: Cyclic dinucleotides (CDNs), which signal through the STING (Stimulator of Interferon Gene) pathway, are a novel class of adjuvants that have been shown to induce anti-tumor responses in vivo. The in-vivo tumor response to CDNs in a squamous cell head and neck cancer model is not well documented. In this study, we examined the anti-tumor immune responses generated by natural and synthetic CDNs on SCCVII squamous cell tumors in a murine model.

Methods: SCCFVII tumor bearing C3H/HeOUJ mice (n = 5 per group) were treated with synthetic or natural CDN intratumorally to assess their antitumor effect. The mice underwent three injections with either RR-CDG (synthetic cyclic-di-guanine), CDG (natural cyclic-di-guanine), R848 (TLR 7/8 agonist), or phosphate buffered saline (control), and the in vivo tumor growth rate was followed. Splenocytes were analyzed for cytokine profile using flow cytometry. In addition to measuring the anti-tumor immune response, the direct toxicity of the CDNs was measured by performing in vitro dose response cell viability assays.

Results: The RR-CDG and CDG treatment groups showed significantly decreased tumor size when compared to the R848 and PBS treatment groups ($p<0.05$). The splenocytes from the RR-CDG treated mice showed an enhanced TH1 response, as determined by increased expression of IFNγ, when compared to the CDG, R848, and PBS treatment groups. In vitro tumor cell killing assay showed that there was no direct tumor cytotoxicity effect in response to CDNs. CDNs demonstrated an indirect enhanced systemic immunological effect on tumor cells.

Conclusion: Synthetic and natural CDN treated mice had significantly reduced tumor volumes when compared to R848 (TLR7/8 agonist) and control treated mice. Mice treated with synthetic and natural CDNs also showed increased splenocyte secretion of IFNγ and a predominant Th1 response when compared to mice treated with R848 (TLR7/8) agonists or controls, supporting the use of intratumoral injection of CDN into HNSCC patients.

Ilona Juan, MS2 Mentor: Marie Hardwick, PhD

Basic Science

Yeast Augmented Network Analysis (YANA) to Identify a Therapeutic Target for Parkinson's Disease

A mutation in the human EIF4G1 gene (a gene that is conserved in yeast) is linked to a heritable form of Parksinson's disease (PD), yet the implications of this mutation in terms of disease management are at present unknown. Here we use our novel Yeast Augmented Network Analysis (YANA) approach in which a candidate gene can be tested against a panel of single gene knockouts to characterize the genetic interaction networks of the candidate gene. First, we individually express the wild type and disease variant forms of human EIF4G1 in our fission yeast model and use high-throughput methods to classify fission yeast modifiers of EIF4G1. By expressing the wild type and disease variant forms of the EIF4G1 gene in the background of 5000+ individual gene knockouts and analyzing the growth rates of these constructs, we were able to identify those genes that demonstrated a significant genetic interaction with EIF4G1. Second, we analyze validated protein-protein interaction databases in both fission yeast and human systems to construct EIF4G1 genetic networks. Finally, from these networks we were able to identify NEDD4 as a genetic modifier of EIF4G1 and potential therapeutic target for PD. The significance of NEDD4 as an E3 ubiquitin-protein ligase, in addition to its role in neuronal development as a neural precursor cell, warrants further study of its implications in PD progression, development and/or treatment. Our study demonstrates the power of synthetic genetics using our YANA approach to comprehensively survey thousands of potential disease gene modifiers and identify novel targets in the pharmacotherapeutic management of PD.

Rabia Karani, MS2 Mentor: Richard Semba, MD

Basic Science

The proteome of normal human retrobulbar optic nerve

Background: The retrobulbar optic nerve is a white matter tract that conveys visual information to the brain. A detailed investigation of the proteome of the normal human retrobulbar optic nerve will facilitate studies of the biology and pathophysiology of the optic nerve.

Methods: We created a resource by conducting an in-depth proteomic analysis of retrobulbar optic nerve from five adults. After fractionating and digesting proteins extracted from the retrobulbar optic nerve, peptides were analyzed using state-of-the-art mass spectrometry.

Results: We identified 2,711 proteins in the human retrobulbar optic nerve, and twenty-one protein isoforms. Proteins included central nervous system proteins such as the astrocytic marker glial fibrillary acidic protein, several proteins expressed by oligodendrocytes (laminin, proteolipid protein, and fibronectin), and myelin proteins (myelin basic protein, myelin-associated glycoprotein). Structural proteins included those involved in neuronal protection and regeneration (α crytallins A and B, dedicator of cytokinesis proteins, ciliary neurotrophic factor) and paranodal structural proteins (neurofascin, contactin, α, β, and γ adducins, septin 2, endophilin, ankyrin β, spectrin). Proteins associated with disease included proteins seen in open-angle glaucoma (thioredoxin, heat shock protein-70), and proteins associated with optic neuritis (aquaporin-4).

Conclusion: The MS proteomics data have been deposited in ProteomeXchange with accession number _____ for future research access.

Lyonell Kone, MS2 Mentor: Arun Venkatesan

Basic Science

Screening for GBM specific pro-inflammatory cytokines in murine macrophages

Background: Glioblastoma (GBM) is one of the most common and lethal brain tumors in adults. Recently, there has been interest in a subpopulation of cells that comprise up to 30% of the tumor mass and have been shown to display a potent anti-inflammatory state; these are known as Tumor Associated Macrophages (TAMs). TAMs are recruited from the vasculature and induced into an anti-inflammatory state by tumor cells. They secrete growth factors, angiogenic factors and anti-inflammatory cytokines, all of which promote tumor growth and survival. We suspect that converting TAMs into a pro-inflammatory state would hamper tumor growth and survival. While there are many well-known pro-inflammatory cytokines, it is unclear whether they would be able to induce a pro-inflammatory state in a GBM microenvironment.

Objective: Identify cytokines that can promote a pro-inflammatory state in the presence of GBM conditioned media.

Methods: GBM conditioned media (GBM-CM) was produced by collecting media that was bathed in GBM cells for 3-4 days. It was then used to induce macrophages into an anti-inflammatory state, which was confirmed by PCR and a YFP reporter gene. Nitric oxide production was used to identify a pro-inflammatory state.

Results: First, we found that 25% GBM-CM was able to induce an anti-inflammatory state in macrophages. We then used 25 % GBM-CM to identify two out of three cytokines that would prevent this anti-inflammatory state and induce a pro-inflammatory state. Unfortunately, we later found that non-conditioned GBM media was also able to induce an anti-inflammatory state.

Conclusion: We identified two cytokines that prevented the anti-inflammatory induction of macrophages by GBM-CM. Unfortunately, non-conditioned GBM media was also able to induce an anti-inflammatory state. It is therefore unlikely that GBM-CM is a good method for replicating the anti-inflammatory environment of GBM tumors.

Andrew Luksik, MS2 Mentor: Rafael Tamargo, MD

Basic Science

The role of haptoglobin in vasospasm following subarachnoid hemorrhage.

Vasospasm is a significant cause of morbidity and mortality following aneurysmal subarachnoid hemorrhage (SAH), affecting 20% to 40% of those who survive ruptured cerebral aneurysms. Haptoglobin is a plasma protein that binds free hemoglobin and promotes clearance of this toxic molecule by macrophages. Humans have two alleles for the haptoglobin gene: Hp1 and Hp2. Previous studies have shown that haptoglobin type plays a critical role in the pathogenesis of vasospasm, but how it does this is still uncertain. An inflammatory-mediated process, vasospasm is more severe in transgenic mice with Hp2-2 genotype, and growing clinical evidence suggests that humans with an Hp2-2 genotype have worse outcomes following SAH. Using an established SAH mouse model where blood drawn from the femoral artery is injected into the cisterna magna, we compared outcomes of SAH in wild-type mice (Hp1-1) and Hp2-2 mice. Mice of both genotypes received one of three subarachnoid injections: normal saline, Hp1-1 blood, or Hp2-2 blood. Severity of subsequent vasospasm will be measured by behavioral assessments, arterial patency, inflammatory markers, and extent of apoptosis. This experimental paradigm will allow us to determine whether vasospasm is a result of the haptoglobin genotype of the blood in subarachnoid space or of the haptoglobin genotype of the recipient animal. We hypothesize that vasospasm is mediated by the type of haptoglobin present in subarachnoid blood rather than by the scavenging response to SAH at the genetic level. Our hypothesis is supported by data suggesting that Hp2-2 protein is less efficient at binding hemoglobin, and by previous animal studies showing that Hp2-2 protein is proinflammatory. Our initial work establishes the feasibility of the surgical technique, having successfully completed the procedure in 9 mice per experimental group per genotype, 54 in total. Better understanding the role of haptoglobin in vasospasm may improve treatment of subarachnoid hemorrhage.

Emily Murphy, MS2 Mentor: Gul Dolen, MD PhD

Basic Science

Molecular profiling of murine nucleus accumbens inputs using recombinant Rabies virus

Social networks play a crucial role in determining the health of an individual. The strength of these networks has a greater effect on mortality than smoking cessation, BMI, or physical activity; thus, the question of what motivates such social behaviors is of great clinical significance. Recent work demonstrates that the coordinated activity of the nucleus accumbens (NAc) and the dorsal raphe nucleus (DRN) is required for reinforcement of social rewards. Further investigation of this interaction requires manipulations that are selective to both DRN neurons as well as inputs to the NAc. In order to unite the worlds of the DRN transcriptome and the NAc connectome, we have developed an approach for connectivity-defined cell type identification. We independently demonstrate the stability of the iTRAP transgene, a fusion fluorescent-ribosomal protein expressed conditionally in cells expressing Cre recombinase. Through stereotaxic injection of a Rabies Cre virus in adult mice, we achieved retrograde, conditional labeling of neurons innervating the target injection area, here the NAc. We then selectively molecularly profiled DRN neurons projecting to the NAc through performing IP for the iTRAP fusion protein-mRNA complexes. Obtaining this molecular profile will permit us to better characterize DRN-dependent social reward, and the behavioral phenotypes that may result from defects of this system. The iTRAP method supplies a tool for characterizing neurons in a connectivity-dependent manner, and here we demonstrate its successful identification and profiling of DRN neurons associated with social reward reinforcement.

Powell Perng, MS2 Mentor: Michael Lim, MD

Basic Science

Therapeutic Effect of local and Systemic Carmustine on Anti-PD-1 Immunotherapy in a Murine Brain Glioma Model

Background: Immunotherapy has produced unprecedented response rates in several human cancers and may be useful as an adjunctive treatment for glioblastoma (GBM). We examine the therapeutic benefit of combining anti-PD1 immunotherapy with systemic or locally-administered wafer of Carmustine (BCNU) chemotherapy.

Methods: Murine glioma cells were grown and implanted in the basal ganglia of mice as previously described (Zeng et al.). We randomly assigned mice into seven treatment arms with 10-20 mice in each arm: (1) no treatment; (2) systemic BCNU; (3) local BCNU wafer; (4) anti-PD1 antibody; (5) anti-PD1 antibody + systemic BCNU; (6) anti-PD1 antibody + local BCNU; (7) empty wafer. Drug doses were prepared as previously described (Zeng et al., Pradilla et al.). Anti-PD1 was dosed in treatment arms 4, 5, and 6 on days 10, 12, and 14 post-tumor implantation. Mice in treatment arms 2 and 5 received injected BCNU 3x/week for two weeks starting on day 14. Mice in treatment group 3 and 6 were each implanted with a single BCNU wafer on day 14; mice in treatment group 7 were implanted with an empty polymer wafer on day 14. Survival in each treatment arm was followed and analyzed using Kaplan-Meier survival curves and compared using the log-rank test.

Results: The median survival for mice in the no-treatment arm and empty-wafer arm were 25 days and 23 days, respectively. Median survival for mice that received anti-PD1 therapy, systemic BCNU, and BCNU wafer were 35 days, 43 days, and 28 days, respectively. Mice that received systemic BCNU + anti-PD1 therapy had a median survival of 45 days. Survival data is not yet available for mice that received BCNU wafer + anti-PD1 therapy.

Conclusion: There may be therapeutic benefit to combining anti-PD1 immunotherapy with locally-administered BCNU wafers. Systemic chemotherapy may counter immunotherapy by inducing global immunosuppression.

Cole Sterling, MS2 Mentor: Betty Tyler

Basic Science

Assessing intracranial delivery of carboplatin and dichloroacetate for the treatment of glioblastoma multiforme in rodents

Background: Glioblastoma multiforme (GBM) is the most common and aggressive form of primary brain cancer. Intracranial multidrug therapy remains an underexplored approach to treatment. Here we compare two intracranial delivery methods—polymers and microcapsules—for the release of carboplatin and dichloroacetate (DCA) in rats with GBM. This particular drug combination has been effective in treating various cancer cell lines in vitro, but has not been tested on any GBM cell line and has not been tested in vivo. Although DCA is not approved for cancer therapy, it has shown promise in this arena based on its ability to increase oxidative phosphorylation, reactivate mitochondrial-driven apoptosis, and chemosensitize cells to carboplatin.

Methods: First, we use an MTT assay to show that this drug regimen may be particularly effective for the treatment of GBM when DCA is applied at least 24 hours prior to carboplatin. Next, we demonstrate the efficacy of this drug regimen in vivo by using intracranial polymers.

Results: In the MTT assay, pre-treatment with DCA—treating cells with DCA 24 hours prior to carboplatin application—was more effective than co-treatment with DCA. Median effective dose values were 14.4 mM and 35.0 mM, respectively.

In vivo, polymeric delivery of the drugs improved median survival by 14 days compared to the control group. However, these findings were less clear when delivering the same drugs with microcapsules.

Conclusion: Due to errors we encountered when loading and sealing the microcapsules, only limited quantities of the drugs were released from these devices. While this drug regimen appears promising for the treatment of GBM, we must determine proper microcapsule preparation techniques before we can accurately assess their use in multidrug delivery.

Sharif Vakili, MS2 Mentor: Nathan Crone

Basic Science

Electrocorticographic Correlates of Metaphysics and Cognitive Dissonance

Background: First described in 1959, Cognitive Dissonance has classically been defined as the neuropsychological phenomenon that takes place when holding contradictory thoughts simultaneously, such as justifying a purchase while experiencing buyer's remorse. Studies have looked at the concept in order to see its evolutionary role in human behavior as well as its effects on decision making and economic models. However, the underlying neurobiology of Cognitive Dissonance remains poorly understood, and has only been investigated by three recent fMRI-limited studies.

This study updates the definition of Cognitive Dissonance as a perception of an axiom violation to develop an original electrocorticography (ECoG) paradigm for revealing a novel neuroelectrophysiological biomarker. ECoG has a strong foundation in literature for high-resolution analysis of spatiotemporal dynamics in neural processing. Here we leverage these powerful techniques to characterize electrophysiological correlates of Cognitive Dissonance.

Methods: Epilepsy neurosurgery patients receiving ECoG were enrolled. To elicit dissonance, patients were presented 125 True/False logic questions that revealed an answer key the moment the question was answered. Some questions had rigged answer keys with incorrect answers. Upon presentation of the incorrect answer key, a perception of logic violation and therefore dissonance was induced. The task was presented as an IQ test that was just tricky enough for the subject to not realize it was rigged.

Results: Electrodes located in the posteroinferior frontal gyrus exhibit trends of 100Hz gamma-band activity 200 milliseconds after dissonance onset.

Conclusion: Cognitive Dissonance neural correlates were discovered using a unique perspective that regards metaphysical properties of existence (like axioms and logic rules) as environmental pressures life evolves in interaction with. Consequently, this signal is described as a biomarker of metaphysics. Tracing this marker phylogenetically can provide insights toward the evolution of cognition and rationality. Clinically, this signal has potential use with brain-machine interfaces, such as triggering the abortion of incongruent subject tasks.

Frances Wang, MS2 Mentor: Luis Garza

Basic Science

Elucidating mechanism of skin type regulation for the prevention and treatment of stump site dermatosis in amputees

There currently exits no therapy to address the root cause of stump site dermatosis, which is due to the inability of stump skin to withstand pressure and friction generated by prosthesis and socket-limb interaction. To encourage prosthetic use in amputees, conversion of skin identity at the stump site from non-volar (nonpalmoplantar; back of hands and top of feet) to volar (palmoplantar; palms and soles) skin would allow it to withstand friction, pressure and irritants. Volar keratinocytes express KRT9, a keratin that provides structural support. Here, we investigate fibroblast genes such as LMX1b and PAX9 that regulate KRT9 expression in keratinocytes, with the goal of converting non-volar skin to volar skin in amputees. It has been found that the gene LMX1b is highly expressed in non-volar fibroblasts, whereas PAX9 is highly expressed in volar fibroblasts. We found that non-volar keratinocytes expressed KRT9 when co-cultured with volar fibroblasts, PAX-9 transfected non-volar fibroblasts and LMX1b knockdown volar fibroblasts. Our study indicates epidermal keratinocyte KRT9 regulation by signals from dermal fibroblasts, which suggests the possibility of treating stump site dermatosis with genetically modified volar fibroblasts.

Adela Wu, MS2 Mentor: Alfredo Quinones, MD

Basic Science

In vivo study assessing the migratory capacity of mesenchymal stem cells

Background: Glioblastoma (GBM) is the most common, recurrent, and invasive type of primary brain cancer in adults. Stem cell therapy is an attractive treatment option, since mesenchymal stem cells (MSCs) from bone marrow and adipose tissue can target and migrate towards GBM cells. This tropism to cancer cells suggests that modification of MSCs to deliver anti-cancer particles to cancer cells may be a potential therapy. A limitation to their use, however, is low efficiency of MSC localization to the brain when administered systematically. We proposed that human adipose-derived MSCs (hAMSCs) administered via intrathecal and intranasal routes would be viable, exhibit glioma cell tropism, and exhibit superior homing to the site of tumor.

Methods: An in vivo study to examine the migratory capacity of MSCs to the cranial region via four different routes of administration (intranasal, tail vein, intrathecal, and cardiac) was performed. Luciferase-labeled hAMSCs were administered on day 0 via the four routes of administration. Each administration group included five mice, which were monitored for whole-body and intracranial fluorescence signal of delivered MSCs over five days. A non-parametric one-way ANOVA test was performed across the different routes of administration, followed by a Dunn's Multiple Comparison test to assess the p-values for individual pairs within each group to measure significance across time.

Results: We found that the intranasal ($p=0.02$) and intrathecal ($p=0.005$) administration routes had significantly greater cranial flux signal compared to other routes. Furthermore, there was a significant increase in signal over time (from day=0 to day=3) within the nasal administration group.

Conclusion: This in vivo study assesses that intranasal and intrathecal administration routes potentially demonstrate the greatest delivery efficacy in the context of developing stem cell therapy for aggressive brain cancer.

CLINICAL RESEARCH POSTER ABSTRACTS

Listed Alphabetically

Nathaniel Bales, MS3 Mentor: Anne Murphy, MD

Clinical Research

Retrospective Chart Review for Comparison of Broad Panel and Specific Genetic Testing in Children with Inherited Hypertrophic Cardiomyopathy

Hypertrophic cardiomyopathy (HCM) is a genetic disease of the sarcomere that can be found in both children and adults, and is characterized by thickening of heart muscle. There are many mutations associated with HCM, and genetic testing is often employed in HCM patients and their families. In children who are not the index case of HCM in their families, current recommendations call for genetic testing of only those genes that have been identified as mutated in family members. Although not characterized extensively, clinical experience suggests that de-novo mutations of HCM-related genes in children are possible, as are undiscovered mutations derived from untested parents.

To determine if younger HCM patients with family histories of HCM should receive broad-panel genetic testing, or testing limited to only familial mutations, a chart review was conducted of all patients who received HCM genetic testing at JHH between 2006-2013. In total, 242 patient charts were analyzed for presence of HCM, age at diagnosis, family history of cardiovascular disease, personal and familial genetic findings, and echocardiogram results.

A total of 81 patients with sarcomere gene mutations were identified. The remainder of patients did not have a mutation identified, or had mutations in genes not related to the sarcomere. Of the 81 patients with mutations, 66 had a clinical diagnosis of HCM. Importantly, 8 patients had >1 pathogenic or likely-pathogenic mutation, including 6 patients who were diagnosed with HCM as children. In this analysis, the likelihood of a child with HCM having more than one mutation is 25% (6/24).

The large number of children with multiple mutations suggests that broad-panel rather than targeted genetic testing is warranted in children with HCM even if they are not the index case. Identification of all genetic contributors to HCM may play an important role in individual and family management of HCM.

Jarred Bressner, MS2 Mentor: Paul Sponseller, MD MBA

Clinical Research

Orthopaedic management of the spine in patients with Loeys Dietz Syndrome

Background: Loeys Dietz Syndrome (LDS) is a newly defined genetic connective tissue disorder. We sought to determine the incidence of scoliosis in LDS patients and investigate the potential of bracing and surgery in their spinal management.

Methods: Patients were selected from the Johns Hopkins Hospital LDS database. For the bracing study, inclusion criteria were definitive diagnosis of LDS, Risser 0, 1, or 2, one year minimum follow up time, and recommended wear of at least 18 hours per day. Outcome endpoints were skeletal maturity, surgery, or study completion. Success was determined by curve progression of less than 5 degrees. 19 patients met the inclusion criteria, (13 female, 6 male).

For the surgery study, the pre-operative and post-operative spine was characterized, and intra-operative, post-operative, and hardware complications were recorded. A total of 19 patients met the inclusion criteria, (11 female, 8 male).

Results: 62% of LDS patients met criteria for scoliosis (88 of 141). Mean age at commencement of bracing was 9±3 years. Mean pre-bracing cobb measurements were 21°±12 (among PT, MT, and TL/L). Post-bracing mean cobb measurements were 34°±22 with mean changes of 12°±21 . Mean rates of progression were 5°±9 per year. There was no significant difference between the ages of successfully braced patients versus unsuccessfully braced patients ($p=0.85$). Additionally, there was no significant difference among pre-braced cobb angles when comparing patients who were successful to those who were not ($p=0.42$ and $p=0.15$ for MT and TL/L respectively). Surgical outcomes were notable for increased blood loss and greater propensity for hardware failure ($p<0.05$ for both).

Conclusion: Bracing was considered a failure in 70% of patients. At present, 50% of the study population has required surgery despite bracing attempts. Surgery remains a viable option, however, LDS patients are at increased risk for hardware failure and demonstrate increased intraoperative blood loss.

Nicholas Calotta, MS2 Mentor: E Gene Deune, MD, MBA

Clinical Research

Severe Carpal Tunnel Syndrome: Does Endoscopic Release Compare Favorably to Open Release for these Patients?

Background: Diagnosis of carpal tunnel syndrome (CTS) involves electrodiagnostic evaluation (electromyography/nerve conduction study). Test results include a disease grading from 'mild' to 'severe'. Treatment is subsequently influenced by this grading. In patients with 'severe' CTS, surgery is recommended; open carpal tunnel release (OCTR) is employed more often than endoscopic release (ECTR), partly due to previous anatomic studies. However, the effectiveness of ECTR has never been studied in this patient population. Here we present the first series of patients with severe CTS and aim to demonstrate the appropriateness and effectiveness of ECTR.

Methods: We conducted a retrospective, cohort study of CTS cases. Patients with severe CTS were grouped according to surgical procedure (ECTR vs. OCTR). An additional cohort was comprised of patients with non-severe CTS receiving ECTR. Our primary outcome variable was patient report of complete resolution of pre-operative CTS symptoms at latest follow-up. Groups were compared using Chi-square tests.

Results: 306 cases of CTS were studied. Patients with severe CTS receiving ECTR (n = 39) were comparable to patients receiving OCTR (n = 99) in terms of sex, diabetes and smoking. These patients showed a higher rate of complete symptomatic resolution following ECTR (81.6%) compared to OCTR (39%; $p < 0.001$). Among patients receiving ECTR, those with severe CTS had complete resolution at a higher rate compared to those with non-severe CTS (n = 168, 60.0%; $p = 0.013$). Mean follow-up was 10.7 months.

Conclusion: This study provides encouraging data to suggest ECTR compares favorably to OCTR and is appropriate for patients with severe CTS. As this is retrospective data, further investigation is needed in a randomized population. With this, ECTR could become more widely considered for severe CTS treatment.

Sophia Chen, MS2 Mentor: Anne Lidor, MD

Clinical Research

Assessment of Post-Discharge Complications after Bariatric Surgery: a NSQIP Analysis

Background: Little is reported about post-discharge complications (PDC) following bariatric surgery. We sought to identify the rates of PDC, associated risk factors, and their influence on early hospital readmission.

Methods: Using American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database (2005-2013), patients ≥ 18 years of age who underwent bariatric surgery with a primary diagnosis of morbid/severe obesity and BMI ≥ 35 were identified. PDC was the primary outcome, defined as an event for which the time interval from surgery to complication was greater than that from surgery to discharge. Hospital readmission was the secondary outcome. The association between PDC and various patient factors was explored using multivariable logistic regression.

Results: 113,898 patients were identified with the overall 3.18% 30-day PDC rate. PDC rates decreased significantly from 2005-6 (4.63%) to 2013 (2.99%) ($p < 0.001$). On average, PDC occurred 10 days post-operatively, with wound infection (49.43%), reoperation (30.72%), urinary tract infection (16.86%), shock/sepsis (12.38%), and organ space surgical site infection (11.03%) being the most common. Open gastric bypass [GBP] patients had the highest PDC rate (8.46%). 51.62% of patients who experienced PDC were readmitted. The factors most strongly associated with increased odds of PDC were: BMI ≥ 50 (AOR: 1.49, 95% CI: [1.34-1.66]), steroid use (1.44, [1.11-1.86]), procedure type (open GBP 4.50, [3.90-5.19]; laparoscopic GBP 2.19 [1.96-2.44]), pre-discharge complication (1.65, [1.36-2.00]), prolonged length of stay (1.74, [1.58-1.91]), and prolonged operative time (1.41, [1.31-1.51]).

Conclusion: Although the rate of PDC after bariatric surgery is low, it accounts for a significant number of readmissions. Given that most PDC are infection-related, adopting best practices for prevention of surgical site infection and catheter-associated urinary tract infection, and standardizing protocols for outpatient monitoring of patients identified to be at high risk of experiencing PDC, should be considered to optimize perioperative patient care and enhance surgical quality outcomes.

Chris Cottrell, MS2 Mentor: Kerry Stewart, EdD

Clinical Research

Effect of Smartphone App Usage on Adherence to 10,000 Steps Program

Background: Cardiovascular disease (CVD) is the leading cause of death for women in the United States. Obesity has contributed substantially to a rise in CVD risk and to the development of diabetes. In addition to caloric restriction, national health guidelines advise the reduction of total and abdominal obesity through increased physical activity. Communication technologies such as smartphones offer a potentially transformative approach for addressing common barriers to changing health behaviors by delivering convenient, individually tailored, and contextually meaningful behavioral interventions. However, rigorous clinical trials isolating the effect of technology modalities are limited. This study compared the effects of text messages versus multimedia messages in helping obese women adhere to the 10,000 steps walking program.

Methods: All subjects were be provided with a FitBit pedometer and a smartphone with the FitBit app installed for their use during the study. The two devices provided experimenters with an accurate measure of steps walked per day for each participant, and the smartphone allowed each participant to receive her daily message. Waist and hip circumferences, height, weight, and BP were measured before each participant began the three-month walking program, and again after they completed it. Participants were randomized to one of two groups: one group received daily text messages during the three-month walking period, while the other group received daily multimedia messages.

Results: Pending. Primary outcomes include number of steps walked per day and waist circumference reduction.

Conclusions: Due to funding limitations, this study did not have a control group. Also, many of the women were over 50 and were unfamiliar with smartphone technology. If this study was repeated, a control group would be included, a more user-friendly format for multimedia messages would be used, and all participants would be educated about smartphone use to ensure competence and increase compliance.

Kristin Darwin, MS2 Mentor: Geetanjali Chander, MD MPH

Clinical Research

Depressive symptoms are associated with poorer antiretroviral adherence and less viral suppression among hazardously drinking HIV-infected women

Background: We examined socio-demographic, substance use, and mental health correlates of antiretroviral therapy (ART) adherence and viral suppression among HIV-infected women with and without hazardous alcohol use.

Methods: We performed a secondary analysis of baseline, 6-month, and 12-month data collected from HIV-infected women receiving care in the Johns Hopkins HIV Clinic between 2006-2011. We defined hazardous alcohol use as >7 drinks/week or binge drinking in the last 90 days. Outcomes included ART adherence (defined as missing a dose of ART in the prior three days) and viral suppression (HIV1-RNA <400 copies/mL). We assessed anxiety and depressive symptoms using the Hospital Anxiety and Depression Scale (HADS). Other independent variables included age, race, housing status, marijuana, cocaine, and heroin use. Stratifying by hazardous alcohol use, we performed multivariable logistic regression using Generalized Estimating Equations to account for clustering.

Results: Of 385 women, 115 were hazardous drinkers at baseline. The median age of the sample was 46 and 86% were African American. Hazardous drinkers were more likely to use cocaine ($p<0.001$), marijuana ($p=0.002$), heroin ($p<0.001$), were less likely to have stable housing ($p=0.002$), and had higher anxiety ($p=0.003$) and depressive symptoms($p=0.003$). In multivariable analysis, depressive symptoms among hazardous drinkers were associated with higher odds of ART nonadherence (OR 1.18;$p=0.03$) and lower odds of viral suppression (OR 0.86;$p=0.05$). Hazardously drinking women with stable housing were more likely to have an undetectable viral load (OR 2.46;$p=0.04$). Among non-hazardous drinkers, cocaine (OR 0.53;$p=0.04$) and marijuana use(OR 0.64;$p=0.05$) were associated with decreased viral suppression. Other independent variables were not significantly associated with outcomes.

Conclusion: Among hazardously drinking HIV-infected women, depressive symptoms are associated with lower antiretroviral adherence and viral suppression. These findings underscore the importance of screening for depressive symptoms among hazardously drinking women. Recognition and treatment of these co-occurring conditions among HIV-infected women may improve outcomes.

Judy Doong, MS2 Mentor: Charles Limb, MD

Clinical Research

Impaired Recognition of Musical Sound Quality Deterioration in Cochlear Implant Users: Sample Rate and Comb-Filtering

Background: Music perception mediated by cochlear implant (CI) remains limited, with reductions in sound quality and impairments in timbre perception. In this study, the impact of sample rate and comb-filtering manipulations on sound quality were quantified for CI users and normal hearing (NH) subjects.

Methods: Seven CI users and ten NH controls were enrolled for sound quality perception evaluation. Sound quality was measured using Cochlear Implant-Multiple Stimulus with Hidden Reference and Anchor (CI-MUSHRA), a sound quality assessment method. Two sets of test stimuli from real-world musical stimuli were created by manipulating sample rate and comb-filtering separately. Sample rate modifications were created with six different sample rates from a reference stimulus. Comb filtering manipulations attenuated a set of harmonically-related frequencies and six different versions were created from a reference stimulus. A total of seven versions, including reference, were presented to the listener for a given musical stimulus. Listeners rated stimuli from 0 to 100 based on sound quality differences perceived between stimuli versions. Twenty-five musical stimuli (5s duration) were presented for both sample rate and comb-filtering manipulations.

Results: Compared to NH subjects, CI users were generally worse at differentiating sound qualities between stimuli based on sample rate and comb-filtering. NH listeners could differentiate between all of the stimuli versions (all pairwise comparison yielded $p<0.01$), while CI users could not. Specifically, for sample rate, CI-users could not differentiate between five of the seven versions (p-value>0.05 for pairwise comparison between adjacent stimuli versions). For comb-filtering, CI users could not differentiate between four of the seven versions (p-value>0.05 for pairwise comparison between adjacent stimuli versions).

Conclusion: CI users have impaired ability to detect sound quality deterioration based on sample rate and comb-filtering manipulations. These factors should be considered when developing CI sound-processing strategies directed towards improving CI-mediated music perception.

Ankur Doshi, MS2 Mentor: Rachel Salas, MD

Clinical Research

Implementing a Clinical iPad Application to Detect Sleep Disorders is Feasible Across Multiple Non-Sleep Outpatient Clinics

Background: Despite the prevalence of sleep disorders and chronic sleep deprivation, up to 70 million Americans remain undiagnosed, misdiagnosed, or untreated due to low awareness among the general population and limited sleep medicine exposure for healthcare providers. To address this issue, we sought to develop a mobile health sleep-screening tool and test its feasibility in outpatient clinics.

Methods: MySleepScript is a clinical iPad App developed to allow providers to screen for sleep disorders in their patients. MySleepScript uses standardized sleep questionnaires to calculate a "level of concern" and provide suggested referrals. Using satisfaction surveys, we sought to determine the feasibility of implementing MySleepScript into clinics.

The app was conducted in 5 Johns Hopkins outpatient clinics (Urology, Neuroinfectious Disease, Transverse Myelitis, Headache, Multiple Sclerosis) from 07/2014-11/2014. Patients were asked to answer questions on the app regarding sleep habits, behaviors, and environment during intake. Directions were provided within the app. Upon completion, the PSQI and "level of concern" were explained to the patient and forwarded to the provider. Patients were then asked to complete satisfaction surveys. Descriptive statistics were used to analyze the satisfaction surveys.

Results: Of 46 patients enrolled, 71% were men, 58% Caucasian, and 80% were follow-up. 61% completed the app within 15 minutes (82% within 20 minutes). Positive results were collapsed based on responses of strongly agree or agree. 92% of patients found the app easy to use, 79% preferred the app platform to paper, 75% felt the app enhanced communication regarding sleep, and 79% found the output to be helpful. 87% of patients recommend that their provider continue using the app. No difference was found among clinics with respect to time or satisfaction.

Conclusion: This pilot demonstrates the utility and feasibility of a mobile health sleep-screening tool conducted across a diverse patient population with uniform demonstration of increased overall patient satisfaction.

Megan Gornet, MS2 Mentor: Lawrence Lenke, MD

Clinical Research

Does Size Matter? A Comparison of Preoperative MRI in Adolescent Idiopathic Scoliosis (AIS) Patients With Curves <80 vs ≥80°

Background: Preoperative MRI in AIS patients may be performed to evaluate for neuroaxis abnormalities, as these may be risk-factors for neurological injury during surgery. While some institutional policies require preoperative MRI in all AIS patients regardless of curve size, the necessity of routine preoperative MRI in AIS patients is still controversial.

Methods: A surgical cohort of adult and pediatric deformity patients from two institutions treated with spinal fusion and instrumentation surgery was established. Two patient groups based on curve size (< or ≥80°), as evaluated by spine radiograph measurements, were compared on MRI screening rates and presence of abnormalities (syringomyelia, Chiari malformation, tumors, tethered cords, and perineurial cysts) detected by MRI screening. In multivariate logistic regression, we also evaluated whether MRI screening was associated with clinical factors including age, gender, and atypical curve types.

Results: 559 AIS patients were evaluated with 83% female, mean age=15 years. The presence of MRI abnormalities was similar in patients with large curves (16.7%) compared to small curves (15.4%; p=0.8). Adjusting for clinical factors confirmed that large curve size does not increase odds of MRI abnormality (OR [95%CI]: 1.07 [0.45-2.59]; p=0.8). Still, physicians were 2.2 times more likely to obtain an MRI with larger curves (82.8%) compared to smaller curves (37.5%) (OR [95%CI]: 7.6 [3.7-15.6]; p<0.0001).

Conclusion: We did not find a higher incidence of neuroaxis abnormalities on preoperative MRI in AIS patients with large curves, although surgeons more often obtained MRI in large curve patients. These findings suggest that the decision whether or not to perform preoperative MRI screening in AIS patients should be made irrespective of curve size, which has potential implications for cost-saving practices among orthopedic surgeons treating AIS. Further studies will evaluate outcomes in practices that require preoperative MRI versus those that allow elective preoperative MRI.

Alexis Graham, MS2 Mentor: Marie Thearle, MD

Clinical Research

Increasing Protein Intake during Overfeeding Increases Energy Expenditure, Satiety, and Urinary Cortisol

Background: Dietary macronutrient composition may augment individual variation in the energy expenditure (EE) response to caloric intake above energy needs contributing to differences in adiposity.

Methods: Sixty subjects with normal glucose regulation had measures of 24hr EE and macronutrient oxidation in a whole room indirect calorimeter during energy balance and 5 different 24hr overfeeding (OF) diets with macronutrient compositions of 26C/44F/30P (%Carbohydrate/%Fat/%Protein); 50C/30F/20P; 75C/5F/20P; 20C/60F/20P; 51C/46F/3P, randomly administered with 3-day washout periods in between diets, and providing 200% of energy needs. Urinary cortisol was determined with each diet, and a visual analogue scale determining hunger sensations was given after each diet.

Results: Compared to energy balance, EE increased with OF (9.8±7.2%; p=<.0001; 2-way ANOVA). Protein content explained 38% of the variance between low (3%), normal (20%), and high (30%) protein OF diets with increases in EE of 3.1±6.6%, 10.4±6.0%, and 14.4±7.2%, p<0.0001, respectively. When protein content was held constant at 20%, increase in EE was highest with the high carbohydrate (75%) diet compared to the high fat (60%) diet (14.3±6.0%, 7.9±8.0%, respectively; p<.0001). There was no difference in %increase in EE between the high protein and high carbohydrate diets (p=0.9). Protein oxidation positively associated with urine cortisol (ρ=0.34, p<.0001), even after adjusting for age, sex, race, diet and body composition but negatively with hunger scores (ρ=-0.26, p=0.03). The individual EE increase averaged over all 5 OF diets was negatively associated with %fat (ρ=-0.34; p=0.003), even after adjusting for age, sex, race, and diet.

Conclusion: When overeating, macronutrient composition of calories consumed influences the EE response. Although overconsumption of protein leads to increased EE and satiety, it also increases cortisol production. This increase in cortisol may be due to the increased demands of the body to process protein, a macronutrient for which it has minimal storage capacity compared to carbohydrates and fat.

Alice He, MS2 Mentor: Charles Limb, MD

Clinical Research

Cochlear Implant Users Require Exaggerated Pitch Contours to Identify Mandarin Tones

Background: Cochlear implant users (CIs) demonstrate significant impairment in pitch perception. This is particularly evident in tonal languages, such as Mandarin Chinese, in which meanings of words are encoded by pitch contours. We used exaggerated tone contours to determine the minimum pitch range needed for normal hearing listeners (NHLs) and CIs to discriminate among Mandarin tones.

Methods: To test participants' abilities to discriminate tone contours in both controlled and realistic settings, we created two series of sound stimuli. Pure tones modeled after the four Mandarin tones (flat, rising, dipping, and falling) were created using Praat software, and speech tokens of the four tones were voice-recorded by native Mandarin speakers. We then increased and decreased the pitch range of both pure tones and speech tokens to produce varying pitch contours. Nine NHLs and 8 CI participants were presented with the sound stimuli through loudspeaker in an acoustically treated sound booth and were asked to identify via touchscreen the tone that best represented the sound heard. The pitch range was adaptively decreased until participants could no longer consistently identify tones with >70% accuracy.

Results: With pure tones, CIs required a significantly higher pitch range to attain >70% accurate tone discrimination as compared to NHLs (CI=41.72Hz, SD=31.1; NHL=3.98Hz, SD=1.6; $p<0.001$). With speech tokens, CIs required a 59.58Hz range (SD=44.3), which is also significantly higher than the required range for NHLs (5.06Hz, SD=9.0; $p<0.001$). NHLs performed significantly better at pure tone identification ($p<0.05$), while CI performance did not vary between pure tone and speech token identification ($p>0.05$).

Conclusion: Compared to NHLs, CIs required significantly greater pitch ranges to identify pitch contours modeled after Mandarin tones. Our study was limited by the lack of Mandarin-speaking CI users available for testing. Future studies should investigate methods to integrate exaggerated pitch contours into CI technology to improve tonal language perception.

Alice Hung, MS2 Mentor: Judy Huang, MD

Clinical Research

Differences in Functional Outcome Across Subtypes within Spetzler-Martin Grade II Arteriovenous Malformations (AVMs)

Background: The Spetzler-Martin grading system for brain arteriovenous malformations(AVMs) is widely utilized to characterize and predict outcomes after AVM treatment with different modalities, despite its original intention for surgical prognostication only. AVMs are graded by size(S), eloquence(E) and deep drainage(V). Grades II-IV include heterogeneous lesion subtypes, thereby limiting the predictive value for functional outcome when using this grading system. While previous studies have demonstrated heterogeneity of outcomes within grade III AVMs, no studies have focused on grade II AVM subtypes. We aim to delineate how functional outcomes differ among these subtypes.

Methods: We retrospectively reviewed patients with AVMs at the Johns Hopkins Medical Institutions between 01/1990 and 07/2013. Grade II AVMs were divided into 3 subtypes: group 1(S2V0E0), group 2(S1V0E1), and group 3(S1V1E0). Baseline characteristics were compared across subtypes. Functional status was assessed using the modified Rankin Scale(mRS) for pre-treatment and last follow-up. Differences in mRS between the two time-points were compared.

Results: A total of 165 grade II patients(28.8%) were retrieved from 572 graded patients. After accounting for missing data, our cohort consisted of 128 patients(77.6%). Mean age of all patients was 39.5 years, with 61 male patients(47.7%). Fifty-four patients presented with hemorrhage(42.2%). No significant difference between subtypes was observed for pre-treatment mRS(p=0.163), treatment modalities(p=0.943), and follow-up durations(p=0.148). No significant difference in mean mRS at last follow-up was observed across subtypes(mean=1.38, p=0.484). A significant difference in proportion of patients with worsening mRS was observed between groups 1 and 3(p=0.032). Changes in mRS for surgically treated patients demonstrated a similar trend between groups 1 and 3(p=0.081).

Conclusion: Subtypes of grade II AVMs portend different gains in functional outcome after treatment. Group 1(S2V0E0) patients had the best functional outcome gain from treatment, while group 3(S1V1E0) patients has the worst performance. The modified Spetzler-Martin grade is useful in further stratifying treatment risks within grade II AVMs.

Dvone Jackson, MS2 Mentor: Danny Song, MD

Clinical Research

The Feasibility of Radiation Dose De-Escalation for the Treatment of Very-Low Risk Prostate Carcinoma

Background: Several randomized controlled trials examining dose-escalated (≥78 Gy) radiotherapy (RT) for men with localized prostate cancer have shown improvement in biochemical endpoints but the effect on metastasis-free (MFS) and prostate-cancer specific survival (PCSS) is less clear. Additionally, higher-dose RT likely exposes patients to an increased risk of gastrointestinal (GI) and/or genitourinary (GU) toxicity. Whether patients with pretreatment prognostic factors that place them at very-low risk for failure following treatment derive benefit from dose-escalated RT is unclear. To better answer this question, we evaluated our experience with conventional dose RT (median = 73.8 Gy) for men with NCCN-defined very-low risk prostate cancer.

Methods: We completed a chart review of 890 men treated with RT at JHH between 01/92 and 12/06. Of these, 57 men met NCCN very-low risk criteria. We performed Kaplan-Meier analysis for the following endpoints: BFFS (Phoenix criteria), MFS and PCSS. Further, to assess for a dose-threshold effect, we stratified within the very-low risk cohort at 72 Gy and performed Cox regression analysis to compare survival outcomes across dose strata.

Results: In aggregate, the very-low risk 5-year BFFS was 95.2%. We could not find a significant difference in the BFFS between those receiving ≤72 Gy or >72 Gy (HR = 0.38, 95% CI = 0.07 – 2.07). MFS and PCSS were 100% at 5 and 10 years, irrespective of RT dose.

Conclusion: 5-year BFFS was 95.2% for the very-low risk cohort, with no metastasis or prostate cancer associated deaths at 10 years. We were not able to detect a dose threshold effect for any of the endpoints. For those very-low risk patients who undergo RT, prospective evaluation of de-escalated dose should be explored.

Nicole Jiam, MS3 Mentor: Charles Limb, MD

Clinical Research

Feasibility of Flat-Panel CT Imaging for Individualized Pitch Mapping in Cochlear Implant Users

For the past 50 years, advances in cochlear implant technology capitalized on the tonotopic organization of the auditory system, particularly with respect to the cochlea. Greenwood's function has been used to describe the place-pitch frequency map of the cochlea, and theoretically describes an ideal logarithmic relationship between spatial location along the Organ of Corti and neural frequency response. Despite this relationship, cochlear implant users demonstrate significant impairments in pitch perception. Part of this difficulty may be attributed to the fact that implant insertions are performed blindly, and that frequency mapping takes place without incorporating the actual physical location of each electrode within the cochlea for each individual patient. Instead, a standard default map is typically applied to the frequency allocation for CI users, which does not account for the individual variability in cochlear lengths, electrode bending or kinking within the cochlea, or altered distances from the spiral ganglion neurons. Flat-panel CT imaging is a new imaging tool that provides high-quality images and improved spatial resolution. In this study, we used post-operative FPCT imaging to analyze the individual variability in electrode contact placement and frequency mapping. We reported on 5 patients with 7 cochlear implants (Med-El standard 31.5mm arrays) who underwent FPCT imaging in 2013. Using DICOM image processing software and 3D curved planar reformation, we calculated theoretical frequencies based on each electrode contact location and compared those values to their actual maps. Our analysis revealed that individual FPCT information may allow improvements in CI mapping for preservation of pitch information for 75% (57/76) of the electrode contacts. The basilar electrodes rendered the greatest variance from the theoretical values, with a maximum of 12,000 Hz difference from expected value. To our knowledge, this is the first study that demonstrates the mathematical discrepancy between theoretical and actual cochlear implant placement with respect to pitch mapping.

Sarah Joo, MS2 Mentor: Meredith Atkinson, MD

Clinical Research

Hepcidin as a Mediator of Cardiovascular Risk in Children with Systemic Lupus Erythematosus and Lupus Nephritis

Background: Up to 80% of children with systemic lupus erythematosus (SLE) develop kidney disease, which is associated with increased risk for anemia, cardiovascular disease, and death. Hepcidin, an iron-regulatory protein, may contribute to lupus co-morbidities including anemia and atherosclerosis. This study measures hepcidin and quantifies if levels are associated with complications including arterial stiffness in children with SLE. It evaluates if subjects with lupus nephritis (LN) have higher levels and evidence of arterial stiffness compared to those without LN.

Methods: Cross-sectional analysis with hepcidin was measured via ELISA in 12 children with SLE, recruited from the pediatric rheumatology clinic at the Johns Hopkins Children's Center. Arterial stiffness was quantified with carotid-femoral pulse wave velocity (PWV). Anemia was defined by WHO criteria (Hgb <11.5 g/dL in 2-11-year-olds, <12 in >12-year-olds). Pearson chi2 or paired t-testing was used for comparison of proportions or means, and linear regression (LR) for association between hepcidin and complications.

Results: The cohort was 100% female and 75% black with mean (SD) age of 14.8 (3.7) years. 42% (n=5) had a biopsy-proven diagnosis of LN. There were no significant differences in race, age, or % anemic between those with and without LN. Overall mean (SD) hepcidin was 65.3 (50.3) ng/mL. In univariate LR, hepcidin was significantly positively associated with diastolic BP only (p=0.04). Patients with LN demonstrated a non-significantly higher hepcidin level than those without nephritis (87.4 vs. 49.6 ng/mL, p=0.21). A non-significant trend towards higher BP and PWV was also noted in those with LN.

Conclusion: Hepcidin levels are positively associated with diastolic BP in children with SLE. Non-significant increases in hepcidin, BP, and PWV were noted in subjects with LN. Significance is limited by sample size, and a goal of ongoing recruitment is to increase power to observe the association between hepcidin and arterial stiffness and modifiers of this association.

Maria Kryatova, MS2 Mentor: Bernard Cohen, MD

Clinical Research

Nasal Infantile Hemangiomas: Characteristics, Complications, and Outcomes

Background: Fifty percent of infantile hemangiomas (IH) – the most common benign infantile tumor – arise on the head and neck. While nasal IH pose unique complications – airway compromise and later psychosocial stress if the resolution is incomplete or a lengthy process – they are understudied. We aim to characterize nasal lesions by type, depth, and location and determine which characteristics are associated with complications and are predictive of outcome, specifically with respect to presence of IH or residua at the start of kindergarten.

Methods: We performed a retrospective chart review of all patients seen by Pediatric Dermatology at JHH between 2001 and 2014 for nasal IH (N=89). A telephone interview was also conducted. SPSS Statistics 22 was used to analyze the data using Fisher's Exact Test.

Results: The telephone survey had a 71% response rate. Most IH were focal lesions (87%), of mixed depth (58%), and were located on the nasal tip (58%). Most patients had at least one treatment type (80%). By the start of kindergarten, IH had resolved in 70%, but 78% of these children still had residua (telangiectasia, fibrofatty mass, or scarring). Segmental and indeterminate IH were more likely to have complications ($p=0.014$) and received more treatment types ($p=0.025$) than focal lesions. Mixed IH were more likely to ulcerate than deep or superficial lesions ($p=0.011$). Mixed and deep IH received more treatment types than superficial IH ($p=0.022$), but were more likely to be present at kindergarten ($p=0.064$). Of those IH that resolved, mixed and superficial left more residua than deep ($p=0.040$).

Conclusion: IH of segmental and indeterminate type and IH of mixed depth have the most complicated clinical course; these lesions should be identified as high risk and monitored and treated accordingly. Since most nasal IH resolve by kindergarten, parents may be appropriately reassured.

Ishaq Lachin, MS2 Mentor: Christopher Wu

Clinical Research

Alternative Medical Practices in Post-Operative Pain Management

Background: As healthcare costs rise and patients seek alternatives to traditional medications, new interventions continue to be explored for the management of post-operative pain. We conducted a systematic review of the literature surrounding post-operative pain management using alternative practices.

Methods: We identified randomized control trials with dates of inclusion up to 11/2013 that measured pain scores in adults and had a clearly defined intervention vs control. We evaluated the quality of the articles (Cochrane and Jadad scores), region of surgery, patients' age, mode of intervention, and visual analog scores (or equivalent) for intervention and control. Secondary outcome of anxiety reduction was also extracted. Data was grouped based on mode of intervention and compared based on reduction in pain scores.

Results: We identified 13 acupuncture (including electric) articles, 15 music articles, 9 massage articles, 7 relaxation articles, and 16 miscellaneous articles. Acupuncture had 8/13 (61.5%) articles showing statistically significant reduction in pain, particularly on the first day, or after the fourth day. 13/15 (86.7%) music articles demonstrated significant reduction in pain, which was most effective within the first few hours. 5/7 (71.4%) music articles also showed significance in reducing anxiety, particularly within the first few hours. 8/9 (88.9%) massage intervention articles showed a significant reduction in pain in the days (>2) after intervention was started, but not immediately so. Relaxation exercises had significant reduction in pain in 4/7 (57%), but only immediately after intervention.

Conclusion: This systematic review demonstrated that complimentary therapies can reduce pain after surgery, and future studies should explore whether multiple modalities can be used together to reduce pain in different time frames in the post-surgical period.

Katherine Levandoski, MS2 Mentor: Annie Grossberg, MD

Clinical Research

Favorable Long-Term Outcomes in Pediatric Patients with Atypical Spitz Tumors Treated with Wide Excision

Background: Atypical Spitz tumors (ASTs) are melanocytic lesions of uncertain malignant potential. While treatment generally involves wide excision with clear margins, AST may also be treated aggressively with sentinel lymph node biopsy (SLNB) and completion lymphadenectomy. A shortage of data on rates of recurrence in pediatric patients treated with wide excision contributes to uncertainty regarding management of ASTs.

Methods: We surveyed the Johns Hopkins Department of Pathology's database to identify pediatric patients who were diagnosed with AST and treated with wide excision between 2001 and 2012. Medical records were reviewed to collect data on demographics, lesion location and features, pathology, treatment, and follow up. After obtaining consent from the patient or legal guardian, a survey was administered to obtain additional information regarding family history of skin cancer, frequency of follow-up care with a dermatologist, and clinical outcomes, including treatment complications, recurrence, and development of new dermatologic or medical conditions.

Results: Twenty-seven patients (63.0% female) were included in this study. Mean age at excision was 10.0 ± 4.9 years (range 3.9 – 18.2). Mean follow up time was 4.6 years (range 1.1 – 9.3 years). There were no reports of recurrence, new AST, or metastases.

Conclusion: We report one of the largest series of pediatric patients with AST treated using wide excision. All remain free of recurrence after a significant follow-up period. Our data suggest that wide excision with clear margins may be sufficient in the routine management of pediatric AST, and that more aggressive procedures, such as SLNB and subsequent completion lymphadenectomy, may not be not warranted.

Jacob Light, MS2 Mentor: James Handa, MD

Clinical Research

Novel Subretinal Findings in Stargardt Disease Using Spectral Domain-Optical Coherence Tomography (SD-OCT)

Background: Stargardt disease (SD) is the leading cause of inherited macular dystrophy with progression into adulthood. Retinal pigment epithelium (RPE)/photoreceptor atrophy and subretinal flecks are classic signs. Using SD-OCT, we examined the subretinal space of SD patients in areas devoid of atrophy or flecks to elucidate changes that may precede these classic findings.

Methods: Patients with an ICD9 code for SD with SD-OCT imaging from 2009 to 2014 were identified. Patients with retinal comorbidities or macular atrophy involving the entire OCT scan area were excluded. Unaffected eyes of age-matched controls were used for comparison. The largest of 5 measurements in unaffected areas in each OCT scan line, taken at 500µm intervals across the macula, was used to determine subretinal space thickness (Bruch's membrane to ellipsoid line). Two-way repeated measures ANOVA was used to analyze differences in subretinal thickness between SD patients and controls. An intraclass correlation was calculated using repeated measurements in 10 randomly-selected eyes. Additionally, two independent observers scored the appearance of the apical process interdigitation line in patients and controls. The chi-square test was utilized to compare the rates of abnormal scores between groups, and the Kappa statistic was employed to assess inter-rater reliability.

Results: Thirty-eight patients (mean age 35.7) and 26 controls (34.1) were identified. Patients showed subretinal thickening relative to controls at 1500, 2000, and 2500µm superior and inferior to the fovea ($p<0.05$). The intraclass correlation was 0.88 ($p<0.0001$). An abnormal interdigitation line (indistinct/interrupted) was noted in 89.3% of patients compared to 23.1% of controls ($p<0.0005$), and the Kappa statistic was 0.89 ($p<0.0001$).

Conclusion: Patients with Stargardt disease show changes in subretinal thickness and morphology on SD-OCT relative to controls in macular regions without atrophy or subretinal flecks. These findings may serve as useful metrics for future prospective studies or early clinical disease detection.

Melanie Major, MS2 Mentor: Gedge Rosson, MD

Clinical Research

The Effect of Timing on Breast Reconstruction Outcomes in Diabetic Women: A Comparison of NSQIP and Johns Hopkins Patient Data

Background: We sought to determine the effect of timing (immediate versus delayed) on post-operative morbidity in diabetic women undergoing breast reconstruction following mastectomy.

Methods: We reviewed the National Surgical Quality Improvement Program (NSQIP) databases from 2005-2012 for all diabetic women undergoing breast reconstruction. Univariable and multivariable logistic regression was used to estimate the risk of 30-day complications in the immediate versus delayed reconstruction groups. Additionally, we retrospectively reviewed Johns Hopkins Hospital (JHH) diabetic patients undergoing breast reconstruction from 2005-2014. We used Fischer's exact test to estimate the association of reconstruction timing with both 60-day and long-term complications.

Results: In NSQIP, 1,408 diabetic women underwent breast reconstruction: 958 (68%) immediate and 450 (32%) delayed. In the immediate group, 11% of patients developed a 30-day post-operative complication compared to 8% of patients in the delayed group (p=0.08). On multivariable analysis, the odds of developing 30-day complications were significantly higher for the immediate group compared to the delayed group (OR [95%CI]: 1.68 [1.04-2.72], p=0.03). This association persisted for 30-day surgical morbidity (OR [95%CI]: 1.75 [1.06-2.90]; p=0.03) but not for 30-day medical morbidity (p=0.9).

In the JHH cohort, 117 reconstructions were performed in 52 diabetic women: 60 (51%) immediate and 57 (49%) delayed. Among immediate reconstructions, 30% developed 60-day complications compared to 11% of delayed reconstructions (p=0.01). In long-term follow-up (median 9 months, range 0.5 – 94), 35% of immediate reconstructions developed a complication versus 12% of delayed reconstructions (p=0.005). Deep incisional surgical site infections, reconstruction failures, and seromas were notably increased in the immediate group (p<0.01 for all).

Conclusion: Among diabetics seeking breast reconstruction, delaying the reconstructive surgery from the mastectomy may optimize outcomes by decreasing postoperative morbidity. It also appears the 30-day postoperative time point available in NSQIP does not fully reflect the magnitude of the long-term complications these diabetic patients will develop seen in local experience.

Madeleine G. Manka, MS2 Mentor: E. James Wright, MD

Clinical Research

Does Use of a Second Cuff Improve Artificial Sphincter Effectiveness? Evaluation Using a Comparative Cadaver Model

Background: The artificial urinary sphincter (AUS) is recognized as the most effective long-term solution for men with severe stress incontinence. It is widely believed that inserting a second urethral cuff is more efficacious, but this supposition is backed by little empirical evidence. In this study, we directly compare the functionality of a single versus tandem cuff in a cadaver model.

Methods: The AUS was inserted into 4 cadavers using standard clinical techniques. The bulbar urethra was dissected using a perineal approach. Distal and proximal bulbar urethral circumference was measured. The membranous urethra was transected. 4.5cm cuffs were placed in the distal and proximal positions and connected to the pressure reservoir and control pump. Retrograde leak point pressure (RLPP) was measured sequentially across the distal cuff, proximal cuff, and two tandem cuffs by inserting a catheter and raising the attached bag of fluid until leakage was seen across the transected urethra (cm H2O). A Friedman test was used to compare RLPP between the three cuff configurations, a paired t test to compare distal and proximal urethral circumference, and a Pearson correlation to compare urethral circumference to RLPP.

Results: Mean RLPP across the distal, proximal and tandem cuffs was 70.25, 77.75, and 76.75 cm H2O respectively ($p=0.14$). Mean urethral circumference of the distal and proximal bulbar urethra was 4.78 and 5.83 cm respectively ($p =0.019$). There was a strong positive correlation between urethral circumference and RLPP ($r = 0.75$).

Conclusion: The tandem cuff does not appear to improve leak point pressure. In addition, the proximal bulbar urethral circumference was significantly greater than the distal circumference. Increasing urethral circumference was strongly correlated with increasing RLPP. Therefore, the perceived benefit of a second urethral cuff may reflect the function of the more proximal cuff alone. In our model, a tandem cuff did not increase effectiveness of the AUS.

Rouzbeh Mashayekhi, MS2 Mentor: Martha Zeiger, MD

Clinical Research

Does microRNA 146b-5p expression level predict central lymph node metastasis of papillary thyroid cancer?

Background: Papillary thyroid cancer (PTC) is the most common type of thyroid malignancy and central lymph node metastases (CLNM) have been associated with a worse prognosis. Currently there are no reliable preoperative factors that can predict CLNM. Many patients undergo prophylactic central lymph node dissection (CLND), which may be associated with increased morbidity. In this prospective study, we examined microRNA 146b-5p (known to be overexpressed in PTC) to determine its usefulness in predicting CLNM. Our hypothesis was that microRNA 146b-5p expression level in PTC tissue samples is associated with CLNM.

Methods: Two hundred fifty three PTCs from patients who underwent total thyroidectomy and CLND at Johns Hopkins, Mayo Clinic, Weill Cornell and University of Michigan were studied. The following clinicopathologic features: age, gender, tumor size, multifocality, CLNM, extrathyroidal extension (ETE), AJCC stage, lymphovascular invasion (LVI), and PTC subtypes were collected. RNA was extracted, the concentration assessed using Qubit Flourometer, and the expression level of microRNA 146b-5p was quantified with Reverse Transcriptase PCR and Quantitative PCR.

Results: On univariate analysis, factors correlating with CLNM in classical PTC included microRNA 146b-5p ($p<0.05$), tumor size >2 cm ($p<0.01$), tumor multifocality ($p<0.01$), LVI ($p<0.001$), positive surgical margins ($p<0.01$), and ETE ($p<0.001$). Multivariate analysis showed microRNA 146b-5p ($p<0.05$), tumor multifocality ($p<0.01$), LVI ($p<0.001$), and ETE ($p<0.01$) to be statistically significant predictors of CLNM. Multivariate analysis only for predictors available preoperatively (microRNA 146b-5p, gender, age, and tumor size) showed microRNA 146b-5p ($p<0.05$) and tumor size ($p<0.05$) to be statistically significant predictors of CLNM.

Conclusion: We conclude that microRNA 146b-5p expression level can predict CLNM in PTC. microRNA 146b-5p can potentially be a helpful prognostic tool to help surgeons make more informed pre-operative clinical decisions for patients with PTC and decide whether CLND would be a necessary part of the operation.

Russell Maxwell, MS2 Mentor: Michael Lim, MD

Clinical Research

A Retrospective Analysis of Progression to Brain Metastasis According to BRAF-V600 Mutational Status

Background: Brain metastasis (BM) is a common occurrence in patients with malignant melanoma and carries a poor prognosis. Melanoma has a high frequency of BRAF-V600 oncogene mutations, which have been shown to be associated with the uncontrolled proliferation, radioresistance, immune evasion, and disease progression in melanoma. However, the clinical relevance of BRAF-V600 mutational status in BM progression is not well understood.

Methods: We searched pathology, radiation oncology, and neurosurgical records at the Johns Hopkins Hospital (JHH) to identify 225 patients with diagnoses of melanoma whose BRAF status (BRAF-WT or BRAF-V600) had been classified. Patient demographic and clinicopathologic data were collected from the JHH cancer registry and electronic medical records. Primary outcome measures were the presence of BM and time to BM following initial melanoma diagnosis. We tested BRAF-V600 status as a predictor of BM and time to BM using univariate as well as multivariate modeling to account for known prognostic factors. Kaplan-Meier curves were constructed to summarize the impact of BRAF-V600 vs. BRAF-WT status on time to BM.

Results: Out of the 225 patients, 142 (63.1%) harbored a BRAF-V600 mutation and 83 (36.9%) were BRAF-WT. BRAF-V600 patients were found to have a younger age at diagnosis (P = 0.0021), a female predominance (P = 0.0037), a more advanced stage cancer (P = 0.023), and more lymph node involvement (P = 0.015). Compared to BRAF-WT patients, BRAF-V600 patients were discovered to have a greater odds of developing BM (unadjusted OR = 1.55; 95% CI = 0.75-3.20, P = 0.24), but this result did not reach statistical significance. Further results from univariate and multivariate are still pending. Time to BM results using Kaplan-Meier protocols are also still pending.

Conclusion: As our results presently suggest, BRAF-V600 mutational status appears to not increase the odds of BM in melanoma patients.

Jessica Moore, MS2 Mentor: Stephen Yang, MD

Clinical Research

Complex Esophageal Reconstruction Procedures Have Similar Outcomes to Routine Esophagectomy

Background: While most patients undergoing esophagectomy possess an undisturbed stomach for reconstruction, other patients have a history of major gastric procedures or other complicating factors. These cases require complex esophageal reconstruction (CER), defined as restoring esophageal continuity using a non-gastric conduit, in a previously operated field, and/or following esophageal diversion. This study compares the outcomes of CER versus non-CER (NCER), which uses an undisturbed stomach for reconstruction.

Methods: We performed a single-institution retrospective cohort study comparing 75 CER to 75 NCER patients from 1995-2014 matched for cancer versus benign disease. Distributions of demographic characteristics, comorbidities, and complications were compared between CER and NCER. Associations with complications and 30/90 day mortality were estimated using logistic regression. Overall survival (OS) was illustrated using Kaplan-Meier method and Cox proportional hazards regression.

Results: While patients were similar in age, sex, and pre-op comorbidities, more non-white patients underwent CER (p=0.04). Most NCER patients had adenocarcinoma (44%) or Barrett's high grade dysplasia (39%); CER patients had other benign disease (44%) or squamous cell carcinoma (24%; p<0.001). CER had higher rates of reoperation (29% vs. 11%, p=0.004), pneumonia (5% vs. 0%, p=0.04), systemic or surgical site infection (34% vs. 18%, p=0.02), and GI complications (25% vs. 11%, p=0.02) and a longer median length of stay (LOS, 18 vs. 9 days, p<0.001) than NCER. Mortality for CER and NCER at 30 days (1% vs. 1%, OR[95% CI] = 1.0[0.1-16.3]), 90 days (7% vs. 3%, OR[95% CI] = 2.6[0.49-13.9]; p=0.25) and overall (HR=1.56[0.89-2.74]; p=0.12) were similar.

Conclusion: Compared to NCER, CER patients had higher rates of return to the OR, more postoperative infections and GI complications, and longer LOS. However, 30-day, 90-day, and OS were similar. Therefore, CER should be offered to patients with acceptable risks and anticipated long-term survival and is a viable option despite its apparent complexity.

Ankur Narain, MS2 Mentor: Edward McFarland, MD

Clinical Research

Examination of Peri- and Post-operative Complications in Patients With Implantable Cardiac Devices After Total Shoulder Arthroplasty

Background: The presence of an implantable cardiac device, either a pacemaker or defibrillator, in a patient undergoing shoulder arthroplasty is of concern to the surgeon. Risks of this procedure include device disruption and peri- and post-operative complications in an at-risk population. The goals of this study were to evaluate the medical complications, surgical complications, and functional results of shoulder arthroplasty in patients with devices.

Methods: This is a retrospective cohort study derived from a population of 599 shoulder arthroplasties. All patients with devices who underwent shoulder arthroplasty and had minimum one-year follow up were evaluated. Medical records were reviewed for peri- or post-operative complications related to device presence. One-year post-operative clinical results were evaluated using shoulder outcome measures (VAS for pain and satisfaction, range of motion, ASES, WOOS and modified Constant score). Student's t-test was used to test differences between continuous variables. Chi squared test of association was used to test differences between categorical variables. Shapiro-Wilk test was used to check the normality assumption.

Results: There were 11 patients with devices who underwent 15 arthroplasties. There were 7 women and 4 men with an average age of 69.3 (range: 47-88) and follow-up average of 30 months (range 12-51). Of the 15 cases, 6 (40%) had devices ipsilateral to the surgical side. In that population, medical complications included tachycardia (1, 16.7%), bradycardia (1, 16.7%), and hematoma (1, 16.7%). Surgical complications included perioperative fracture (1, 16.7%) and transfusion (1, 16.7%). Length of stay averaged 4 days (range 2-8). There were statistically significant improvements in passive abduction ($p=.003$), active abduction ($p=.003$), passive flexion ($p=.007$), active flexion ($p=.008$), passive external rotation ($p=.011$), active external rotation ($p=.043$), and combined passive external rotation ($p=.033$).

Conclusion: As the largest study ever conducted on this topic, these results indicate that shoulder arthroplasty can be safely and effectively performed in patients with devices.

Suresh Kevin Nayar, MS3 Mentor: Babar Shafiq, MD, MSPT

Clinical Research

Multidisciplinary Rehabilitation of Hip Fractures: Bridging the Gap between Orthopaedics and Physical Therapy

Although the operative management of hip fractures has evolved considerably in the past half-century as our understanding of hip fracture biology, biomechanics, and fixation methods have improved, recommendations made by physicians and physical therapists on the rehabilitation of hip fractures are often given in isolation with little communication across disciplines. This review focuses on five major components of the rehabilitation of hip fractures, including: the benefits and timing of physical therapy, early weight bearing, rehabilitation facilities, predictors of functional outcome, and the pharmacologic management of fracture healing. The following recommendations are given by level of evidence and may guide executable protocols for physicians and therapists as well as promote understanding and communication across specialties.

Level A:

• Patients who undergo physical therapy see significant improvements in functional outcome, including improved strength, balance, and ambulation as well as decreased length of hospital stay compared to those without therapy.

• If tolerated, weight bearing should begin immediately after surgery in all hip fracture subtypes.

• Physical therapy can begin immediately after surgery, regardless of weight bearing status.

Level B:

• Multidisciplinary rehabilitation programs, whether home-based or inpatient, generally offer greater improvements in functional and quality of life outcomes compared to conventional acute postsurgical hospitalized care with no further treatment.

• Scheduled pain control in rehabilitation programs increases functional performance compared to those not receiving adequate pain medication.

• Self-reported measures of improvement may not correlate with performance-based measures.

• Despite rigorous training aimed at improving psychosocial functioning, a patient may still have a permanent decrease in confidence in their ability to function following hip fracture.

Level C:

• While there is no clear benefit of bisphosphonates, vitamin D, and calcium supplementation, preliminary evidence suggests that parathyroid hormone and strontium ranelate may accelerate fracture healing.

• If used for a short duration, NSAIDs can provide effective analgesia without compromising bone remodeling.

Mohamud Qadi, MS3 Mentor: Adrienne Scott, MD

Clinical Research

Effect of prior ophthalmic surgery on open globe injuries

Objective: To review the epidemiology and detect the impact of prior corneal, cataract, retinal, and refractive surgeries on visual recovery in patients with open globe injuries.

Design: Retrospective case review.

Participants: We searched the Johns Hopkins electronic medical records and found 39,000 ophthalmic surgeries and 4,000 open-globe injuries from January 1, 1997 to November 1, 2014. 400 patients who underwent ophthalmic surgeries had subsequent open globe injuries. 79 patients out of these 400 had prior ophthalmic surgeries for corneal transplant, cataract surgery, retinal surgery, or refractive surgery in the same eye.

Methods: Gender, age, dates of prior ophthalmic surgeries, date of open-globe injury, initial uncorrected visual acuity (UCVA), initial best-corrected visual acuity (BCVA), type of open-globe injury, location of open-globe injury, cause of open globe-injury, and type of open globe repairs, were evaluated using logistic regression models for final UCVA and final BCVA.

Main Outcome Measures: Two main visual outcomes were assessed: final UCVA and final BCVA.

Results: A prognostic model for the impact of prior ophthalmic surgeries on open globe injuries was constructed. Multiple logistic models were performed for final visual acuity. The strongest predictive factors for enucleation as a final visual outcome were having prior history of corneal transplant surgery, mainly penetrating keratoplasty (PKP) and Descemet's Stripping Endothelial Keratoplasty (DSEK). The greatest predictors for better final visual acuity were prior history of cataract surgery (phacoemulsification and extracapsular).

Conclusion: Patients who have prior corneal transplant surgery have worse visual outcomes after subsequent open globe injury compared to other types of ophthalmic surgeries. This should be useful in counseling patients and making clinical decisions regarding open globe injury management in patients with prior ophthalmic surgeries. This also demonstrates the importance of appropriate counseling when considering ophthalmic surgical interventions in patients at risk for ocular trauma, especially children.

Nick Rosculet, MS2 Mentor: Joseph Califano, MD

Clinical Research

The Neutrophil To Lymphocyte Ratio Is A Prognostic Indicator For Head And Neck Squamous Cell Carcinoma

Background: Background: There is a growing body of evidence showing that inflammatory response can play an important role in cancer progression. The neutrophil to lymphocyte ratio (NLR) has been shown to have prognostic significance for a variety of cancers, with higher values correlating with poor outcomes. This study aimed to determine the prognostic significance of this inflammatory marker for patients with head and neck squamous cell carcinoma (HNSCC).

Methods: Methods: A retrospective cohort study was performed on 123 consecutive patients treated for HNSCC with primary chemoradiation therapy between 2007 and 2014 at a single institution. The NLR was calculated from complete blood counts performed between the date of HNSCC diagnosis and the initiation of treatment. Analysis was performed using Cox proportional hazards regression and outcomes were evaluated based on recurrence-free survival and overall survival.

Results: Results: Mean age was 61 years with 89.4% male, 10.6% female, 89.4% Caucasian, 10.6% African American, 68.3% smoking history, 31.7% non-smokers, 81.2% drinking history, 18.8% non-drinkers, average stage T2, and median NLR of 2.7. In univariate analysis, NLR of less than the median was significantly associated with recurrence-free survival (p-value=0.023) and with overall survival (p-value=0.021).

Conclusion: Conclusions: This study has identified that the NLR is an indicator of both recurrence-free and overall survival in HNSCC. This finding supports the role of the host immune response in cancer progression. The NLR, easily calculated from routine lab values, can help clinicians stratify patients and predict responses to treatment. Further investigation is needed to identify whether the NLR's prognostic value is affected by other clinical factors including gender, age, race, and HPV status.

Anthony Serritella, MS2 Mentor: Michael Streiff, MD

Clinical Research

An Analysis of VTE Prophylaxis Practice in Oncology Patients after Implementation of a Standardized Mandatory Computerized Clinical Decision Support Tool

Background: Venous thromboembolism (VTE) is an important cause of morbidity and mortality in oncology patients. Prophylaxis reduces the risk of VTE by 60% but many patients are not prescribed risk-appropriate VTE prophylaxis. We developed mandatory computerized clinical decision support-enabled, service-specific (CCDS) order sets to improve our institution's VTE prophylaxis performance. The order sets require providers to complete checklists to assess VTE risk factors and contraindications to pharmacologic prophylaxis. The order sets then display the risk-appropriate VTE prophylaxis regimen for each patient. The purpose of this retrospective study is to evaluate VTE prophylaxis and events rates in hospitalized cancer patients admitted using a CCDS medical oncology VTE order set.

Methods: We retrospectively collected prescription and clinical data on patients admitted to the solid tumor and hematologic malignancy services at the Johns Hopkins Sidney Kimmel Comprehensive Cancer Center from October 17, 2010 (date of order set implementation) through June 30, 2014. A two-sided student's t test or chi-square test were used for analyses.

Results: 7920 patients were admitted from 10/17/2010 to 6/30/14. The mean age was 57 years and 46% were female. The median length of stay was 4 days. Solid tumor service providers were more likely to prescribe risk-appropriate VTE prophylaxis and patients on the solid tumor service were more likely to be assessed as high-risk for VTE. Pharmacologic prophylaxis was more common on the solid tumor service, while ambulation was more common on the hematologic malignancy service. Risk-appropriate VTE prophylaxis was high on both services. Data on objectively-confirmed hospital-acquired VTE will be presented at the meeting.

Conclusion: We report the largest analysis to date of VTE prophylaxis practices in hospitalized cancer patients. Significant differences in perceived VTE risk and prescribed prophylaxis were noted between services. Use of a computerized decision support-enabled VTE prophylaxis order set was associated with high rates of appropriate VTE prophylaxis.

Harita Shah, MD/PhD or Student in Residence Mentor: Lisa DeCamp, MD, MSPH

Clinical Research

Healthcare Activation and Health Literacy in Low-Income Spanish- and English-Speaking Parents of Young Children

Background: Patient engagement is heralded as an important means of healthcare reform. A key component of engagement is patient activation: the confidence, skills, knowledge, and willingness to manage one's health and healthcare. Adults with greater activation have better health outcomes and lower healthcare costs. However, parent activation has not been well-studied. Its possible associations to language and health literacy may offer additional insight into pediatric health and healthcare disparities.

Objectives: 1) To compare parent activation between Spanish- and English-speaking parents

2) To explore the association between health literacy and parent activation

Methods: We surveyed parents of publicly-insured children (6 months-5 years) who were patients at an urban general pediatric clinic for ≥6 months. Parents completed an orally-administered survey in English or Spanish according to preferred language. The survey included sociodemographics, the Parent-Patient Activation Measure (0-100), and the Newest Vital Sign (NVS) health literacy measure (0-6, dichotomized low (0-1) and marginal/adequate (2-6)). Student's t-test, chi square analyses and linear regression were used to examine associations between activation score, health literacy level, and sociodemographics.

Results: 121 parents participated (Expected enrollment: 350 parents by January 2015). 64% were immigrant Latinos with Spanish-language preference. Mean activation score was lower among Spanish-speaking parents than English-speaking parents (mean=73(SD=18), mean=81(SD=16) respectively; p=0.02), with no difference in activation by education or immigrants' years in the US. Parent activation was lower in parents with low health literacy compared to marginal/adequate health literacy (mean=71(SD=18), mean=80(SD=17) respectively) after controlling for language and education($p<0.05$).

Conclusion: Parent activation in this sample of low-income parents was greater than activation in adults. Parents' limited understanding of health information due to language and/or health literacy may reduce their ability to engage in their child's healthcare. Further study is needed to explore the relations between parent activation, parental health literacy, and child health outcomes.

Liyang Tang, MS2 Mentor: Howard Francis, MD

Clinical Research

Does Emotional Intelligence Affect Cochlear Implant Outcomes in Older Adults?

Background: Hearing loss has been associated with dementia, social isolation, and functional decline. Cochlear implants (CI) in patients with bilateral hearing loss have been shown to increase speech perception and quality of life. However, some patients have more gains than others. Emotional intelligence has been positively correlated with quality of life and this study aims to determine the role that it may play in determining CI outcomes.

Methods: Adults with bilateral, severe to profound sensorineural hearing loss who are 65 years and older and received a single cochlear implant at Johns Hopkins Hospital were recruited to participate. Patients with congenital deafness, bilateral CI, and who do not speak English were excluded. Emotional Intelligence (EI) was measured using the TEIQue-SF survey. Outcomes included the AZbios audiological measurements and quality of life measured using the Glasgow Benefit Inventory. Outcomes were collected between 5 and 13 months after surgery. Pearson correlation coefficients and t-tests were performed.

Results: To date, 26 out of the 48 eligible patients have been approached about the study and 18 have returned completed surveys (response rate: 69%, female: 27.8%, average age: 73.6). While EI is not associated with quality of life, it has a negative, though statistically insignificant, correlation with post-operative AZbios scores ($r= -0.39$, $p= 0.12$). Age at time of surgery, however, has a significant negative correlation with post-operative AZbios scores ($r= -0.55$, $p= 0.02$) and is marginally associated with higher EI ($r= 0.42$, $p= 0.08$).

Conclusion: Older patients tend to have higher EI, but worse objective audiological outcomes. This finding suggests that the greater optimism and motivation of older patients do not necessarily translate into better auditory outcomes within the first year after CI surgery. Structured rehabilitation and other interventions are needed and may generate improved outcomes at later time points.

Trinh Trang, MS2 Mentor: Kate Puttgen, MD

Clinical Research

Multicenter Retrospective Cohort Study of Topical Timolol for Treatment of Infantile Hemangiomas

Background: Infantile hemangiomas (IH) are the most common benign vascular tumors in children. While most IH will involute on their own, a significant minority require medical and/or surgical treatment. The first-line treatment option for complicated IH is propranolol, a non-selective β-blocker. More recently, the topical β-blocker timolol has been proposed as an alternative for small cosmetically sensitive IH.

Methods: The efficacy of timolol in the treatment of IH has not yet been evaluated in a large cohort of patients. The objective of this multicenter, retrospective observational study is to assess response of IH color, size, volume and overall appearance in pediatric patients treated with topical timolol between 2010 and 2013 who were seen by pediatric dermatologists at 7 tertiary referral centers across the United States. Data were available for 732 patients. The cohort was 27.40% male and 72.60% female. 82.88% were white, 5.45% Hispanic, 3.11% black, and 2.72% were Asian. 17.45% were born pre-term, 65.79% full term, and 0.28% post-term. 74.83% have localized IH and 5.23% have segmental IH on the head and neck, and 19.94% with IH on the body. Drawing on medical records and clinical photographs, we assessed the functional and aesthetic outcomes of IH using a visual analog scale (VAS), ranging from -100 (IH is doubled in size or color) to 100 (IH is completely resolved). Size/volume and color were assessed separately.

Results: Our results show that IH respond significantly to timolol, with the mean response in size/volume increasing from mean baseline of 10.98 to 26.46, 38.52, and 41.10, and the mean response in color increasing from mean baseline of 21.27 to 39.17, 53.19, and 54.69 at 1-2, 3-6, 6-9 months into treatment and at the last visit, respectively.

Conclusion: Our results indicate that timolol is effective in treating IH, especially small and superficial cases, with no serious adverse effect.

Kevin Yuqi Wang, MS4 Mentor: Izlem Izbudak

Clinical Research

Tract-specific Diffusion Tensor Imaging in Cervical Spondylotic Myelopathy After Decompressive Spinal Surgery

Background: Prior studies assessing cervical compressive myelopathy (CCM) using diffusion tensor imaging (DTI) obtained fractional anisotropy (FA) and mean diffusivity (MD) measurements by placing regions of interest (ROI) covering nearly the whole cross sectional area of the spinal cord. However, DTI in the spinal cord has the advantage of differentiating white matter funiculi and grey matter. The aim of this study was to compare DTI metrics of the cervical spinal cord using tract-specific ROIs in patients with CCM to those measured in healthy volunteers.

Methods: Magnetic resonance (MR) imaging of the cervical spinal cord was performed in 4 symptomatic patients with CCM and in 5 healthy volunteers. FA and MD were calculated on both axial and sagittal DTI acquisitions with ROIs encompassing the hemicord and whole cord, respectively. Region-specific FA and MD measurements were also calculated on axial imaging with ROI placement in the anterior, lateral, and posterior regions of the spinal cord to approximate the locations of the anterior grey matter, corticospinal tract, and dorsal column, respectively. Measurements were obtained at the C2-C3 spinal level in healthy volunteers, and at the level of most severe compression in CCM patients. Non-parametrical statistical testing was used to compare patients and controls.

Results: Mean FA was significantly lower in CCM patients prior to surgery than in healthy controls in lateral ROIs ($p=0.050$). Mean MD was significantly higher in CCM patients prior to surgery than in healthy controls in posterior ROIs ($p=0.014$). There was a trend toward higher FA value and lower MD value in lateral ROIs in patients after surgery compared with before surgery ($p=0.068$).

Conclusion: Preliminary results suggest that patients with CCM may demonstrate region-specific changes in DTI metrics when compared to healthy controls. DTI may be a promising modality for providing additional information beyond that of conventional MR imaging in patients with CCM.

Ophelia Yin, MS2 Mentor: Mindy Christianson, MD

Clinical Research

Polycystic Ovary Syndrome Does Not Appear to Affect Menopausal Transition Symptoms

Background: Polycystic ovary syndrome (PCOS) is the most common endocrinopathy in reproductive-aged women and is characterized by anovulation, hyperandrogenism, and polycystic ovaries. Since previous studies on PCOS have focused on younger populations (<45 years), the impact of PCOS during the menopausal transition remains poorly understood. This study aims to determine the influence of PCOS on common midlife symptoms such as hot flashes.

Methods: Data was analyzed from an ongoing cohort study of 639 midlife women ages 45-54 years. Subjects completed detailed questionnaires each year on hot flashes and other common midlife symptoms. Subjects were contacted by telephone and identified as having a history of PCOS using the Rotterdam criteria. Chi square analysis and multivariate logistic regression models were used to analyze the effect of PCOS on the menopausal transition.

Results: Of 474 women screened for PCOS, 50 (10.6%) met diagnostic criteria. Of these, 44 PCOS and 349 controls were included in the final analysis. Average PCOS subject age was 48.4 and body mass index (BMI) was 26.3, with 86% Caucasian and 14% non-Caucasian. PCOS subjects had increased frequency of menses (p=0.009) and higher rates of alcohol use (77% vs. 61%, p=0.049) compared to controls. Multivariate logistic regression analysis demonstrated that PCOS was not associated with increased odds of hot flashes, vaginal dryness, urinary symptoms, or sleep disturbances. The only positive predictor of hot flashes was current smoking status with an odds ratio of 1.68, p-value 0.02, 90% CI [2.1, 2.6].

Conclusion: A history of PCOS was not associated with hot flashes or other midlife symptoms in this study. These data suggest that other factors, such as smoking habits, are more important in determining hot flash and other symptom risk during midlife and that PCOS may have no specific impact on the menopause transition.

HISTORY OF MEDICINE

POSTER ABSTRACTS

Listed Alphabetically

Ambar Mehta, MS2 Mentor: Randall M. Packard, PhD

History of Medicine

A Historical Analysis of New York City's Tuberculosis Epidemic

Starting in the 1980s, an insidious tuberculosis epidemic began to creep under the radar in New York City (NYC), slowly infiltrating the city from person to person. When the epidemic finally reached a peak in 1992, many blamed the city's withering public health infrastructure, the rise of poverty, the reduction in social services, and other structural factors. A retrospective analysis of literature discussing these aforementioned factors reveals that many believed that immigration constituted a minor role in the epidemic. However, most reports never investigated the true contribution immigration had on the epidemic. Immigrants, or those who were born outside of the United States, often come from countries with high tuberculosis prevalences. Consequently, they hold the potential to harbor latent tuberculosis. In this report, we analyzed immigration data from the 1970s till the early 2000s. Our sources included the annual NYC Tuberculosis Reports and the The Newest New Yorkers book series, both published by the NYC Department of Health. We argue that immigration held not an insignificant influence on the epidemic. Further research should investigate the role of immigration in this epidemic, and elucidate any potential causative links between being foreign-born and incidence in the epidemic. Such studies can suggest the need for improvements in detecting and resolving tuberculosis in immigrants.

Ayresleigh Rowland, MS2 Mentor: Daniel Todes, PhD

Medical Humanities

Mind, Matter, and Motherhood:
Shifting Paradigms of Puerperal Insanity in the Early 20th Century

In this paper I explore a nosological shift in the history of mental illnesses associated with reproduction from 1890 to 1940. Through a close reading of medical journals and manuals, I examine how an evolving narrative reflected new etiological theories and changing views of the female body and psyche.

With the adoption of the Kraepelinian diagnostic system around 1910, psychiatrists and obstetricians agreed that scientific medicine required the replacement of the imprecise term “puerperal insanity” with new disease categories based on the correlation of physical lesions with symptomatology. This revision of psychiatric disease classification prompted a rethinking of the etiology of insanities associated with reproduction. Before 1910, puerperal insanity was thought to arise primarily from pathology of the reproductive organs. From this perspective, predisposing factors, such as a positive family history, increased the probability of previously “normal” woman becoming unbalanced. By 1920, doctors located the pathophysiological process in the woman’s nervous tissue. Insanity itself served as proof of a woman's inherently deficient, weak “make-up” or “constitution,” which became apparent only when the great strain of reproduction brought about its collapse. The act of diagnosis retrospectively labeled the patient as mentally pathological. Later, in the 1920s and 30s, followers of psychoanalytical theory sought to discover the early signs of a defective nervous constitution before insanity manifested. Their case studies describe women with strange personalities incapable of adjusting their minds to meet the demands of maternity. Medical literature published on this subject gradually evolved into an evaluation of the quality of women's brains, their weakened mental resistance and neurotic leanings. The narrative of reproductive insanity ceased to be an unpredictable tragedy visited upon all classes of women and became the inevitable failure of an abnormal mind to resist stress and adapt to motherhood.

Mary Smith, MS2 Mentor: Mooney, PHD

History of Medicine

The East Baltimore Medical Plan: A look at the realtionship between JHMI and the East Baltimore Community

In a time of racial strife and community unrest after the Baltimore riots of 1968, the creation of a prepaid comprehensive health plan for East Baltimore was approved by the Joint Board of Trustees at Johns Hopkins Hospital. The East Baltimore Medical Plan was lauded as one of the first entirely collaborative efforts between Johns Hopkins Hospital, local black physicians, and the East Baltimore community to improve the healthcare of a largely African American East Baltimore population.

This research examines the ways in which the creation of the East Baltimore Medical Plan was shaped by the dynamics of the complex relationship between Johns Hopkins Hospital, local black Physicians, and the East Baltimore community. The strain between these three constituencies is revealed through a close examination of, correspondence, meeting minutes, program proposals, newspapers, and journal articles between 1965 and 1972. I demonstrate that there were clear disagreements between these groups over the definition and extent of the proposed collaboration.

These tensions impeded the fostering of successful relationships between the three parties and hindered the growth and progress of the East Baltimore Medical Plan. Although a comprehensive plan was never realized, two tangible outcomes of this collaboration were the East Baltimore Medical Center and the East Baltimore Community Corporation, both of which continue into the present day as fully functioning entities.

Problems of contention, race relations, and disenchantment between community citizens and its service providers still exist in the area around the Johns Hopkins Hospital. This project draws upon historical research to shed light on potential solutions and compromises to overcome these rifts.

Alex Stone, MS2 Mentor: Graham Mooney, PhD

History of Medicine

Crowded: The Development of Emergency Medicine at the Johns Hopkins Hospital

Emergency medicine as a specialty at the Johns Hopkins Hospital stemmed from an effort to move patients out of the emergency room. Following WWII, the number of patients seeking care in emergency rooms grew steadily in Baltimore. At the Johns Hopkins Hospital, the provision of service was limited by the small size of the emergency department, the lack of clearly defined leadership, and the inexperience of the residents and interns. In reports about the emergency department's problems, discussion of misuse of the emergency room predominates over the issues of limited space and personnel. The hospital leadership believed that patients receiving primary care in the emergency room was the main driver of the crowded conditions that patients experienced.

For years, the Johns Hopkins Hospital suffered from a negative opinion in the East Baltimore community, in part due to long wait times in the emergency department. Following the 1968 race riots, hospital leaders looked to improve the local reputation of the hospital. They focused on moving non-emergency cases out of the emergency department because they believed that primary care dispensed there was inefficient. A director of the Emergency Services was appointed to streamline the emergency room and to divert patients to other outpatient clinics. These efforts paved the way for emergency medicine to gain a place as a specialty at Hopkins.

This paper uses institutional primary sources from the Alan Chesney Memorial Archives in addition to newspaper articles and published interviews in order to focus on the period between 1953 and 1975. In addition to telling a history of emergency medicine at the Johns Hopkins Hospital, this paper explores how the definition of an emergency differed between the medical establishment and the community, a question that remains relevant today. One limitation of this research is the limited material describing the patient perspectives.

Crystal Wang, MS2 Mentor: Randall M. Packard, PhD

History of Medicine

Investigating the etiology of dengue hemorrhagic fever in Thailand from 1950-1967

Following the 1958 outbreak in Bangkok, Thailand, Dr. Scott Halstead believed that the antibody-dependent enhancement (ADE) theory explained the mechanism behind dengue hemorrhagic fever (DHF) and dengue shock syndrome (DSS). This theory argued that after an infection to one dengue serotype, an individual was predisposed to shock when infected a second time with different dengue serotype. 50 years after his theory was proposed, the ADE theory continues to remain the dominant theory. However, it is viewed as a partial and incomplete explanation for DHF/DSS, especially in the wake of more contemporary evidence. Therefore, it is important to reexamine the history of dengue and how the ADE theory came to be supported historically, since the theory behind the disease will ultimately drive future interventions. Specifically, my goal is to answer the following questions: which theories emerged on the etiology of DHF in Thailand in the 1950s and 1960s and why? How did the hypersensitivity hypothesis come about and why was it accepted as a valid explanation for DHF/DSS?

Through a combination of scientific literature published between 1950-1970, oral histories, and archival collections from the Walter Reed Army Research Institute, I will explore how DHF was first characterized, and trace which observations led researchers to construct hypotheses regarding its etiology. I will discuss which scientific, social, cultural, or political factors might have influenced how researchers developed their hypotheses, and then attempt to explain why Halstead's theory became the dominant hypothesis by the 1970s. I will also describe the debate surrounding his hypothesis, including the reactions and opinions of others in the larger dengue and medical field, and why other alternative hypotheses were not supported. In doing so, the story of DHF in Thailand provides insight into the creation, life, and death of new theories and the production of new information.

MEDICAL HUMANITIES, BIOETHICS, and the HEALING ARTS POSTER ABSTRACTS

Listed Alphabetically

Christopher Bailey, MS4 Mentor: Donna Magid, MD

Medical Humanities

Automated social media for learning: Facebook push notifications for Radiology correlation and education during Gross Anatomy

Background: The integration of Radiology into the Anatomy course provides an excellent clinical corollary to solidify anatomic relationships, introduce clinical relevance, and foster early interest in imaging. We sought to incorporate easily accessible, readily mastered daily samples of relevant material closely correlated with the Anatomy course's day-by-day plan.

Methods: A set of imaging-centered clinical cases that reinforce high yield anatomic concepts was generated on the Medical Imaging Resource Center (MIRC) software (RSNA). A Facebook (Facebook, Inc., Menlo Park, CA) Page was created and promoted to first-year medical, biomedical engineering, and medical illustration students, all of whom enrolled in Anatomy. Students were asked to voluntarily "Like" the Facebook Page, which would allow them to receive push notifications. To deliver questions daily, we employed Buffer (bufferapp.com), a tool that permits the scheduled release of content ("Posts") onto Facebook Pages. Metrics provided on Facebook, including total "Likes", Page views, and link clicks, were used to assess participation.

Results: At its launch on August 19, 2014 the Facebook Page was "Liked" by 148 people; evidently, Facebook users outside of the target demographic also viewed the content. Number of people who viewed each Post ranged from 74 to 181 (mean 134, SD 30), with 20 to 59% (mean 45%, SD 12%) of Post viewers clicking on the link. With regard to student satisfaction, over 80% of students felt that the cases were relevant, interesting, and enhanced their understanding of anatomy and appreciation for imaging as a diagnostic tool.

Conclusion: Facebook combined with Buffer provides an efficient, low-cost, and automated technique to deliver educational material to students. This novel approach has been well received by students, citing greater understanding of both anatomy and Radiology and interest in the field. Given the ubiquity of Facebook and ease of the method, this approach is widely applicable to other educational scenarios.

Zachary Obinna Enumah, MS2 Mentor: Obarrio, PhD

Medical Humanities

Healing Systems, Attitudes and Perceptions in Nyarugusu Refugee Camp, Kigoma, Tanzania

Background: Tanzania's refugee policies have imposed restrictions on both the freedom of movement and residency, as well as the right to earn a livelihood. For many, access to adequate education, healthcare and other human rights are denied. The purpose of this study was to investigate the health-related perceptions, attitudes and reported behaviors of refugees living in Nyarugusu camp, Kigoma Tanzania, which currently serves 65,000 refugees primarily from the Democratic Republic of Congo.

Methods: The project was undertaken using a multi-method approach. Forty refugee healthcare educators employed by the International Red Cross participated in two semi-structured town hall meetings that lasted approximately one hour each. Town hall meetings data was

supplemented by participant observation, interviews, and archival research conducted at the United Nations High Commissioner for Refugees (UNHCR) Resource Center in Tanzania and at the University of Dar es Salaam East Africa Research Collection. Open coding was conducted using Nvivo and memos were written and compiled using constant comparison method. This analytic process resulted in the generation of thematic domains.

Results: Two major thematic domains emerged from this study: 1) positive perceptions and attitudes and 2) negative perceptions and areas of concern. Several positive subthemes also emerged, such as free services, specialized pre-natal care, and extensive healthcare education. By contrast, negative themes included concerns over pharmaceutical resources and personnel, tensions between doctors and patients, delays in seeking care, and questions about the role of faith traditions, such as blood transfusions for Jehovah's witnesses.

Conclusion: The use of a participatory assessment model to qualitatively examine healthcare systems in a refugee camp resulted in a nuanced understanding of the health care experiences of this vulnerable population. Engaging stakeholders is a first step in improving health care for refugees. Future work should focus on perspectives of other stakeholder groups such as traditional healers.

Niyati Mamtora, MS2 Mentor: Ed Bessman, MD

Medical Humanities

Catching Waves: The Perspectives of Physicians Who Surf

Background: Physician burnout is a serious problem in the USA. Two major strategies to reduce the risk of burnout have been identified in the literature: exercise and spirituality. Surfer culture is unique in that surfing is a spiritual discipline as well as a sport. This project examined how being part of the surfer culture affects the lives of physicians who surf.

Methods: Recruitment involved contacting various surfer's medical associations who then emailed information to their members about my study. Those agreeing to participate were interviewed via phone, Skype, or in person to gain an understanding of participant's experiences with both surfer and medical culture and how surfer culture has impacted their sense of purpose, stress levels, and work/life balance. Transcribed interviews were carefully read and coded. This analytic process resulted in the generation of thematic domains

Results: 15 American physicians and 6 European physicians were interviewed. Analysis to date has resulted in the following thematic domains.

• Surfing added balance to participants' lives

• Surfing allowed participants to be present and in nature which released the built-up stress related to their work.

• Surfer doctors reported being more compassionate to patients and coworkers with regular surf sessions.

• Most participants approach risk management in terms of calculated risks. They mainly believe risks are a part of life and it's up to the individual to make informed decisions.

• Most participants live in cultures that accept surfer culture and they do not hide their identity as surfers-doctors in the medical or surfer culture. If they did, it was during their training/early years.

Conclusion: Surfing physicians reported lower stress levels and more empathy toward patients when they were surfing regularly. Participants reported physical exercise, necessity of being in the moment, and being in nature as the reasons why surfing counterbalanced medicine's stresses.

Maxine Norcross, MS3 Mentor: Emily Frosch, MD

Medical Humanities

LiveWell in a Learning Community: A Student-Driven Curriculum Supporting Self-Care

Introduction: At the Johns Hopkins University School of Medicine, previous attempts to incorporate restorative practices into the medical school curriculum have received poor reviews. However, past curricula were created by faculty without a student needs assessment. We conducted a wellness needs assessment and found that students desire learner-driven programs that teach self-care strategies and include faculty role-models. Based on these results, we designed an interactive workshop series to promote self-care within our learning community.

Program description: Program goals were to 1) establish a forum for discussion of well-being, 2) foster reflection and self-awareness, and 3) promote development of wellness practices among medical students. We piloted the program "LiveWell Workshops" in Fall 2013 with five monthly workshops on topics chosen by students: self-care, sleep hygiene, doubt, stress management, and relationships. Each workshop lasted 60 minutes, included dinner, and consisted of brief didactics led by both students and faculty, reflective exercises, and group discussion.

Program evaluation: N=172 students (74% of MS1 class, 55% of MS2 class) attended at least one workshop. Attendance per workshop ranged from 24 - 91 students (mean 61, SD 26). Among workshop participants, 81% found the presented information useful, 70% agreed that the workshops addressed their concerns, 70% planned to try strategies that were discussed, and 88% would recommend the workshops to a peer. Participants reported positive outcomes including learning that other students share their concerns, the importance of self-care, and specific strategies to improve well-being. Suggested program improvements were more opportunities for small group discussion.

Discussion: The pilot of LiveWell Workshops was well-attended and received favorable reviews. Key elements to program success include a needs assessment, student-driven program development, and collaboration between students and faculty. Student leaders are planning to expand the program next year and measure program impact on individual learners and our learning community.

John Schimek, MS2 Mentor: Yoram Unguru, MD

Medical Humanities

Helping Hands: Peer advice for parents of pediatric oncology patients

Background: Parents of pediatric oncology patients value relationships with other parents who have had a child with cancer and understand their unique situation. By analyzing the advice offered new parents in these relationships, a new intervention could be created to help parents cope with a new diagnosis. The purpose of this project was to describe the nature of parents' advice and inform the production of an innovative intervention – a "handbook" - for parents of newly diagnosed children.

Methods: We analyzed the advice of 149 parents of children with cancer attending Camp Sunshine, a camp for children with life-threatening illnesses and their families. Parents drew an outline of their hand on which they wrote advice they would offer to new pediatric oncology parents. Hands were created at camp sessions devoted to: general oncology (N=47), brain tumor (N=3), Spanish speaking oncology (N=69), and off treatment (N=30). A content analysis of the 'hands' was performed independently by two investigators who met to compare coding and resolve differences. This process resulted in the generation of thematic domains.

Results: Themes that emerged from the projects fell into three categories: how to approach medical care, how to live each day, and how handle relationships with other people. Previously unidentified advice themes emerged with our methods, particularly in the category of interactions with other people with themes focused on other family members including siblings of the sick child.

Conclusion: Novel advice themes for parents of pediatric oncology patients were identified through a creative project at a camp for families of children with cancer. In the future, these themes may inform the production of a "handbook" to be used to help parents of newly diagnosed children cope during a time of drastic change.

PUBLIC HEALTH
and COMMUNITY SERVICE
POSTER ABSTRACTS

Listed Alphabetically

Laura Anzaldi, MS2 Mentor: Adam Kaplin, MD

Public Health and Community Service

Tracking Purpose in Life of Those Affected by Multiple Sclerosis Who Are Members of an Online Support Network

Background: Multiple sclerosis is a debilitating autoimmune CNS disease with cognitive impairment, high levels of inflammation, depression and disability. Purpose in life (PIL) is a promising idea that has been correlated with improved neurodegenerative outcomes, lower levels of inflammation, and lower rates of disability. This is a preliminary exploration into the possibility of using PIL to improve the health of MS patients. Because community involvement has also been shown to correlate with increased PIL, we have partnered with myCounterpane, an up-and-coming online MS support network. We aim to (1) assess how purpose in life changes over time with use of myCounterpane, and (2) determine how graphical feedback of one's PIL trends affects survey response rates.

Methods: 100 new users (MS patients and MS caregivers) of myCounterpane will be recruited to join the study as they join the site. All participants will be prompted to complete monthly anonymous surveys that collect general demographic information and quantify their PIL using Crumbaugh and Maholick's PIL scale. Half of the participants will be randomly assigned to see a graphical summary of their PIL trends at the completion of each survey. Participants will receive surveys for one year.

Results: No results yet

Conclusion: We have not yet deployed the survey due to several challenges. The project changed course significantly over the summer with numerous set-backs, highlighting the importance of flexibility. It was also sometimes challenging to coordinate with the myCounterpane team, especially when they had different priorities and had limited resources to contribute to our project. There were significant misunderstandings at times - clear, frequent communication in writing was crucial. We have overcome most of these challenges and hope to launch the survey in the coming weeks.

Karun Arora, MS2 Mentor: David Friedman, MD, PhD, MPH

Public Health and Community Service

Providing High-Volume, High-Quality, Low-Cost Cataract Surgery in Sub-Saharan Africa

Background: Cataract is the leading cause of treatable blindness in Sub-Saharan Africa. Aravind, the world's largest eye hospital based in India, and the Wilmer Eye Institute are collaborating to provide managerial and clinical guidance and financial support to selected centers in rural Kenya, Ethiopia, Nigeria and Zambia to increase the quantity and quality of cataract surgery. My role was to collect baseline data at each center so that the impact can be tracked objectively over time.

Methods: Data collected included numerical data, such as number of surgeries performed, outpatients seen, screening camps conducted, and glasses sold in the two years prior to the collaboration. Detailed information was also collected regarding the processes in place, including pre-, intra-, and post-operative procedures; monitoring of surgical outcomes; patient flow; management of screening camps; human resources, equipment, medical record system, written protocols, and other infrastructure; and fee structure, options for indigent patients, and financial systems.

Results: In brief, all sites could benefit greatly from improvements in each process area listed above. However, each site faces area-specific and developmental stage-specific challenges. The relatively new institute in Kenya is still trying to gain trust and recognition in the community. In Ethiopia and Zambia, one primary limitation is the lack of trained ophthalmologists. In Ethiopia, the availability of equipment is another major hurdle. In Nigeria, where manpower and equipment are more readily available, the primary challenge is poor management.

Conclusion: Developing cataract surgery programs is challenging and requires tremendous attention to detail. The Aravind model of conducting efficient screening camps to identify persons requiring care and of providing care to all who need it by using a higher-paying, private arm to subsidize a lower-cost, public arm is extremely effective, but requires local adaptations. Goodwill built among the community, effective systems, and proper management can greatly impact the success of an institute.

Marcelo Cerullo, MS3 Mentor: Adil Haider, MD

Public Health and Community Service

Assessing the association between insurance and management of pediatric blunt splenic injuries

Background: Prior research has demonstrated the efficacy and safety of non-operative management for pediatric splenic injuries (PSI). Repeated studies have documented an association between insurance status and hospital course. Though every state has set up its own Children's Health Insurance Program (CHIP), enrollment rates have varied. We investigated how state CHIP enrollment influences the effect of individual insurance status on in-hospital management of PSI.

Methods: The rate of enrollment into CHIP from 1999 to 2011 was calculated by applying the Savitzky-Golay smoothing algorithm to US Census state-level data. Discharge records of pediatric patients (<18 years) with ICD-9 codes for non-penetrating splenic injury were selected from the 2009 Kids' Inpatient Database (design weights applied to produce national-level estimates). The effect of insurance status on PSI management was evaluated by logistic regression (adjusting for demographic, hospital, injury-specific confounders). A hierarchical model was constructed to evaluate the latent effect of enrollment rates on the effect of insurance status.

Results: A total of 2843 patients with PSI in 39 states were included. Adjusted odds of mortality were higher in children who underwent operative management compared to children who underwent non-operative management (95%CI: 4.51-14.07). Lack of insurance was not associated with mortality, (95%CI: 0.62-3.05), though uninsured children had 1.4 (95%CI: 1.16-2.91) times greater adjusted odds of undergoing operative management compared to insured children, and continued to demonstrate greater odds of undergoing operative management even when clustering by state was controlled for in the hierarchical model (95%CI: 1.09-3.10). Faster state-specific enrollment rate resulted in lower odds of operative management ($p<0.05$).

Conclusion: Uninsured children are more likely than insured children to receive operative management for blunt splenic injury, regardless of their state's rate of enrollment into CHIP. However, children in faster enrolling states are less likely to undergo operative management overall, highlighting the importance of measures aimed at increasing insurance uptake.

Cody Cichowitz, MS2 Mentor: Chris Hoffmann, MD

Public Health and Community Service

Assessing Continuity of Care from Hospital to Community in South Africa

Background: In southern Africa post-discharge mortality remains high for medical patients, despite improved access to health practitioners and medications, including antiretroviral therapy. A cohort of 300 patients was recruited from a semi-rural hospital in South Africa for a prospective study designed to identify modifiable factors that impact medication uptake and adherence, readmission, and mortality during the six months following hospital discharge. The purpose of this study is to describe the enrollment data for the first 183 patients recruited for the larger prospective study.

Methods: A team of nurses and health counselors recruited 300 patients from the adult medical ward at Tshepong Hospital. At the time of study enrollment, demographic and admission data were collected, and participant's completed a survey that assessed prior health care utilization and access to the medical system. Enrollment data for the first 183 participants was described with percentages.

Results: The most common chief complaint leading to hospital admission involved the respiratory system (32%), followed by the nervous system (23%). During the six months prior to study enrollment, 72% of participants reported seeking medical care and 26% of participants had been hospitalized. At the time of enrollment, 44% of participants were HIV positive, 48.2% of participants had at least one chronic medical condition (excluding HIV), and 60% reported being on a prescribed medication. Finally, 47% of participants stated that there were times that they wanted to seek medical care but could not access the health care system.

Conclusion: In order to understand and improve hospital and post-discharge mortality in southern Africa, it is necessary to first recognize that patients present to the hospital with complex medical needs and patterns of health care utilization. The presence of chronic conditions and comorbidities increases the demands placed on providers and health systems caring for adult medical patients, including those with HIV.

Pujan Dave, MS2 Mentor: Pradeep Ramulu, MD PhD

Public Health and Community Service

Ability of Bottle Cap Color to Facilitate Accurate Glaucoma Patient-Physician Communication Regarding Medication Identity

Background: Bottle cap color is a primary cue used by patients and physicians to communicate about topical ophthalmic medications. However, it is unclear if cap color facilitates accurate patient-physician communication, particularly amongst individuals with glaucoma who might have color vision deficiency.

Methods: Glaucoma patients provided color descriptions of 11 distinct medication bottle caps. Patient-produced color descriptors were presented to three physicians, and each physician was asked to match the color descriptor to the medication they thought the color descriptor used to describe. The frequency of patient-physician agreement, occurring when all three physicians accurately matched the color descriptor to the correct medication, was calculated for each medication. Multivariate regression models evaluated whether patient-physician agreement decreased with extent of better-eye visual field (VF) damage and/or of color vision deficiency as determined by Hardy-Rand-Rittler (HRR) score and Lanthony D15 index (D15 CCI).

Results: The 100 glaucoma patients studied provided a total of 102 unique color descriptors to describe the 11 tested bottle cap colors. Among individual patients, the mean number of medications demonstrating patient-physician agreement was 6.1/11 (55%). Agreement rates across patients were less than 15% for 4 medications (prednisolone acetate, betaxolol, brinzolamide/brimonidine, and latanoprost). Lower HRR scores and higher D15 CCI (both indicating worse color vision) were associated with greater VF damage ($p<0.001$). Severity of better-eye VF damage and of color vision deficiency were both associated with a lower likelihood of patient-physician agreement in univariate analyses ($p<0.05$ for all), while greater color vision loss was the only significant predictor in multivariate models (odds of agreement = 0.90 per 1 point decrement in HRR score; $p<0.001$).

Conclusion: Physician understanding of patient medication usage based solely on bottle cap color is frequently incorrect. Healthcare providers should be aware of potential errors based on communication using bottle cap color alone to protect patients from both confusion and harm.

Timothee Fruhauf, MS2 Mentor: Amy Tsui, PhD; Caroline Moreau, MD, PhD

Public Health and Community Service

Predictors of Contraceptive Use Among Youth Ages 15-24 in Ghana

Background: Despite high unmet need for contraception, Ghanaian female youth are often excluded from reproductive health programs. Identifying the correlates of their contraceptive use is a critical step in understanding Ghana's paradoxical drop in total fertility rate and stable contraceptive prevalence rate, in the context of delayed childbearing. On that basis, this research aims to identify the factors related to contraceptive use among sexually active women ages 15-24 in Ghana, using data from Performance Monitoring and Accountability 2020/Ghana.

Methods: This analysis used nationally representative cross-sectional data collected through a mobile device-based surveillance system monitoring family planning progress. The association of age, region, urban/rural, marital status, education, and wealth with ever use of contraception among sexually active youths was assessed through bivariate and multivariate regression analyses. Associations were also explored in relation to current use of contraceptives among youths in need of contraception. Odds ratios and confidence intervals were computed.

Results: Age, region, marital status, and education were significantly correlated to contraceptive use among sexually active youths and youths in need of contraception (p-value < 0.05) in bivariate analyses. However, only age, marital status, and education remained significant factors in the multivariate regression: sexually active women who were 20-24 years old, married, or had attended higher education had greater odds of ever using contraceptives than women who were 15-19 years old (OR:2.05, 95%CI:1.51-2.80, p:0), unmarried (OR:1.71, 95%CI:1.28-2.28, p:0), and less educated (OR:2.40, 95%CI:1.51-3.82, p:0). Age was the sole factor of current contraceptive use among youths in need (OR:1.58, 95%CI:1.06-2.35, p:0.025).

Conclusion: Use of contraceptives by sexually active youths in Ghana remains an issue, especially for young unmarried women. Further research is needed to identify the barriers to their contraceptive use and build tailored programs for this subgroup. Promoting female education should continue to improve contraceptive use, potentially via enhanced access to health services and information.

Jasmine Holmes, MS2 Mentor: Eric Bass, MD, MPH

Public Health and Community Service

Project Perfect Fit: Quality Improvement Initiative of the Lose Dat Program

Background: Addressing the disparity of opportunity and educational resources that lead to poor health choices amongst urban populations is one of the core objectives of many public health initiatives. The goal of this project was to train community health workers (CHWs) to lead one such initiative, the Lose Dat Program, a community weight loss/health maintenance program. In relinquishing control to CHWs, we aimed to make it a more efficacious, sustainable, community-centered healthcare service.

Methods: The director of the Louisiana Community Health Worker Training Institute held three weekly group facilitation-training sessions with eight CHWs prior to the initiation of the program along with five subsequent practice sessions. Each CHW's group facilitation's skills were assessed weekly by program directors and participants using oral feedback, session evaluations, and participant comments against the objectives of the three-week course (leadership, verbal/non-verbal communication, discussion facilitation, conflict resolution, time-management, team-building), along with the clarity of the presentations, and the effectiveness of program. Records of constructive criticisms, suggestions, and impartial observations were compiled and reviewed by the core leadership and CHWs.

Results: Qualitative data reveal three major effects by the end of six weeks. First, CHWs with higher session attendance, who facilitated more frequently, consequently receiving more consistent feedback, facilitated with more clarity, confidence, and less reliance on physician input. Second, participant participation in sessions increased as indicated by participant active engagement in discussions, question asking/answering, and sharing of relevant personal anecdotes. Lastly, the efficiency of the program improved, one measure of which was streamlined organization of weekly sessions.

Conclusion: Observation of CHWs yields that CHW skill development is aided by assessment feedback, associated with higher rapport amongst community participants, and CHW team building and experience is possibly linked to increased program efficiency, suggesting that the transition of leadership to CHWs in the Lose Dat Program is both sustainable and beneficial.

Seema Kacker, MD/PhD or Student in Residence Mentor: Catherine Juillard, MD MPH

Public Health and Community Service

Socioeconomic Correlates of Trauma:
An Analysis of Emergency Ward Patients in Yaoundé, Cameroon

Background: Injury is a significant cause of morbidity and mortality in sub-Saharan Africa, but underlying social and economic factors are not well understood. The relationship between socioeconomic status (SES) and outcomes was evaluated using a prospective registry of patients presenting to the largest trauma hospital in Yaoundé, Cameroon.

Methods: Trauma patients(n=2855) visiting Central Hospital were surveyed regarding demographic and socioeconomic background, nature and severity of injuries, and treatment outcomes. A wealth score was estimated for each patient, corresponding to an index constructed from the urban Cameroonian Demographic and Health Survey. Logistic regression was used to evaluate the effects of SES on care-seeking behavior, injury severity, and treatment outcome.

Results: Patients aged 1-89 presented with road traffic injuries(59.8%), falls(7.76%), and penetrating trauma(6.16%), and had higher SES than the broader urban Cameroonian population. Within the Yaoundé sample, being in the lowest SES quintile was associated with an increased likelihood of having sought care elsewhere before presenting to the hospital(aOR=2.77, $p<0.001$), after controlling for background and injury characteristics. Patients in the lowest SES quintile were also more likely to present with moderate/severe injuries(aOR=5.41, $p<0.001$), and were more likely to be transferred to the operating room.

Conclusion: Patients presenting to this trauma center were wealthier than the broader community, suggesting the presence of potential barriers to care. Poorer patients were more likely to have severe injuries and more likely to need surgery, but were less likely to seek care immediately from a major trauma center.

Sunaina Kapoor, MS2 Mentor: Maunank Shah, MD

Public Health and Community Service

Cost-effectiveness of Isoniazid Preventative Therapy for HIV-infected pregnant women in India

Background: Pregnancy increases the risk of active Tuberculosis (TB) infection particularly in HIV-infected women. Co-infection can result in increased morbidity and mortality for both mother and child. Isoniazid preventative therapy (IPT) may reduce progression to active TB in HIV-infected individuals, but confers risks of drug toxicity in pregnant women and added costs. Globally, India has the highest incidence of TB and a high burden of HIV. The cost-effectiveness of IPT for HIV-infected pregnant women in India is unknown.

Methods: An economic evaluation was performed using a decision-analytic model to determine the cost-effectiveness of 6 months antepartum IPT among HIV-infected pregnant women (all assumed to be on anti-retroviral therapy) in India. We compared two prevention strategies with current practices in India (no IPT): Intervention 1 (IPT for all HIV-infected women regardless of CD4-count) and Intervention 2 (IPT for HIV-infected pregnant women with CD4-counts ≤200 cells/µl). Primary outcomes were anticipated costs, disability-adjusted life years (DALYs), active TB cases, and TB related deaths. Cost-effectiveness was represented using incremental cost-effectiveness ratios (ICERs).

Results: Both interventions were found to improve health outcomes compared to no IPT. Intervention 1 resulted in the greatest improvement in health outcomes with 21 TB cases averted per 1000 patients and 10 TB deaths averted per 1000 patients at an incremental cost of $20.26 per individual. Intervention 2 also showed improved health outcomes with 3 TB cases averted per 1000 patients and 2 TB deaths averted per 1000 patients at an incremental cost of $2.01 per individual. Both Intervention 1 and 2 were highly cost-effective compared to no IPT with ICERs of $177.72 and $201.00/DALYs-averted respectively, at a willingness-to-pay threshold of Indian per capita GDP ($1500/DALYs-averted).

Conclusion: Implementation of 6 months of IPT for HIV-infected pregnant women (regardless of CD4-count) is a highly cost-effective strategy for TB prevention compared to current practices in India.

Rabia Karani, MS2 Mentor: Aruna Chandran, MD MPH

Public Health and Community Service

Occupational Hazards to Ambulance Providers in Turbulent Settings in Low and Middle-Income Countries

Background: Ambulance providers in low and middle-income countries face many physical and psychological stresses. This study reviews the hazards faced by providers working in turbulent settings in low and middle-income countries, and also highlights specific dangers faced by providers in Karachi, Pakistan.

Methods: The first portion of this study was a systematic literature review of studies that reported hazards to ambulance providers operating in turbulent settings in low and middle-income countries. The initial search yielded 16643 studies, of which 48 studies described relevant data. The second portion of this study involved conducting in-depth interviews with 30 ambulance providers in Karachi, Pakistan. These providers were selected by convenience sampling and represented providers from one of two non-profit ambulance services, or from the emergency department at Aga Khan Hospital.

Results: Our review of the literature divulged five main categories of hazards. Threats to ambulance providers from attacks on ambulances were a key cause of mortality. Exposures to biological hazards, radiation, and accidents were also a significant contributor to morbidity. Psychiatric consequences such as PTSD and chronically high stress levels were seen in many providers. Misuse of ambulances to provide non-medical transport, or by rerouting from hospitals, led to significant loss of time for providers. Finally, work related conditions such as involvement of laypeople in accidents, low pay, poor roads, and an unbalanced lifestyle further contributed to hazards. These dangers were all present for ambulance providers in Karachi as well. However, a hazard unique to ambulance providers in Karachi was their duty to transport mentally ill people to asylums, without any medical assistance or support.

Conclusion: Our study highlights hazards to providers who are often the first line of care for patients. Our findings demonstrate a need for protection of ambulance providers in low and middle-income countries, both by pre-hospital care systems and local and international governments.

David J. Lee, MS2 Mentor: Haider, MD and Siddiqui, MD

Public Health and Community Service

Disparities in Patient Satisfaction based on Race, Gender, Education, and Payer Satatus

Background: Measurement of patient experiences with satisfaction scores has evolved as an objective measure of the quality of care. Patient satisfaction (PS) can influence adherence to treatment plans for patients and now influences pay-for-performance for providers. Research has shown that disparities exist in PS by demographic characteristics, but have not accounted for differences in response rate by demographics. This study analyzed disparities in PS while accounting for non-responders.

Methods: Press Ganey survey results for patients discharged form Johns Hopkins Hospital since 2008 were linked to administrative hospital data through a unique patient identifier. The data was dichotomized to top scores (5=top score; 1-4=not top score). A univariable analysis of top scores was performed for variables of interest such as race, gender, education, and payer status. This was followed by a multivariable logistic regression controlling for age, service, length of stay, severity of illness, along with the variables of interest. Weighting for non-response was done performing a logistic regression for predictors of response. These weights were then applied to the multivariable model for top scores.

Results: For the domain of questions that looked at physician care, African-Americans (.805-OR), females (.912-OR), patients with less than a (HS) education (.893-OR) and Medicaid patients (.784-OR) were all associated with greater dissatisfaction after weighing for non-response. In the domain of nursing care, African-Americans (.832-OR), females (.855-OR), and patients with less than a HS education (.898-OR) were all associated with lower top scores. All results were significant with a 95% confidence interval. These results were mostly reflected across all domains. Race and sex were the most important predictors of satisfaction.

Conclusion: PS scores continue to be lower among AA, female sex, Medicaid patients, and lower education patients. This study shows that disparities seen in satisfaction get slightly reduced after adjusting for variable response rates by different demographics.

Erina Lie, MS2 Mentor: Katherine Puttgen, MD

Public Health and Community Service

Propanolol Use in the Management of Infantile Hemangiomas

Background: Infantile Hemangioma (IH) is the most common neoplasm of infancy. Currently, there are no evidence-based guidelines for treatment. For decades, patients were managed only with high-dose corticosteroids when warranted until 2008 when propranolol was introduced and rapidly adopted. No studies have examined if age and morphology at presentation correlate with clinical choice of therapy or the latter's association with procedural management. This study aimed to determine if propranolol use is associated with younger patients, higher-risk lesions, and fewer laser and surgical interventions.

Methods: Retrospective cohort analysis on a sample of 155 patients aged 0-18yo with last clinical IH visit between January 2008 and February 2013. Hemangioma Severity Scale (HSS) and Hemangioma Dynamic Complication Scale (HDCS) were used to assess overall severity and complications severity, respectively. Demographics were compared using Fisher's exact and Kruskal-Wallis tests. We used multinomial logistic regression to determine associations between treatment choice and age at presentation, HSS, HDCS, laser, and surgical interventions.

Results: Patients on propranolol or observation present older than those on steroids or combination of propranolol and steroids (median 6.6months-old vs. 2.5months-old, p=0.0001). Adjusted for age, patients with higher severity had higher odds of receiving combination therapy (OR=1.46, 95%CI 1.14-1.86), propranolol (OR=1.23, 95%CI 1.03-1.46), and steroids (OR=1.18, 95%CI 1.02-1.36), and patients with more severe complications had higher odds of receiving steroids (OR=2.01, 95%CI 1.10-3.69). Patients on combination therapy were more likely to undergo laser (OR=6.60, 95%CI 1.37-31.8) and surgery (OR=5.88, 95%CI 1.23-28.2) relative to observed patients.

Conclusion: In our cohort, propranolol (combination and stand-alone) was used in patients with more severe lesions (size, location, complication, pain, and/or disfigurement risk) but fewer severe complications. Patients on propranolol were neither younger nor more likely to undergo procedures unless also treated with steroids. Future studies can explore treatment associations with outcome to further establish benefits of care and evidence-based therapy guidelines.

Sandra Lopez, MS2 Mentor: Joseph Lopez, MD

Public Health and Community Service

Impact of Conflict of Interest in Plastic Surgery: An Analysis of Research Outcomes

Background: Conflict of interest in medicine is defined as a "set of conditions in which professional judgment concerning a primary interest tends to be unduly influenced by a secondary interest". Concerns over conflict of interest remain, as it may influence patient care, clinical practice, and research. Studies in several fields have demonstrated that industry funding is associated with the publication of manuscripts with positive findings. This association has not been fully explored in plastic surgery. The purpose of our study is to assess whether commercial funding in plastic surgery is associated with the publication of a positive outcome in established literature.

Methods: Manuscripts in three major plastic surgery journals published from January 2013 to January 2014 were reviewed in this study. Articles outlining basic science and clinical research were included. Reviews, anatomical studies, case reports, brief communications, technical notes, editorials, and ethics commentaries were excluded. Articles included in the study were classified based on surgical subspecialty, self-reported conflict of interest, level of evidence, and study design. Included abstracts were blinded and analyzed by three experts who graded the reported findings as positive, negative, neutral, or not applicable. Discrepancies in the grading of a study outcome were resolved by consensus. Statistical analysis was used to assess whether commercial funding is associated with a positive outcome.

Results: Analysis is currently in progress, it is clear there is a limited amount of articles that have reported having conflict of interest.

Conclusion: Currently in progress and will be dependent upon final results. Some limitations of this study include that only three journals were reviewed and the fact that inherent bias may exist amongst the experts who subjectively graded the reported research findings. It would be helpful to include a larger array of articles. Further research analyzing the impact of conflict of interest on plastic surgery outcomes is needed.

Sally Mahmoud, MS2 Mentor: Jonathan Golub

Public Health and Community Service

Assessing Minneapolis efforts to treat refugee, immigrant, and US Born patients for Latent Tuberculosis: a retrospective cohort study

Background: The global health community has pledged to eliminate tuberculosis as a public health problem. Despite the advancement that has been made in TB control, we are still far from eradicating the disease. In order to combat tuberculosis, we must target the reservoir of latently infected patients. Reactivation of latent TB represents >70% of new cases of active TB cases in the US.

Methods: Our objective was to determine the proportion of refugees, immigrants, and US born patients at Hennepin County Public Health Clinic (HCPHC) successfully completing latent tuberculosis infection (LTBI) treatment, and to identify factors associated with treatment completion (i.e. diagnostic tool, age, gender, treatment regimen, etc.) We completed a retrospective cohort analysis of individuals who received LTBI care at HCPHC for between April 1, 2011 and March 31, 2014.

Results: Among 900 patients diagnosed with LTBI, X% of refugees, Y% of non-refugee foreign-born, and Z% of US-born patients completed LTBI treatment. In multivariate analysis, refugees/immigrants/US born had greater/lesser odds of LTBI treatment completion (Adjusted Odds Ratio X; 95 % CI X-Y $p < 0.001$) adjusting for age, gender, and treatment regimen.

Conclusion: These results suggest that LTBI treatment completion is excellent/subpar at HCPHC. Efforts to improve LTBI care should be tailored to different risk groups at HCPHC.

(The results and conclusions are still in progress)

Andres Mallipudi, MS2 Mentor: Kathleen Page, MD

Public Health and Community Service

Caregiver Administration of Non-Prescription Antibiotics to Children in Baltimore's Latino Population

The increased prevalence of antibiotic use and the rise of multi-drug resistant bacteria comprise some of the world's leading public health concerns. The cause of this medical dilemma is multifactorial, but one of the primary contributors is the injudicious dispensing and use of antibiotics. The Latino population is well known to consume antimicrobial drugs at increased rates, compared to other ethnic groups, as a result of their cultural preferences with regards to antibiotics. This phenomenon has also been shown to result in an increase in Latino parents' desire for antibiotics from their children's pediatricians. However, whether Latino parents are more likely to obtain and use non-physician obtained antibiotics (NPOAs) to treat their children remains unknown. This project aims to determine whether Latino parents are more likely to provide or suggest the use of NPOAs to their children compared to non-Latino parents. The lack of research on NPOA administration to children in the United States necessitates the creation of a validated question set on this topic. The survey questions regarding the participants' use of antibiotics, perceptions and knowledge of antibiotic usage, and history of NPOA administration to their children were developed with the aid of infectious disease, pediatric, and public health experts. Questions regarding demographic information will be based on previously validated surveys that were used in our target populations. The validated survey resulting from the project will be used to generate data on the rates of NPOA administration in Baltimore's Latino and non-Latino adult caregiver population, and correlate these findings to their and their children's education level, household income, access to healthcare, immigration status, and various other demographic indicators.

Anita Ram, MS2 Mentor: Margaret Chisolm, MD

Public Health and Community Service

Predictors of Cigarette Smoking Reduction among Pregnant, Drug Dependent Women

Background: Smoking cigarettes during pregnancy is extremely common among opioid-dependent women, with nearly 95% reported to smoke during pregnancy. Despite the widespread prevalence, cigarette smoking is often under-addressed in this population. The purpose of this study was to determine the factors associated with successful cigarette smoking reduction among opioid-dependent pregnant women.

Methods: This study is a secondary data analysis of opioid-dependent pregnant women (N=118) enrolled in a randomized controlled trial of a contingent behavioral incentive (CBI) shaping schedule. We dichotomized participants into the "successful reduction" group (SR group) or the "non-successful reduction group" (NSR group) based on whether they were able to meet a smoking reduction target of 50% or greater. We then used SPSS to run independent T samples tests and chi-squared tests to compare groups.

Results: Participants in the SR group had significantly higher CO levels at baseline ($p=0.039$), less cocaine use in the past 30 days at baseline ($p=0.022$), and fewer lifetime attempts to quit smoking ($p=0.016$). With regards to treatment characteristics, participants in the SR group were more likely to be in the CBI study arm of the trial ($p=0.019$), have lower CO levels at delivery ($p<0.001$), and were more active in the trial. Participants in the SR group attended more days of treatment ($p=0.043$) and provided more urine samples ($p=0.014$).

Conclusion: The results from this study suggest that incentive programs for smoking reduction are helpful, but other factors may contribute to successful smoking reduction such as cocaine use at baseline, smoking levels at baseline, lifetime quit attempts, and willingness to participate in the study. Future interventions should target opioid-dependent women who were less successful in smoking reduction, perhaps through the addition of more potent incentives, pharmacologic treatments, more frequent monitoring, and/or intensification of substance abuse treatment for women who concurrently use cocaine.

Anu Ramachandran, MS2 Mentor: Maunank Shah, MD PhD

Public Health and Community Service

Evaluating the Cost Effectiveness of Implementing CRAG-LFA as a Screening Tool for Cryptococcal Meningitis among HIV patients in Uganda

Background: Cryptococcal meningitis (CM) constitutes a significant source of mortality in resource-limited regions. One million cases occur annually, representing 10-30% of HIV-related death in prevalent regions. Between hospitalization, monitoring, and medications, CM is an extremely difficult opportunistic infection to manage. Mortality remains high due to late diagnosis, suggesting a need for early diagnostic intervention.

Recently, the cryptococcal antigen lateral-flow assay (CRAG-LFA) was developed to detect cryptococcal antigen in serum. Important questions remain about how to implement CRAG-LFA to maximize screening capability and cost-effectiveness. We seek to establish cost-effectiveness of CRAG screening in Uganda and explore clinical and epidemiological factors contributing to optimal implementation.

Methods: A decision-tree model was constructed to compare three strategies in our cohort (HIV+ Ugandans with CD4<100): Standard of care (no screening), intervention with CRAG-LFA screen followed by treatment, and primary prophylaxis. Costs were based on estimates from Uganda. Effectiveness of each intervention was measured in disability-adjusted life years (DALYs) and assessed on cost per DALY averted, or incremental cost-effectiveness ratio (ICER).

Results: CRAG-LFA screening cost $1.48 more than standard of care and $226 less than primary prophylaxis and reduced the rate of cryptococcal-associated mortality by over 40% vs. standard of care and 15% vs. primary prophylaxis.

CRAG-LFA screening was associated with an ICER of $5.88 per DALY averted, making it extremely cost-effective. Several modeled situations reduced the ICER to cost-saving levels below zero.

Conclusion: CRAG-LFA screening is extremely cost-effective with the potential to prevent significant morbidity from CM in vulnerable populations. It improved CM detection by 70% and reduced mortality by 40% while increasing costs by less than $2.00 per patient. Furthermore, the barriers to implementation in a rural clinic are relatively low, as the test does not require training, a cold chain, or consistent power supply. Together, this provides strong evidence for the implementation of CRAG screening in these settings.

Samantha Roman, MS2 Mentor: Emily Frosch, MD

Public Health and Community Service

Attitudes and Experiences of Internal Medicine Residents in Managing Comorbid Medical and Psychiatric Disorders

Background: Although primary care physicians are increasingly responsible for managing patients' psychiatric disorders, many feel ill-equipped to treat psychiatric disorders due to a lack of medical knowledge, clinical experience, and communication skills. Furthermore, identification and treatment of psychiatric disorders varies widely by provider. This study examined experiences and attitudes of internal medicine residents regarding ambulatory patients with comorbid medical and psychiatric disorders in order to inform residency training program development.

Methods: An anonymous survey was piloted within the Johns Hopkins Medicine-Pediatrics residency program, and subsequently administered in-person and on-line to residents in the Johns Hopkins Osler and Bayview Internal Medicine residency training programs August 2014-November 2014. Respondents used Likert scales to indicate their level of agreement with various statements regarding management of psychiatric disorders.

Results: 42 residents (33.1%) responded to the survey. Residents approximated that nearly 40% of their ambulatory patients have been diagnosed with ≥1 psychiatric disorders and, varying by diagnosis, these disorders have a moderate to great impact on patients' other medical problems. Almost all residents agree they are expected to identify psychiatric disorders in their ambulatory clinics; 85% and 57.5% agree they are expected to treat psychiatric disorders with pharmacological and non-pharmacological therapies, respectively. Yet, nearly two-thirds feel that too little time is devoted to mental health training in their program, and many, particularly those who have not had a psychiatry rotation, consider a lack of confidence in identifying and treating psychiatric disorders barriers in their clinical practice. Additional barriers were identified by residents, several of which are significantly different between programs.

Conclusion: Our results suggest that internal medicine residents may benefit from additional psychiatric training, which could be customized to address barriers specific to each program. However, this study is limited by the small sample size and relatively low response rate, and may not be generalizable outside of Johns Hopkins.

John Schulz, MS2 Mentor: Scott Berkowitz, MD, MBA

Public Health and Community Service

Medicare Accountable Care Organizations' Public Reporting and Composition of Shared Savings Plans

Background: When accountable care organizations (ACOs) in the Medicare Shared Savings Program (MSSP) achieve their cost and quality goals, they may share in the savings with Medicare. However, actual shared savings plan composition and other ACO characteristics remain relatively unexplored.

Methods: Key ACO descriptive characteristics were abstracted from publically available websites for all 338 active MSSP ACOs launched through January 2014. Performance Year 1 results were then analyzed for 2012 and 2013 ACOs to assess for associations between the generation of savings and ACO characteristics or shared savings plan features. For comparisons of categorical variables a chi-square test was used and for comparisons of means an unpaired t test was utilized.

Results: Of current MSSP ACOs, 313/338 (93%) maintain a website which includes composition and other organizational details, and 284/338 (84%) provide at least basic commentary regarding a shared savings plan. 176 /338 (52%) reported detailed allocation percentages; 81/338 (24%) suggested plans were "to be determined". On average, ACOs reporting detailed allocations planned to give 63% (range: 0-100%, SD=26.3) to participants and 33% (range: 0-100%, SD=25.6) to infrastructure. ACOs including hospitals planned to give a larger average percentage to participants than those without (69% vs. 58%, p=0.01). Based on year 1 MSSP results, ACOs planning to give >50% to providers were more likely to have generated savings (p=0.03) as were ACOs with >10 participants (p=.009).

Conclusion: Most MSSP ACOs are meeting CMS reporting requirements. While shared savings plans vary widely, those that distribute a majority of their savings to providers, and those with greater than 10 participants, were more likely to have generated savings. Although there may be no single model for ACO success, continued investigation of predictors for generating savings may inform future shared savings models.

Arnav Srivastava, MS2 Mentor: Adil Haider, MD

Public Health and Community Service

Exploring Health Care Provider Perspectives on Pain Management in the Emergency Department

Background: A rich and growing literature exists regarding significant racial disparities in pain management in the emergency department (ED). Furthermore, preliminary data collected from the Johns Hopkins Hospital in 2013 found Black patients more likely to be discharged with high pain scores. While racial disparities in outcomes and implicit racial bias have been established, the causal pathways linking these two themes have yet to be explored. Our study's goal is to clarify these mechanisms by which provider bias may influence pain treatment approach and contribute to disparities in pain management.

Methods: Qualitative research was conducted by engaging twenty providers at the Johns Hopkins Hospital ED, including physicians, nurses, and physician assistants, in in-person, semi-structured interviews. After completion, at least two study team members transcribed and manually coded (using Microsoft Word and ATLASti) each interview. Then identification of emergent themes related to pain management strategy, use of opioids, factors related to pain reporting and thematic analysis generated the results portion of the study.

Results: Four major themes have emerged from preliminary analysis the data: 1) Providers view the numerical pain scale (0 -10) as unreliable and providers often dismiss high scores reported by patients; 2) past negative experiences with healthcare and providers, particularly with minority patients, may cause patients to exaggerate their pain reporting in subsequent visits; 3) provider believe that they may unconsciously distrust patients who visually appear to be lower socioeconomic class or lower education; 4) the demographic differences between Johns Hopkins providers and their patients may impede communication and rapport building in the provider-patient encounter.

Conclusion: This study explores a needed understanding of the provider experience that may contribute to racial disparities in pain management in the ED. Further initiatives to qualitatively study the patient pain management experience and quantitatively study some of the emergent themes from this project should be conducted.

Sharif Vakili, MS2 Mentor: Michael Boland

Public Health and Community Service

A Comparison of Systems to Measure Patient Flow through Ambulatory Clinics

Background: Understanding how patients move through outpatient clinics is essential to offering high quality care to a large and ever-increasing patient population. This study compares the costs, benefits, and challenges of two methods for measuring patient flow: 1) a commercial Radio Frequency Identification-Infrared (RFID-IR) system that does not require active patient cooperation and 2) a custom-built, low cost, networked Radio Frequency Identification (RFID) system that requires patients to swipe at proximity card readers located throughout the clinic.

Methods: Readers for both the RFID-IR and RFID systems were installed throughout the clinic. A total of 112 patients presenting to the General Eye Service of the Wilmer Eye Institute were given both RFID-IR and RFID tags. Investigators simultaneously recorded the times at which patients moved in, out, or between rooms. These measurements were considered the standard against which the other methods would be compared.

Results: One hundred twelve patients generated a total of 252 events over the course of 6 days. Both the RFID-IR and RFID systems recorded accurate times compared with the manual recordings as there was no statistically significant difference between the 3 measurements ($p>0.05$ for all comparisons).

The proportion of events correctly recorded by the RFID system (83.7%) was significantly greater than that obtained with the RFID-IR system (75.4%, $p<0.001$). The cause of the missing events using the RFID-IR method was found to be a signal interruption with a front desk transponder. Excluding those data, the RFID-IR system correctly recorded 94.4% of events ($p=0.002$; OR= 3.83 compared to the RFID system).

Conclusion: We found that both RFID and RFID-IR methods are effective at providing patient flow information. The custom-made RFID system was as accurate as RFID-IR and was installed at 10% the cost. Given its significantly lower cost, the RFID option may be appropriate for smaller clinics with more limited budgets.

Tim Xu, MS2 Mentor: N/A

Public Health and Community Service

Public Attitudes toward Rationing of End-of-Life Care by Medicare

Background: About one-quarter of the United States Medicare budget is spent on services for patients in their final year of life. “Rationing” of end-of-life care has attracted heated political debate, as popularized by discussion of "death panels."

Methods: We fielded an online survey among a nationally politically- and demographically-representative sample of 1,000 Americans through the nonpartisan research firm YouGov (October 1-3, 2014). Multivariable logistic regression was used to analyze responses while accounting for age, gender, political identification, race, income, and region. Statistically-significant odds ratios (means) are reported.

Results: Most respondents (79.3%) believed that Medicare should not be able to “ration” spending on end-of-life care. Compared to the 18-29 age group, the 45-64 (OR 0.33) and 65+ (OR 0.41) age groups were less likely to support “rationing”; political identification was not an independent predictor of response. Those who believed that it is too difficult to get necessary care through Medicare were less likely to support “rationing” (OR 0.21). Most respondents believed that Medicare is in immediate financial crisis (29.5%) or that it will be in financial crisis within the next 20 years (54.5%). Compared to Democrats, Independents (OR 2.96) and Republicans (OR 2.08) were more likely to believe that Medicare is currently in financial crisis. Responses regarding the future of Medicare funding were not associated with views on “rationing.”

Conclusion: Respondents who were worried about the care they might receive through Medicare (i.e. believe that it is difficult to receive necessary care) were much less likely to support “rationing” of end-of-life care. Political affiliation was not associated with rationing. When educating the public about Medicare and value-based healthcare, greater care should be taken to separate non-political (e.g. “rationing”) from political issues (e.g. the stability of future Medicare funding).

Tim Xu, MS2 Mentor: Sean Berenholtz MD MHS

Public Health and Community Service

The Surgical Unit-based Safety Program (SUSP) to Reduce Surgical-Site Infections

Background: Surgical-site infections (SSIs) lead to excess morbidity, mortality, and costs. Adapted from the Comprehensive Unit-based Safety Program (CUSP), the AHRQ-funded national Surgical Unit-based Safety Program (SUSP) is a multifaceted intervention designed to prevent SSIs. Participating hospitals educate frontline providers, identify and learn from local defects in safety, partner with a senior executive, and introduce teamwork and communication tools. We report preliminary results from SUSP, now implemented in 195 hospitals across 37 states.

Methods: SUSP is being rolled out sequentially among five cohorts of hospitals in a stepped-wedge cluster design. SSIs in participating hospitals are recorded using the Centers for Disease Control (NHSN) or American College of Surgeons (NSQIP) standardized definitions. We compared baseline and post-intervention SSI rates using the Fisher's exact test and regression models adjusting for hospital characteristics (e.g. size, setting). A difference-in-differences regression model was also used to compare changes in SSI rates to those of a concurrent, non-intervention cohort.

Results: We analyzed data reported using NHSN for 15,126 colon surgeries performed between July 2011 and June 2014; data collection for non-colon surgeries was introduced in later cohorts and is ongoing. SSI rates declined from 5.3% at baseline to 3.5% post-intervention (p=0.001). Among the 84 hospital service lines reporting post-intervention data, 41 showed lower SSI rates post-intervention, 29 were unchanged, and 14 saw an increase in SSIs (Figure). SUSP implementation was associated with a non-significant decrease in SSI rates post-intervention compared to baseline (RR=0.85, p=0.16). In the difference-in-differences model, the post-intervention risk was lower, though not significant (RR=0.62-0.72, p=0.08). Analysis of a smaller group of hospitals reporting data through NSQIP produced similar results.

Conclusion: Preliminary analysis suggests that implementation of SUSP was associated with lower SSI rates, but not after accounting for concurrent controls. Further analysis is needed after additional data collection through August 2015.

Tim Xu, MS2 Mentor: Martin Makary, MD MPH

Public Health and Community Service

Hospital Cost Implications of Increased Utilization of Minimally-Invasive Surgery

Background: Minimally-invasive surgery (MIS) is associated with decreased postoperative complications for common procedures, yet hospital utilization of MIS by procedure varies widely across the United States. We designed a study to calculate the projected cost savings associated with increased MIS utilization.

Methods: We created regression models to compare the costs, length of stay, and risk of complications associated with open and MIS appendectomy, colectomy, and lung lobectomy procedures from the 2010 National Inpatient Sample. Regression parameters were used to project national cost, hospital day, and complication savings based on scenarios in which patients who underwent open surgery were simulated to receive MIS.

Results: MIS cost less than open surgery (mean savings per discharge (95% CI): appendectomy =-$1,528 (-$1,685 to -$1,370), colectomy=-$7,507 (-$8,197 to -$6,816), and lobectomy=-$6,290 (-$7,811 to -$4,769). Savings directly attributable to the decreased risk and cost of complications in MIS procedures were -$668 (43.7%) for appendectomy, -$5,097 (67.9%) for colectomy, and -$2,944 (46.8%) for lobectomy. If lower-MIS hospitals were to increase their utilization to the median utilization of the top tertile (83rd percentile), there would be 4,306 fewer complications, 169,819 fewer hospital days, and $337 million in savings each year. If all hospitals were to increase their utilization by 50%, the estimated savings would be 3,578 fewer complications, 144,853 fewer hospital days, and $288 million.

Conclusion: Increased MIS utilization would result in up to $280-340 million in savings, not including the cost of hospital readmission. Low MIS utilization represents an opportunity to reduce complications and healthcare costs through more appropriate division of labor among surgeons and additional training in MIS technique. The advent of Value-Based Purchasing and global payment schemes will shift the cost burden of complications from payers to hospitals; more appropriate utilization of MIS will allow hospitals to improve publicly-reported patient outcomes and increase profit margins.

Tracy Yang, MS2 Mentor: Joel Gittelsohn, PhD

Public Health and Community Service

Process Evaluation Findings of B'More Healthy Communities for Kids: A Multi-Level, Multi-Component Obesity Prevention Program

Background: B'More Healthy Communities for Kids (BHCK) is a multi-level, multi-component obesity prevention trial directed toward low-income African American youth in Baltimore. BHCK works with small food stores, recreation centers, carryout restaurants, wholesalers, policymakers and families. Participants include youth and adult caregivers residing within one mile of intervention recreation centers.

Methods: Process evaluation is conducted by monitoring 88 implementation standards based on reach, dose delivered and fidelity. Process evaluation data were collected using a number of instruments tailored to each component of the intervention. Guidelines rank each standard in terms of low, medium or high delivery. Main outcome measures consist of comparison of process measures with set standards created by each working group.

Results: Here, we report on findings to date based on two feedback periods. Food store interactive sessions had low reach to the target audience (10-14 year old youth) with 7.4 + 6.2 interactions/session compared to higher reach for adults (17.1 + 6.6). Dose delivered of food samples (28.5 + 14.4) and giveaways (16.2 + 6.2) distributed was medium to high. Carryout restaurant menu redesign obtained medium to high fidelity with 20% healthy side options and 10% healthy entrée options provided on posted menu boards. Recreation centers achieved high reach with 11.6 + 6.1 youth attending educational sessions. The agent-based policy model (ABM) had low to medium reach with one local policymaker including the ABM on a formal agenda in the past year. Wholesalers obtained overall high fidelity by stocking food items that met BHCK nutrition guidelines. Social media and text messaging achieved high reach with 70% of BHCK-enrolled families joining the program.

Conclusion: These findings are used to monitor and modify components during the trial and to assess implementation quality post-intervention. Recommendations for intervention include increased reach of the target population and continued outreach to policymakers with the ABM.