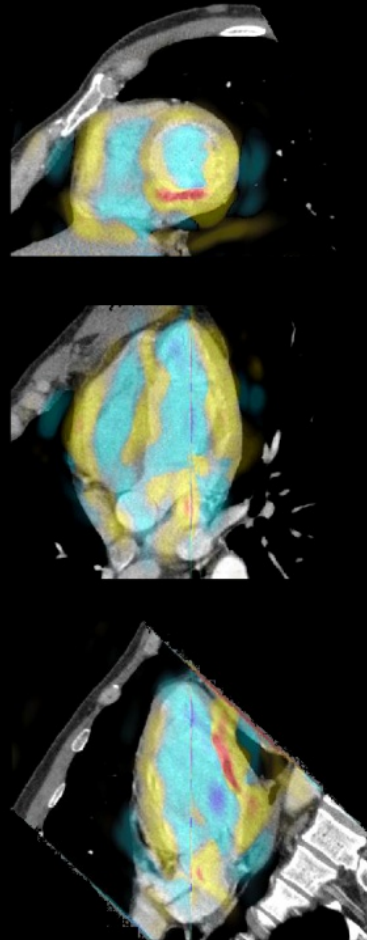


5th Annual Medical Student Research Day



January 24, 2013
Johns Hopkins University School of Medicine
Armstrong Medical Education Building

Cover image courtesy of
Liwei Jiang, MS2

Pictured: A computed tomography (CT) reconstruction of the heart is accompanied by cross-sectional views of myocardial strain, a key measure of heart function.

Cardiovascular disease remains the leading cause of death worldwide, but modern imaging techniques continue to improve detection, monitoring, and outcomes. Advances in motion estimation, a CT image processing technique, have made it possible to improve image quality while reducing radiation dose to the patient. Our laboratory is developing a computational algorithm that employs motion estimation data to calculate myocardial strain, an index of myocardial contractility that quantifies heart function. By displaying the results as semitransparent color maps superimposed upon the short-axis and the two long-axis CT views of the heart, this approach hopes to equip clinicians with a precise yet intuitive tool to assess cardiac health.

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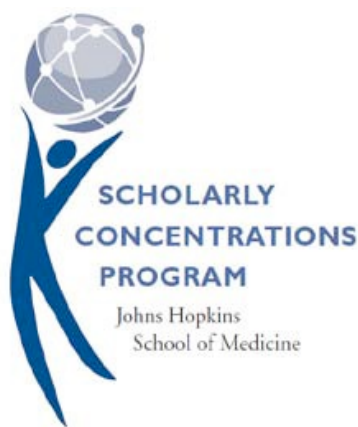
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Medical Student Research Day 2013

We are pleased to have you join us for the 5th 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 four 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	Jon Lorsch, PhD
Clinical Research	Kelly Gebo, MD, MPH Jennifer Haythornthwaite, PhD Steve Sozio, MD, MHS John J. Strouse, MD, PhD
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 <i>AMEB Main Lobby</i>
12:30-2:15 PM	Podium Presentations <i>AMEB Lecture Hall</i>
2:15-3:45 PM	Poster Session <i>AMEB 2nd Floor</i>
3:45-4:45 PM	Concurrent Oral Presentations <i>RM320, 326, 341, 342, 343, 344, 345, 370</i>
4:45-5:30 PM	Keynote speaker, <i>Dr. Charles Limb</i> MSRD Award Ceremony <i>AMEB Lecture Hall</i>

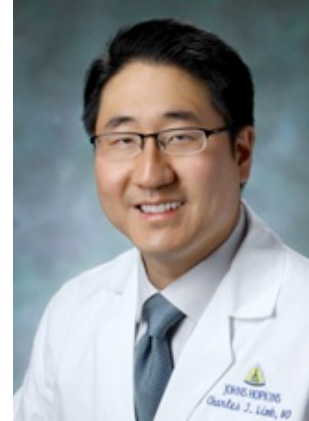
KEYNOTE SPEAKER

Charles J. Limb, MD

*Associate Professor of Otolaryngology-Head & Neck Surgery at
the Johns Hopkins University School of Medicine*

Faculty, Peabody Conservatory of Music

*Director of Research, Neuroeducation Initiative at the Johns
Hopkins University School of Education*



Charles Limb is a true renaissance man who combines his passion for otolaryngology and neuroscience with his love for music to study music perception in deaf individuals with cochlear implants and the neural basis of musical improvisation and creativity. He holds a joint appointment in the Johns Hopkins School of Medicine Department of Otolaryngology-Head and Neck Surgery where he specializes in neurotology and skull base surgery, and the Peabody Conservatory of Music.

Dr. Limb received his undergraduate degree at Harvard University, obtained his medical degree at Yale University School of Medicine and completed his surgical training at Johns Hopkins Hospital. He then completed postdoctoral research fellowships with David Ryugo at the Johns Hopkins Center for Hearing Sciences where he studied the development of the auditory brainstem, and with Allen Braun at the National Institutes of Health where he used functional neuroimaging methods to study neural mechanisms of music production and perception.

Dr. Limb's research on how the brain works during musical improvisation have greatly contributed to our understanding of brain activity underlying human creativity. He is the editor-in-chief of *Trends in Amplification*, the sole journal focusing on auditory amplification devices and hearing aids. He also serves on the editorial board of the journals *Otology and Neurotology* and *Music and Medicine*. His work has been featured by National Public Radio, TED, National Geographic, Scientific American, PBS, the New York Times, CNN, the Library of Congress, Canadian Broadcasting Company, Baltimore Symphony Orchestra, the American Museum of Natural History, and the Smithsonian Institute.

Faculty Judges

Hanan Aboumater, MD, MPH
Assistant Professor of Medicine

Eric Bass, MD, MPH
Professor of Medicine

Jaishri Blakeley, MD
Assistant Professor of Neurology

Mary Catherine Beach, MD, MPH
Associate Professor of Medicine

Zachary Berger, MD, PhD
Assistant Professor of Medicine

Henry Brem, MD
Professor and Chairman of Neurosurgery

Andrew Cameron, MD, PhD
Assistant Professor of Surgery

Joseph Carrese, MD, MPH
Associate Professor of Medicine

Colleen Christmas, MD
Assistant Professor of Medicine

Janice Clements
Professor of Comparative Medicine,
Neurology, Pathology

Sarah Clever, MD, MS
Assistant Professor of Medicine

David Cooke, MD
Associate Professor of Pediatrics

Elizabeth Dzeng, MD, MPH
Fellow in General Internal Medicine

David Friedman, MD, MPH, PhD
Professor of Ophthalmology

Khalil Ghanem, MD, PhD
Associate Professor of Medicine

Kelly Gebo, MD, MPH
Associate Professor of Medicine

Gail Geller, ScD
Associate Professor of Pediatrics

Jeremy Greene, MD
Associate Professor of
the History of medicine

James Handa, MD
Professor of Ophthalmology

Marta Hanson, PhD
Associate Professor of
the History of Medicine

Adam Hartman, MD
Assistant Professor of
Neurology and Pediatrics

Jennifer Haythornthwaite, PhD
Professor of Psychiatry

Craig Hendrix, MD
Professor of Medicine

Mark Hughes, MD, MA
Assistant Professor of Medicine

Lisa Ishii, MD
Assistant Professor of Facial Plastic and
Reconstructive Surgery

Michael Johnston, MD
Professor of Neurology, Pediatrics and
Physical Medicine & Rehabilitation
Senior Vice President and Chief Medical
Officer, KKI

Thomas Koenig, MD

Assistant Professor of Psychiatry
Associate Dean for Student Affairs

Mariana Lazo-Elizondo, MD, PhD, MPH

Assistant Professor of Medicine

Michael Lim, MD

Assistant Professor of Neurosurgery

Jon Lorsh, PhD

Professor of Biophysics and
Biophysical Chemistry

Nisa Maruthur, MD, MHS

Assistant Professor of Medicine

William Matsui, MD

Associate Professor of Oncology

John W. McDonald, MD, PhD

Associate Professor of Neurology and
Physical Medicine & Rehabilitation
Director of International Center for Spinal
Cord Injury

Graham Mooney, PhD

Assistant Professor of
the History of Medicine

Lawrence Nogee, MD

Professor of Pediatrics

Randy Packard, MD

Professor of the History of Medicine

Ben Ho Park, MD, PhD

Associate Professor of Oncology

Kalpana Prakasa, MD

Assistant Professor of Medicine

Lorraine Racusen, MD

Professor of Pathology

Tariq Shafi, MD, MHS

Assistant Professor of Medicine

Steve Sozio, MD, MHS

Assistant Professor of Nephrology

John J. Strouse, MD, PhD

Assistant Professor of Hematology

Patricia Thomas, MD

Associate Professor of Medicine
Associate Dean for Curriculum

Sarah Wheelan, MD, PhD

Assistant Professor of Oncology
Biostatistics and Bioinformatics

Schedule of Podium Presentations

12:30 pm	Joani Christensen, MS3	<i>Using Monocytes Loaded with Indocyanine Green for Non-Invasive Imaging of Cutaneous Inflammatory States</i>
12:40 pm	Aditi Vasan, MS2	<i>Use of Multidisciplinary Services to Address Family Psychosocial Needs at a Pediatric Primary Care Clinic</i>
12:50 pm	Matthew Murrill, MS2	<i>From Panacea to Poison: the Emergence of Groundwater Arsenic Contamination in West Bengal</i>
1:00 pm	Ryan Shields, MS2	<i>Translating a U.S. Medical Curriculum Abroad: A Study on Cultural Dissonance in International Education</i>
1:10 pm	Alessa Colaianni, MS3	<i>A long shadow: Nazi doctors, moral vulnerability, and contemporary medical culture</i>
1:20 pm	Carol Li, MS3	<i>Does BRAF V600E Mutation Predict Aggressive Features in Classic Variant Papillary Thyroid Cancer: Results from Four Endocrine Surgery Centers</i>
1:30 pm	Dannielle McBride, MS2	<i>Provider Beliefs Surrounding Implementation and Sustainability of a Chronic Kidney Disease Registry</i>
1:40 pm	Howard Choi, MS2	<i>Cost-Effectiveness of Xpert MTB/Rif for diagnosing pulmonary tuberculosis in the United States</i>
1:50 pm	Jacob Ruzevick, MS3	<i>Erlotinib inhibits growth in a primary mouse xenograft model of chordoma</i>
2:10 pm	Lauren Thomaier, MS2	<i>Assisted Reproductive Technology: Is There a Biological Plausibility for Increased Risk In Autism Spectrum</i>

Schedule of Concurrent Oral Presentations

Basic Science: Room 320

3:45-3:55 pm	Eugene Shenderov	<i>Tryptophan residues in the hydrophobic channels of human CD1d molecules modulate glycolipid loading and presentation to invariant NKT cells</i>
3:55-4:05 pm	Tamara Ashvetiya	<i>Implantable Bioreactors for the Delivery of Stem Cell-Derived Cytokines to the Post-Infarct Heart</i>
4:05-4:15 pm	John Cooper	<i>Determining the Role of Cytotoxic Necrotizing Factor-1 in the Pathogenesis of Urinary Tract Infections</i>
4:15-4:25 pm	Maimon Hubbi	<i>Lysosomal Degradation of HIF-1alpha Represents a Novel Therapeutic Target</i>
4:25-4:35 pm	Riaz Nadir Gillani	<i>Tumor DNA detection to monitor the response of BRCA-less tumors to PARP1 (poly ADP ribose polymerase) inhibitors</i>

Clinical Research 1: Room 326

3:45-3:55 pm	Claire Zachik	<i>Variability in Rates of Structured Developmental Screening across a Large Primary Care Organization</i>
3:55-4:05 pm	Mays Ali	<i>Poverty Kills: Socioeconomic Disparity in Inpatient Mortality Following Traumatic Injury in Adults</i>
4:05-4:15 pm	Jaleesa Jackson	<i>Overutilization of Chlamydia Tests Among Older Women in an Urban, High Prevalence City</i>
4:15-4:25 pm	Sunitha Suresh	<i>Frailty is Associated with an Increased Risk of Falls in Dialysis Patients of All Ages</i>
4:25-4:35 pm	Sarah K. Wallace	<i>Quantifying the Effect of Cardiopulmonary Resuscitation Quality on Cardiac Arrest Outcome: A Systematic Review and Meta-Analysis</i>

Clinical Research 2: Room 341

3:45-3:55 pm	Hiten Patel	<i>Racial and Sex Disparities in the Treatment of Small Renal Masses</i>
3:55-4:05 pm	Hiten Patel	<i>Comorbidities and Causes of Death in the Management of Small Renal Masses: A SEER-Medicare Analysis</i>
4:05-4:15 pm	Shekhar Gadkaree	<i>Metastatic Brain Tumor Survival and Recurrence by Primary Tumor</i>
4:15-4:25 pm	Joshua Watson	<i>Efficacy of the Orally Delivered, Anti-Parasitic, Mebendazole, in an Intracranial Rodent Gliosarcoma Model</i>
4:25-4:35 pm	Aaron Wild	<i>Concurrent versus sequential sorafenib therapy in combination with radiation for hepatocellular carcinoma</i>

Clinical Research 3: Room 342

3:45-3:55 pm	Emma McDonnell	<i>Patterns of Post-Operative Spirometry in Lung Transplantation</i>
3:55-4:05 pm	Lauren Reader	<i>Association of Uric Acid and Left Ventricular Hypertrophy in Pediatric Hypertension</i>
4:05-4:15 pm	Qing Lina Hu	<i>Endocarditis is Significantly Associated with Patent Foramen Ovale in Patients with Left Heart Valve Procedures</i>
4:15-4:25 pm	Cecillia Lui	<i>Mutations in Alström Protein Promote Persistent Postnatal Cardiomyocyte Replication in Multiple Families</i>
4:25-4:35 pm	Kevin Contrera	<i>Rates of long-term cochlear implant use in children</i>

Clinical Research 4: Room 343

3:45-3:55 pm	Michael Brener	<i>Epicardial Fat is Associated with Duration of Antiretroviral Therapy and Coronary Atherosclerosis in the Multicenter AIDS Cohort Study</i>
3:55-4:05 pm	Justin Bellamy	<i>Severe infectious complications following frontal sinus fracture: the impact of operative delay and peri-operative antibiotic use</i>
4:05-4:15 pm	Julie Ng	<i>IgE-Independent Hypersensitivity Reactions are Associated with Prolonged Survival in Advanced Pancreatic Cancer Patients Receiving a GM-CSF Cell-Based Vaccine plus Cyclophosphamide (Cy) and Cetuximab</i>
4:15-4:25 pm	Eric Dein	<i>Nerve Injury after Total Shoulder Arthroplasty</i>
4:25-4:35 pm	Shiv Gaglani	<i>Using Commercial Activity Monitors to Measure Gait in Patients with Suspected iNPH: Implications for Ambulatory Monitoring</i>

History of Medicine/Public Health: Room 344

3:45-3:55 pm	Julia Cromwell	<i>Autopsy and the Influenza Epidemic at Johns Hopkins Hospital, 1918</i>
3:55-4:05 pm	Kristopher A Kast	<i>The shapes of Proteus: mental illness in English case literature of the 17th and 18th centuries</i>
4:05-4:15 pm	Fidel A. Desir	<i>Survey of partner notification practices for sexually transmitted infections in the United States</i>
4:15-4:25 pm	Erin Hayward	<i>Multi-level influences on environmental health in public housing</i>
4:25-4:35 pm	Samuel Michel	<i>Establishing a rural community health worker training program in San Juan Sacatepequez, Guatemala</i>

Public Health: Room 345

3:45-3:55 pm	Kathryn Miele	<i>QuantiFERON-TB Gold In-Tube Implementation for Latent Tuberculosis Diagnosis in a Public Health Clinic: A Cost-Effectiveness Analysis</i>
3:55-4:05 pm	Joseph Klembczyk	<i>Importance of Environmental Conditions in Lusaka, Zambia's Seasonal Cholera: A Mathematical Analysis</i>
4:05-4:15 pm	William Acosta / Harita Shah	<i>Mortality and long-term virologic outcomes in children and infants treated with LPV/r-based therapy in Panama</i>
4:15-4:25 pm	Yu Tung Wang	<i>Inguinal hernia repair using mesh: the impact of international short-term surgical training in Ghana</i>
4:25-4:35 pm	Wuroh Timbo	<i>Risk Factors for Seclusion and Restraint in a Pediatric Psychiatry Day Hospital</i>

Medical Humanities/Medical Education: Room 370

3:45-3:55 pm	Rhianon Liu	<i>"Am I cut out for this?:" A qualitative analysis of doubt among first year medical students"</i>
3:55-4:05 pm	Rhianon Liu	<i>Doubt among future doctors: a survey of first year medical students</i>
4:05-4:15 pm	Carter Neugarten	<i>At Ease and Dis-ease: Patient Requests for Reassurance</i>
4:15-4:25 pm	Samuel Enumah	<i>Perceptions of short term medical aid in the Dominican Republic: Voices of host community members</i>
4:25-4:35 pm	Tyler Mains	<i>Isolating the impact of Audience Response Systems on learning.</i>

POSTER PRESENTERS

AMEB 2nd Floor

Listed Alphabetically by Research Category

BASIC SCIENCE

#	Name	Title
1	Samiran Bhattacharya	Effect Of Mir141 Expression Modulation On Bladder Cancer Invasive Potential
2	Zachary Cordner	Investigating Morpholino Oligonucleotides As A Novel Approach To The Treatment Of Huntington's Disease
3	Adam Diehl	Investigating The Two-Pronged Role Of HEYL In Breast Cancer Angiogenesis.
4	Jacqueline Douglass	Quantitative Phosphoproteomic Analysis Of The PTEN Signaling Pathway
5	Laurette Fernnou	Evaluation Of The Effects Of Sodium Salicylate On Anemia In Aged Mice
6	Inna Grishkan	Helper T Cells Downregulate CD4 Expression Upon Chronic Stimulation
7	Liwei Jiang	Cardiac Function Analysis Using A 4D Motion Estimation Algorithm For Computed Tomography
8	Nikhil Jiwrajka	Identification Of External Factors That Affect The Fidelity Of Eukaryotic Start Codon Recognition
9	Ian-James Malm	PD-1 Blockade Combined With TEGVAX (TLR Agonists-Enhanced GVAX) Can Induce Regression Of Established Palpable Tumors
10	John Marshall	Matrix Metalloproteinase Expression In Cavity Tissue In A Rabbit Model Of Post-Primary Tuberculosis
11	Ji Qi	The Effect Of Fibroblast Identity On Induction Of Keratin 9 Gene In Human Epithelial Keratinocytes
12	Kanika Trehan	N-Acetylcysteine Enhances Cystic Fibrosis Sputum Penetration And Airway Gene Transfer By Highly Compacted DNA Nanoparticles

13	Vinson Wang	Pelvic Nerve Injury Leads To Marked Changes In Adrenergic And Cholinergic Signaling In The Vagina And Bladder
14	Risheng Xu	Behavioral Effects Of Cocaine Are Mediated By Nitric Oxide-GAPDH Transcriptional Signaling
15	Patricia Zadnik	Bioluminescence As A Surrogate Marker Of Functional Decline In Metastatic Disease

CLINICAL RESEARCH

#	Name	Title
16	Christopher R. Bailey	Quality Of Life Outcomes Associated With Nipple Sparing Mastectomy And Breast Reconstruction
17	Basak Basdag	Postoperative Outcomes And Quality Of Life (QOL) Of Planned Vs. Unplanned Vascular Delay (VD) In Free Flap Breast Reconstruction Surgery
18	Wendy Chen	Long-Term Follow-Up Of Children Treated With The Modified Atkins Diet
19	Wendy Chen	Clinical And Neuropathological Correlates Of Apathy In Alzheimer's Disease (AD)
20	Janet Choi	Long-Term Use Of Cochlear Implants In Older Adults
21	Jason E Cohen	Pediatric Extirpative Renal Surgery: A 12-Year Experience In Maryland
22	Jason E Cohen	Trends In Renal Surgery: Robotic Technology Is Associated With Increased Utilization Of Partial Nephrectomy
23	Nathan Cutler	Auditory Force Feedback Substitution Improves Surgical Precision During Simulated Ophthalmic Surgery
24	Jacob K. Dey	Facial Reanimation Surgery Restores Affect Display
25	Allen Feng	Efficacy Of Sorafenib Combined With Doxorubicin Eluting Bead-Transarterial Chemoembolization For Patients With Unresectable Hepatocellular Carcinoma
26	Shiv Gaglani	Using Commercial Activity Monitors To Measure Gait In Patients With Suspected Inph: Implications For Ambulatory Monitoring

27	J. David Gatz	Pre-Hospital Rapid Sequence Intubation Is Associated With Decreased Mortality In Pediatric Trauma Patients
28	Tiffany Ho	Generational Difference Between Baby Boomers And Silent Generation: Chronic Diseases, Painful Conditions, And Complementary And Alternative Medicine (CAM) Use
29	Minh-Phuong Huynh-Le	Involved Field Radiation Therapy For Hodgkin Lymphoma: Treatment Outcomes At The Johns Hopkins Hospital
30	Kathleen Jee	VEGF Secreted By Hypoxic Müller Cells Promotes MMP-2 Expression In Neighboring Endothelial Cells In Proliferative Diabetic Retinopathy
31	Yike Jin	Local Delivery 2-Deoxy-D-Glucose As A Possible Therapeutic Option: A Preclinical Study
32	Danielle Jones	Outcomes For Upper Eyelid Loading For Treatment Of Paralytic Lagophthalmos
33	Rohan Joshi	Sacral-Alar-Iliac Fixation In Pediatric Deformity: 2 - 5 Year Follow Up
34	Derek Ju	Spinal Surgery For Metastatic Epidural Spinal Cord Compression (MESCC) From Breast And Prostate Cancer Provides Functional Benefits Despite Differing Pathology-Specific Characteristics And Prognosis
35	Saami Khalifian	Trainee Application Appraisal "Just Google It"
36	Bilal Khan	Are Hospitals With Poorer Financial Vitality Treating A Larger Proportion Of Minority Patients?
37	Jennifer Kim	Immediate And Follow-Up Results For 44 Consecutive Cases Of Small (<10mm) Internal Carotid Artery Aneurysms Treated With The Pipeline Embolization Device
38	Alexandra Kornbluh	Challenges In Translating Evidence Into Practice: Pulse Oximetry Policy Implementation In The NICU
39	Joe Lin	Outcomes After Early Treatment Of Cauda Equina Syndrome
40	Stephanie McLaughlin	Correlation Of Menstrual Cycle Phase And Infection Risk In Women Exposed To N. Gonorrhoeae
41	Yuliya Mints	Single Nucleotide Polymorphisms In Proximity To K-Channel Genes Are Associated With Decreased Qtc Variance
42	Kara Mirski	Motor And Cognitive Delay In Duchenne Muscular Dystrophy: Implication For Early Diagnosis

43	Andrew Mo	BMI – Is It Still A Predictor Of Mortality Outcomes In Lung Transplantation Patients Post-Implementation Of The Lung Allocation Score (LAS)?
44	Huzefa Mogri	Incidence Of Donor Derived Malignancies In Post-Transplantation Cyclophosphamide Treatment During Hematopoietic Stem Cell Transplantation
45	Carolyn Mulvey	Increased Flap Weight And Decreased Perforator Number Predicts Fat Necrosis In DIEP Breast Reconstruction
46	David Narotsky	The Relationship Between 25-OH Vitamin D And Peripheral Artery Disease
47	Mira A. Patel	Survivorship After Surgical Resection For Cancer: The Need For Continued Surgical Follow-Up
48	Hiten Patel	Comorbidities And Causes Of Death In The Management Of Small Renal Masses: A SEER-Medicare Analysis
49	Michelle Peng	Three-Dimensional Magnetic Resonance Analysis Of Extraocular Muscles Demonstrates Gaze-Specific Contractile Shape Changes.
50	Lydia Powell	Influence Of Battlefield Military Research On Civilian Trauma Practices: A National Survey
51	Varun Puvanesarajah	Surgical Treatment Of Scoliosis In Osteogenesis Imperfecta Patients May Improve Quality Of Life Compared To Non-Surgical Management
52	Eric Sankey	Long-Term Outcomes Of Fractionated Conformational Radiotherapy In Patients With Meningiomas Of The Cavernous Sinus
53	April N. Sharp	Increased Inpatient Burden And Neurosurgical Demand In Premature Infants With Intraventricular Hemorrhage
54	Jean Suh	Assessment Of Skin Color Patterns And Associated Lifestyle Factors In African-Americans Using Tristimulus Colorimetry
55	Kevin V. Tran	An Efficacy Evaluation Of The Low-Cost Quantum Catch Fundus Camera In Screening For Diabetic Retinopathy
56	Kanika Trehan	Increased Post-Operative Smoking Among Lung Cancer Patients Undergoing Video-Assisted Thoracic Surgery (VATS) Compared To Open Thoracic Surgery
57	Chiedozie Uwandu	Factors Associated With Increased Incidence Of Motor And Sensory Deficits In Patients Who Undergo Meningioma Resection
58	Joanna Wang	Impact On Seizure Control Of Surgical Resection Or Radiosurgery For Cerebral Arteriovenous Malformations

HISTORY OF MEDICINE

59	Timour Al-Khindi	"Too Frankly Human And Not Strict Science": A Tale Of Psychiatry And Eugenics At Johns Hopkins Hospital
60	Robin Bigelow	Cesarean Section Rates And Indications In The Early 20th Century: A Look Through Dr. J. Whitridge Williams' Lens
61	Lena Delle Caron	An Historical Look At Rex Morgan, Md, A Comic Strip That Has Won Readers Over For Its Entertainment And Medical Education
62	Michael Daniel	A History Of Hospital Infection Control: The Study On The Efficacy Of Nosocomial Infection Control
63	Radu Dudas	The Use Of Illustrations In 13th And 14th Centuries Medieval Surgical Manuscripts
64	Andrew Layman	Physician-Explorers And The Maturation Of The Field Of Polar Medicine During The Heroic Age Of Antarctic Exploration (1897-1920).
65	Emily Miller	The History Of Women In Orthopaedic Surgery And Their Impact On The Field
66	Brent C. Pottenger	How Did Care For Intimate Partner Violence (Ipv) Victims Evolve Into An Orthopaedic Medical Issue? Historical Perspective On The Medicalization Of Ipv In Orthopaedic Surgery

MEDICAL EDUCATION: AMEB 1st Floor

#	Name	Title
67	Morgan Broccoli	First Response For The Austere Medical Environment (FRAME)
68	Jonathan Dattilo	Collaboration In Pre-Clinical Medical Education: Crowdsourced Test Content And User-Friendly Software
69	Kanika Trehan	T.H.E. Gooseman: A Simulator For Transhiatal Esophagectomy

MEDICAL HUMANITIES, BIOETHICS, and the HEALING ARTS

#	Name	Title
70	Taylor DesRosiers	Medical Vignettes: The Experience Of A Medical Student
71	Veronica Hocker	Portrayal Of The Pregnant Woman In Popular U.S. Media: A Content Analysis
72	Megan Hosein	Peer Health Workers And HIV Care: How Can Phws Help Reach And Influence At-Risk HIV Patients In Rural Uganda?
73	Pooja Singal	Effective Interventions For Obesity Prevention Across Settings: An Overview Of Federal Guidelines And Current Evidence Base
74	Heather Walls	Asking Awkward Questions: A Survey Of Knowledge, Skills, Attitudes, And Practice Of Sexual History Taking In Johns Hopkins Faculty And Medical Students

PUBLIC HEALTH and COMMUNITY SERVICE

#	Name	Title
75	David Bernholt	Mortality Among Marathon Runners In The United States, 2000-2009
76	Onyinyechi Eke	Integration Of Environmental Assessments Into A Mass Active Case Finding Program In Klerksdorp, South Africa.
77	Nellie Farrow	Improving Emergency Department Throughput By Reducing Unnecessary Orthopedics Consultations
78	José Flores	Ethnic Disparities Persist In The Field Of Plastic And Reconstructive Surgery: An Analysis Of A Large Post-Mastectomy Prospective Cohort
79	Ran Li	Outcomes Of Patients With Eloquent Glioblastoma
80	Tatyana Lyapustina	The Epidemiology And Ecology Of Cholera In Bangladesh: A Reflection
81	Arielle Medford	Development And Cost Implications Of Quality Of Care Indicators For Occupational Injuries
82	Nicky Mehtani	Pilot Study Of "The Evergreen Project," An Attempt To Create Systematic Healthcare Change

83	Sidharth Puri	Impact Of Surgical Video Review In Resident Cataract Surgery
84	Karthik Rao	Factors Associated With Survival And Recurrence For Patients Undergoing Surgery Of Cerebellar Metastases
85	Emma Steinberg	Eating Habits Of Adults In Samborondon, Ecuador
86	Amanda Sun	Modeling The Impact Of Alternative Strategies For Rapid Molecular Diagnosis Of Tuberculosis In Southeast Asia
87	Jeremy Tanner	Effectiveness Of A Multicomponent Care Coordination Intervention On Dementia Caregivers In The Community - A Randomized Control Trial
88	Shannon Walker	Hospital Recommendations To Reduce The Infant Mortality Rate In South Los Angeles
89	Yuqi Wang	Medicare Advantage Chronic Special Needs Plan Effect On Long-Term Nursing Home Utilization
90	J.Corey Williams	Using Stories To Improve Patient Health Education In A Patient-Centered Medical Home Setting
91	Xin Zhou	Maternal And Child Health Outcomes From The Family Spirit Intervention

2012 MSRD Student Awardees

HANSEN BOW

Henry Strong Denison Research Scholar

Microchip-based intracranial temozolomide delivery in a 9L rat glioma model

JACOB RUZEVICK

Harold Lampert Research Scholar

The Haptoglobin 2-2 gene is associated with increased aneurysm formation in a novel model of aneurysm formation

ANNE VAN BEUNINGEN

W. Barry Wood Research Scholar

The role of GDE2 in motor neuron maintenance and survival

MARTHA BRUCATO

Excellence in Medical Student Research

Community Adolescent Sexuality Education (CASE) Program Needs Assessment and Curriculum Update

YARDEN FRAIMAN

Excellence in Medical Student Research

Identification of a Flt-3 Ligand surge in pediatric leukemia patients receiving myelosuppressive therapy.

VALERIE GORDON

Excellence in Medical Student Research

Conditional knockout of Kir4.1 in NG2 cells of the adult brain

ALEXANDER JENSON

Excellence in Medical Student Research

Gender and performance of Community Treatment Assistants in Tanzania

ALLISON KAEDING

Excellence in Medical Student Research

MLL Rearrangement and Age at Diagnosis Are Strongly Associated with High Level Surface FLT3 Expressions and Ex Vivo Sensitivity to FLT3 Inhibition: A Prospective Analysis of 54 Consecutive Infants with ALL.

BRIAN LEE

Excellence in Medical Student Research

External validation of postoperative nomogram for early prostate cancer recurrence following radical prostatectomy

STUART MITCHELL

Excellence in Medical Student Research

Loeys-Dietz Syndrome Affects Bone Microarchitecture

ANGELINE NGUYEN

Excellence in Medical Student Research

Impact of home- and community-based service use on nursing home placement in persons with probable Alzheimer's disease

RALPH PASSARELLA

Excellence in Medical Student Research

Capturing Patient Input on Patient Safety via Novel Machine Learning Tool

AMAR SRIVASTAVA

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Comparisons of features of double-positive disease with anti-GBM disease and ANCA-associated vasculitides

SHARON WEEKS

Excellence in Medical Student Research

Is the Kampala Trauma Score An Effective Predictor of Mortality in Low-Resource Settings? A Comparison of Multiple Trauma Severity Scores

Acknowledgements

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PODIUM PRESENTATION ABSTRACTS

Listed Alphabetically

Cost-Effectiveness Of Xpert MTB/Rif For Diagnosing Pulmonary Tuberculosis In The United States

Background: Among the challenges in worldwide tuberculosis (TB) control is the lack of rapid, accurate diagnostic tests. Cepheid Xpert MTB/Rif™ (Xpert) is a fully automated molecular diagnostic test for TB, offering highly sensitive and specific results within two hours. Although use of Xpert is known to be cost-effective for low- and middle-income countries with endemic TB, the instrument's costs and cost-effectiveness in a high-income country with low TB prevalence such as the United States is unknown. We sought to evaluate the costs and cost-effectiveness of incorporating the Xpert molecular test into TB diagnostic algorithms in the US, compared to existing approaches (sputum microscopy, clinical diagnosis, liquid culture).

Methods: A decision-analysis model compared current TB diagnostic strategies in the US to possible diagnostic strategies incorporating Xpert. Epidemiologic and diagnostic parameters were obtained from the literature; testing costs were obtained by direct observation in mycobacterial laboratories. Cost-effectiveness was represented using quality-adjusted life years (QALYs) and Incremental Cost-Effectiveness Ratios (ICERs).

Results: The cost of Xpert was calculated to be \$98.10 per specimen. Implementation of Xpert testing would increase laboratory costs to \$256 per TB suspect (vs. \$158 without Xpert). However, Xpert testing of a single sputa from TB suspects is expected to reduce total healthcare costs per TB suspect (\$2,673) compared to diagnostic algorithms using only sputum microscopy and culture (\$2,728), and lead to improved health outcomes (6.32 QALYs gained per 1000 TB suspects). Compared to existing molecular assays, implementation of Xpert in the US would be considered highly cost-effective (ICER of \$39,992 per QALY gained).

Conclusion: Despite an initial increase in laboratory costs, TB diagnostic algorithms using Xpert were overall highly cost-effective. This finding, combined with Xpert's high sensitivity, specificity, and speed, supports consideration of Xpert for possible inclusion into tuberculosis diagnosis strategies in the United States.

Using Monocytes Loaded With Indocyanine Green For Non-Invasive Imaging Of Cutaneous Inflammatory States

Background: Distinguishing infection from sterile inflammation currently relies upon subjective interpretation of clinical parameters and microbiologic data combined with nonspecific imaging. Assessing characteristic variations in leukocytic infiltration could provide more specific information. Homing of systemically administered monocytes tagged using the only FDA-approved near infrared dye, indocyanine green (ICG), may be assessed non-invasively using clinically-applicable laser angiography systems to investigate cutaneous inflammatory processes.

Methods: RAW 264.7 mouse monocytes were coincubated with ICG solution. Fluorescence was confirmed microscopically. Homing ability of loaded cells was assessed in vitro using a microplate chemotaxis assay. Labeled cells were injected systemically into mice with induced sterile inflammation (Complete Freund's Adjuvant inoculation) or infection (Group A Streptococcus inoculation) of the hind limb. Whole animal near infrared imaging was completed using a near-infrared laser. Fresh frozen tissue from the area of inoculation was examined microscopically for fluorescence.

Results: Loaded cells were highly fluorescent in the near infrared range. In vitro, loaded cells retained ability to chemotax toward monocyte chemoattractant protein-1 ($p < 0.01$). Following intravascular injection of loaded cells, whole animal imaging revealed local fluorescence at the inoculation site, with significantly different fluorescence ratios in the infection and inflammation model as early as 2 hours after injection ($p < 0.01$) and the difference becoming more pronounced as time progressed. Microscopic examination of locally inflamed tissue revealed punctate areas of fluorescence, consistent with the presence of ICG-loaded cells.

Conclusion: Whole animal near infrared imaging following systemic injection of indocyanine green-loaded monocytes can distinguish cutaneous infection from sterile inflammation. Development of a minimally invasive technique to rapidly image inflammation may lead to new tools to distinguish infectious from sterile inflammatory conditions at the bedside.

Podium Presenter, Medical Humanities, Bioethics, and the Healing Arts

A Long Shadow: Nazi Doctors, Moral Vulnerability, And Contemporary Medical Culture

Background: More than 7% of all German physicians became members of the Nazi SS during World War II, compared with less than 1% of the general population. In so doing, these doctors willingly participated in genocide, something that should have been antithetical to the values of their chosen profession. The participation of physicians in torture and murder in numerous historical instances both before and after World War II is a disturbing legacy seldom discussed in medical school, and under-recognized in contemporary medicine. This research sought to answer the unsettling question: is there something inherent in being a physician that promotes a transition from healer to murderer?

Methods: I read original historical documents as well as histories of Nazi medicine, bioethics and eugenics, visited historical Holocaust sites in Berlin, Krakow, and Auschwitz, attended lectures and discussions about contemporary medical ethics, and reflected on my own experiences with medical culture to identify the key components of medical culture that aided Nazi physicians in their almost unfathomable transition from healers to effectors of genocide. With this historical background in mind, I defined and delineated moral vulnerabilities endemic to contemporary medical culture, and assessed how they were relevant to the Nazi physicians during the Holocaust.

Results: I identified six distinct moral vulnerabilities present within contemporary medical culture that were also contributing factors to so many Nazi physicians' decisions to participate in the Holocaust. These include: the hierarchical nature of medicine, clinical detachment, comfort inflicting pain, use of medical terminology and euphemism, career ambition, and the license to commit acts that would otherwise be considered criminal.

Conclusion: Though nearly all physicians want to save lives and promote health, there are aspects of medical culture that can paradoxically pave the way for us to act immorally and unethically. Being aware of these deleterious aspects will make us safer doctors.

Does BRAF V600E Mutation Predict Aggressive Features In Classic Variant Papillary Thyroid Cancer: Results From Four Endocrine Surgery Centers

Background: Evidence is controversial regarding the association between BRAF mutation and aggressive features such as central lymph node metastases (CLNM) in patients with papillary thyroid cancer (PTC). Despite this, some propose that BRAF be utilized in the management algorithm of PTC. Importantly, no study has incorporated multiple surgery centers that perform routine CLND for PTC and thus have patients who are truly evaluable for the presence of CLNM.

Methods: Consecutive patients with classical PTC who underwent total thyroidectomy and CLND as part of routine practice at 4 tertiary endocrine surgery centers were retrospectively reviewed. BRAF mutation status was determined by pyrosequencing. Standard bivariable analyses examined demographic, patient, and tumor-related factors. Multivariate logistic regression controlling for gender, age, size, extrathyroidal extension (ETE), surgical margin involvement, lymphovascular invasion (LVI) and multifocality examined the odds of CLNM associated with BRAF mutation.

Results: 314 individuals, of whom 238 underwent prophylactic and 76 underwent therapeutic CLND, were eligible for study. 252 (80.3%) patients were positive for the BRAF mutation. 59.1% of BRAF positive vs. 51.6% of BRAF negative patients had CLNM ($p=0.28$). Bivariable analysis demonstrated no significant relationship between positive BRAF mutation and gender, age, tumor size, multifocality, LVI, surgical margin involvement, lateral lymph node metastasis, ETE, or TNM stage. In multivariate analysis, BRAF mutation was not associated with CLNM. Multivariate analysis including only factors available preoperatively (BRAF mutation, age, gender, and size) also showed no significant correlation between BRAF mutation and CLNM.

Conclusion: This is the first multi-institutional study that included only patients who underwent routine CLND and examined the association of BRAF mutation and aggressive features of PTC. Results show that with classical PTC, BRAF mutation is not an independent predictor of CLNM and may not be useful for guiding surgical management. Prospective studies are needed before BRAF mutation analysis should be incorporated into a surgical algorithm.

Dannielle McBride, MS2

Mentor: Delphine Tuot, MD; Deidra Crews, MD; Eric Bass, MD

Podium Presenter, Public Health and Community Service

Provider Beliefs Surrounding Implementation And Sustainability Of A Chronic Kidney Disease Registry

Background: Chronic kidney disease (CKD) is a major public health concern, affecting over 20 million Americans. There is suboptimal delivery of guideline-concordant CKD care in the United States. CKD registries, as an example of team-based care, may offer one way to enhance CKD management. Since primary care providers (PCPs) deliver most CKD care in the US, we sought to (1) explore PCP attitudes and beliefs about CKD registries and team-based CKD care and (2) determine key facilitators of implementing a CKD registry in safety-net primary care.

Methods: We conducted semi-structured interviews of 20 PCPs representing all 16 primary care clinics in the San Francisco Community Health Network (SFCHN), an integrated delivery health care system that serves San Francisco's publicly insured and uninsured residents. An iterative grounded theory approach was used to code transcripts, resulting in a refined set of themes that reached thematic saturation.

Results: Overall, PCPs felt that a CKD registry would aid them in providing high quality care to CKD patients, particularly if it tracked patients who fell out of care or had progressive CKD and provided routine feedback on CKD metrics. Facilitators for successful implementation included changes in clinic flow and employing non-physician health care providers. PCPs cautioned that the unique complexities of CKD, such as differing treatments based on etiology, might limit the benefit of a CKD registry. Nonetheless, they stated that a CKD registry conformed with current primary care priorities such as the provision of team-based care, patient empanelment and participation in quality improvement initiatives would be ideal.

Conclusion: While most PCPs believed that CKD registries could enhance the quality of CKD care, they were cautious about its widespread use because of the complexities of kidney disease. Successful implementation of CKD registries as a means to provide greater guideline-concordant CKD care will require careful attention and PCP champions.

From Panacea To Poison: The Emergence Of Groundwater Arsenic Contamination In West Bengal

Background: Starting in 1966, the widespread drilling of tubewells in India promised to sustain the burgeoning Green Revolution and provide access to microbiologically safe drinking water for thousands of communities across the country. This triumphant utilization of groundwater, however, unexpectedly drew up the naturally present contaminant arsenic particularly in the region of West Bengal. Clear, colorless, odorless, and tasteless, this poison was consumed unknowingly in communities for years before it manifested itself through the characteristic clinical symptoms of chronic exposure in Punjab in 1976, in West Bengal in 1983, and received domestic and international attention in the mid 1990s. It was claimed in 2000 that this tragedy was the world's largest environmental disaster, worse than the radioactive fallout of Chernobyl and the industrial disaster at Bhopal. This study explores the emergence of ground water arsenic as a public health problem in Bengal as well as the Government response to this emerging disaster, including its interactions with media outlets, academic institutions, and international organizations.

Methods: Archival research was conducted at the School of Environmental Studies – Jadavpur University (Kolkata, West Bengal, India) from June to August 2012. Additionally, oral histories were recorded for 11 Indian academics, public health engineers, politicians, reporters and clinicians central to the history of groundwater arsenic in the region.

Results: Three key factors shaped Government response and the public's perceptions of the ground water problem in Bengal: the etiological nature of the source of contamination, the predominance of technocratic solutions, and the fear of widespread panic.

Conclusion: An appreciation for the emergence and mitigation of groundwater arsenic in Bengal provides an important context to understand the current environmental situation in the region and a key event in the history of 20th century water supply programs.

Erlotinib Inhibits Growth In A Primary Mouse Xenograft Model Of Chordoma

Background: Targeting the epidermal growth factor receptor (EGFR) inhibits growth of chordoma.

Chordoma is a tumor that arises in the skull base or sacrococcygeal regions. The prognosis is approximately 6-years. To date, there has never been a study showing efficacy of a chemotherapeutic agent nor is there an FDA approved compound for the treatment of chordoma.

Methods: The patient xenograft was serially passaged in mice. Immunohistochemistry was performed for chordoma markers EMA, S100, AE1/AE3, Ki-67 and brachyury as well as for EGFR. The activity of receptor tyrosine kinases (RTKs) was assessed using a human RTK array. Flow cytometry was completed using a BD-FACSCalibur flow cytometer and analyzed with Flowing Software. Single Nucleotide Polymorphism analysis was completed using the Illumina Human 1M BeadChip. Sequencing of EGFR was completed by PCR. Celltiterglo was used for IC50 analysis. For in vivo experiments, Erlotinib was delivered by oral gavage to mice with the chordoma xenograft. Control mice received a vehicle control. To determine the mechanism of inhibition, an EGFR phosphorylation array was used on treated and control tumors.

Results: The chordoma xenograft maintained the histological, and immunohistological characteristics as the parent tumor as both were diffusely positive for EMA, S100, AE1/AE3, Ki-67 and brachyury. The genomic profile showed no copy number amplifications. EGFR was the most activated of 71 kinases studied despite flow cytometry showing 10% of cells expressed EGFR. Sequencing showed no amplification or activating mutations in EGFR. Erlotinib had the lowest IC50 of all EGFR inhibitors tested. In repeated in-vivo studies, there was a significant difference in the size of tumors treated with Erlotinib versus vehicle (633 vs 2000 mm³, p=0.0002). Mechanistically Erlotinib inhibited phosphorylation of Tyr845 of the EGFR protein.

Conclusion: Targeting EGFR with Erlotinib inhibits growth in chordoma. This is the first study that shows a proof of concept for an effective chemotherapeutic for chordoma.

Translating a U.S. Medical Curriculum Abroad: A Study on Cultural Dissonance in International Education

Background: There has been ample research regarding the experience of minorities and international students in medical schools around the world, but little research has examined the impact of the recent exportation of medical curricula to other countries. Johns Hopkins University School of Medicine (JHUSOM) recently partnered with Perdana University Graduate School of Medicine (PUGSOM) in Kuala Lumpur, Malaysia and implemented the Genes to Society (GTS) curriculum currently in use at JHUSOM in Baltimore. This study explored the perspectives of the first-year medical students currently at PUGSOM focusing on issues of cultural dissonance in their relationships with professors, adapting to the GTS curriculum, and the teaching of patient-doctor communication in a multi-cultural, multi-lingual society.

Methods: In-depth semi-structured interviews with the first class of first-year students at PUGSOM (n=23) were conducted. All interviews were audio recorded. Recordings were subsequently transcribed, independently coded by two reviewers and analyzed for major themes.

Results: Several major themes were identified and included adjusting to an American pedagogy and adapting to the friendliness and openness of the professors. The most prominent theme was the interactivity expected in the classroom and the transition from a “passive” to an “active” learning environment. Students noted that “[PUGSOM] is a whole new, different culture and now we are adapting to the culture.” Clinical teaching involving open-ended questions, patient-centered interviews, and a strong patient-doctor relationship were almost universally accepted by students and deemed appropriate for a Malaysian context. However, many noted that this open communication was often not seen during their clinical experiences in the community due to physician time constraints.

Conclusion: While Malaysian graduate medical students may come from a more passive pedagogical background, they almost uniformly supported an American style curriculum and felt they could confidently apply the lessons and strategies used in clinical teaching when seeing patients in Malaysian clinics.

Assisted Reproductive Technology: Is There A Biological Plausibility For Increased Risk In Autism Spectrum Disorders (ASD)?

Background: Assisted reproductive technologies utilize multiple laboratory interventions to generate a cohort of embryos capable of implantation and development. One such intervention, ovarian stimulation, results in significant changes in the hormonal environment in utero, which persist during peri-implantation. Recent epidemiologic evidence suggests that the high hormonal milieu required for ovulation induction is associated with ASD in the offspring. In this study, using a mouse model, we examine the effect of the peri-implantation hormonal milieu on transcriptomic changes in the fetal cortex.

Methods: Blastocysts from naturally mated mice were flushed and transferred non-surgically into the uteri of pseudopregnant recipients following either natural mating (NM) or mating following treatment with gonadotropins (SO). On post-coital day 17.5, recipient dams were sacrificed. Fetal cortical brain tissue was processed. Microarray analysis was performed on 38 fetal brain samples representing n=3 NM and n=8 SO litters. Ontology studies on transcriptomic data were performed. Confirmatory QPCR was done on genes that exhibited differences between the groups.

Results: Through ontology data analysis, superovulation appeared to affect neuronal migration, neuronal differentiation, regulation of neuronal death and neuronal morphogenesis. 15 targets, which exhibited 1.5 or more log change between the groups, were identified. Of those, genes involved in neuronal migration and differentiation demonstrated statistical significance ($p < 0.05$).

Conclusion: Peri-implantation maternal hormonal milieu appears to have a direct effect on fetal brain development. Although the specific molecular and cellular mechanisms leading to these observations remain to be elucidated, this line of investigation is important in order to understand the pathophysiology of adverse neurological outcomes following assisted reproduction.

Use Of Multidisciplinary Services To Address Family Psychosocial Needs At A Pediatric Primary Care Clinic

Background: Family psychosocial needs can adversely impact children's health, but it is often challenging for physicians to address these needs in the primary care setting. Primary care clinics in high-need communities can address this challenge by incorporating co-located multidisciplinary services targeted to families' needs. This study evaluated the impact of on-site multidisciplinary services at an urban pediatric primary care clinic on families' perceptions of the clinic and adherence to well child care.

Methods: Over a 3 month period, caregivers of patients presenting to the clinic were interviewed regarding their use of and satisfaction with 12 on-site programs. The interview included validated tools assessing caregivers' satisfaction and perception of the clinic as a medical home. Healthcare utilization data was obtained from patient records. Descriptive statistics were used to characterize participating caregivers, and t-tests were used to compare caregiver satisfaction and health care utilization patterns for families who used fewer vs. more than three clinic services.

Results: The majority of the 80 participating caregivers were female (91%), African-American (89%), and had children who were Medicaid insured (84%). Ninety percent of caregivers had used at least one clinic service, and 42% had used three or more. Use of 3 or more clinic services was associated with higher mean satisfaction with the clinic (mean: 31.8 vs. 31.0, $p < 0.05$) and a stronger perception of the clinic as a medical home (mean: 97.6 vs. 93.4, $p < 0.01$). Use of 3 or more services was also associated with an increased number of missed well child care visits (mean: 0.49 vs. 0.20, $p < 0.05$).

Conclusion: Use of the multidisciplinary services at an urban pediatric primary care clinic was associated with greater caregiver satisfaction and increased perception of the clinic as a medical home. Caregivers who utilize many services may face more significant barriers to accessing care, and further integration of co-located services may be needed to improve adherence with well child care.

ORAL PRESENTATION ABSTRACTS

Listed Alphabetically

Oral Presenter, Public Health and Community Service

Mortality And Long-Term Virologic Outcomes In Children And Infants Treated With LPV/R-Based Therapy In Panama

Background: The WHO recommends that all HIV-infected infants receive HAART, and that PIs are used in children previously exposed to NNRTIs. However, there are few studies of young children receiving PI-based therapy in real life resource-limited settings, and data on the timing of HAART initiation among children who survive infancy is scant. Our aim was to evaluate outcomes at the Hospital del Niño, Panama, where since 2002 children below 3 years of age are routinely treated with LPV/r-based therapy, regardless of immunologic status.

Methods: Retrospective cohort analysis of all HIV-infected children enrolled in care between January 1, 1991 and June 1, 2011. Kaplan-Meier method and Cox proportional hazards regression were used to evaluate death, virologic suppression (VL < 400), and virologic rebound.

Results: Of 399 children contributing 2,248 person-years of follow-up, 254 (63.2%) were treated with LPV/r and 95 (23.7%) were never treated with ARVs. Median enrollment age was 0.84 years. Among children who enrolled in care at < 1 year, infant mortality was lower in HAART-treated versus untreated children (22.8/100 py, 95% CI 10.2-50.7 vs. 92.4/100 py, 95% CI 70.4-121.2). In multivariate analysis, improved survival was associated with male gender (HR 0.56, 95% CI 0.33 to 0.96) and treatment with HAART (HR 0.32, 95% CI 0.12 to 0.83). Among children who survived to 1 year of age without HAART, subsequent treatment with LPV/r-based HAART improved survival (HR death 0.07, 95% CI 0.02 to 0.35) compared to no treatment, while the effect of non-LPV/r HAART (HR death 0.32, 95% CI 0.07 to 1.48) did not reach statistical significance. Among children receiving LPV/r, virologic suppression was achieved in 42.1%, 70.5%, and 85.1% by 12, 24 and 60 months of follow up. In multivariate analysis, virologic suppression was not associated with prior exposure to ARVs or age at initiation of therapy. Virologic rebound occurred in 13.5%, 22.2%, and 39.1% of children at 12, 24, and 60 months following initial suppression. No children who achieved virologic suppression after initiating LPV/r died.

Conclusion: Infant mortality was higher in girls, even after adjustment for early HAART. Non-CD4-guided initiation of LPV/r-based therapy improved outcomes among children who survived the first year of life without therapy. Excellent outcomes in children who achieved virologic suppression despite delayed virologic response suggest that virologic monitoring should be used to target adherence interventions rather than to prematurely discontinue LPV/r-based therapy.

Poverty Kills: Socioeconomic Disparity In Inpatient Mortality Following Traumatic Injury In Adults

Background: Several studies have demonstrated race and insurance status as important predictors of inpatient mortality following trauma, but have been limited by their inability to adjust for direct measures of socioeconomic status (SES) and comorbidities. Our study aims to identify whether a relationship exists between SES and inpatient mortality following trauma after adjusting for known confounders including comorbid conditions.

Methods: Patients aged 18-65 with Injury Severity Scores (ISS) of 9 and higher from the Nationwide Inpatient Sample (years 2003 to 2009) were included. ISS was generated by applying the International Classification of Diseases, 9th edition (ICD-9) PIC program. Patients' median household income (MHI) by zip code, available by quartiles (Q1=0-25%; Q2=25-50%; Q3=50-75%; Q4=75-100%), was used as a measure of socioeconomic status. Q4, the wealthiest quartile, was used as the reference group. Multiple logistic regression analyses were performed to determine the relative odds of inpatient mortality for the different MHI quartiles, adjusting for ISS, mechanism of injury, Charlson comorbidity index, and patient demographics, including age, sex, race, and insurance status.

Results: 267,621 patients met inclusion criteria. Patients in lower wealth quartiles had increased unadjusted inpatient mortality rates (Q1, 4.19%; Q2, 3.73%; Q3, 3.66%; Q4, 3.15%; $p < 0.001$). Similarly, patients in Q1 ($n=83,714$), Q2 ($n=68,932$), and Q3 ($n=62,413$) had increased odds of adjusted inpatient mortality, compared to the wealthiest Q4 ($n=52,562$), the reference group (Q1 OR, 1.13; 95% CI, 1.06-1.20; Q2 OR, 1.09; 95% CI, 1.02-1.17; Q3 OR, 1.11; 95% CI, 1.04-1.19).

Conclusion: Median household income predicts inpatient mortality after traumatic injury, with patients in the poorest zip codes experiencing worse outcomes than patients in the wealthiest zip codes. These findings suggest that among patients residing in socioeconomically disadvantaged zip codes, there may be additional mechanisms preventing them from achieving their full survival potential.

Implantable Bioreactors For The Delivery Of Stem Cell-Derived Cytokines To The Post-Infarct Heart

Background: This project focuses on the development of an “implantable bioreactor” for the delivery of stem cell-derived cytokines to the post-infarct heart. The aim of stem cell therapy is to regenerate damaged tissue and to restore cardiac function following a myocardial infarction. We propose that the direct infusion of stem cells into the infarcted artery is not necessary to produce regenerative effects. The delivery of cytokines derived from stem cells growing within the implantable bioreactor may produce a greater therapeutic effect than the direct infusion of stem cells into the infarcted artery.

Methods: Stem cells growing within the bioreactor release cytokines across the fenestrated bioreactor membrane into the external environment. ELISAs were performed on conditioned media collected from outside the bioreactors in order to quantify cytokine production. Significant production of VEGF, FGF-basic, IL-8, and HGF was detected, and a dose response relationship was observed between cytokine production and the number of human mesenchymal stem cells (hMSCs) infused into the bioreactor. Co-infusion of hMSCs with matrigel produced a several-fold increase in cytokine production, indicating enhanced stem cell survival.

Results: Bioreactors containing hMSCs were implanted in pigs for periods of up to six weeks with no sign of rejection. Explanted bioreactors exhibited a different cytokine production profile than comparable bioreactors that had never been implanted in a pig, suggesting that stem cells housed within bioreactors are able to sense environmental conditions and respond by modifying paracrine factor production.

Conclusion: The human umbilical vein endothelial cell tube formation assay, an in vitro angiogenesis assay, showed that stem cell-containing bioreactors produce a significant, dose-dependent increase in the length of the tubule network. Also, bioreactors containing “young” mouse MSCs promote tubule formation to a greater extent than “old” MSCs, indicating greater angiogenic potential. Therefore, it may be beneficial to use allogeneic stem cells from young individuals in future trials.

Severe Infectious Complications Following Frontal Sinus Fracture: The Impact Of Operative Delay And Peri-Operative Antibiotic Use

Background: Purpose: To investigate whether delay in operative management of frontal sinus fractures is associated with increased serious infectious complications. The effects of prolonged peri-operative antibiotics, nasofrontal outflow tract (NFOT) injury, and posterior table involvement were also examined.

Methods: Methods: Retrospective chart review was performed for 242 consecutive patients with surgically managed frontal sinus fractures who presented to the R Adams Cowley Shock Trauma Center between 1996-2011. Patient demographics, surgical management, hospital course, and complications were recorded. All CT imaging was reviewed to evaluate involvement of the posterior frontal sinus wall and NFOT. Serious infectious complications included meningitis, encephalitis, brain abscess, frontal sinus abscess, and osteomyelitis. Delayed operative intervention was defined as greater than 48-hours from admission. Relative risk for each exposure was obtained using multivariable logistic regression analysis adjusting for the strongest covariates

Results: Results: There were 14 (5.8%) serious infections. All patient with serious infections had involvement of both the posterior table of the frontal sinus and nasofrontal outflow tract (NFOT) obstruction. The cumulative incidence of serious infection in these patients with both posterior table and NFOT involvement was 10.8%. Logistic analysis showed that operative frontal sinus management delayed beyond 48-hours was independently associated with a 4.03-fold increased risk for serious infection ($P<0.05$); intraventricular catheter use and acquired soft-tissue infection conferred a 4.09-fold ($P<0.05$) and 5.10-fold ($P<0.001$) increased risk, respectively. Antibiotic use beyond 48-hours post-operatively was not associated with fewer serious infections.

Conclusion: Conclusion: Delay in operative management of frontal sinus fractures in those that require operative intervention is associated with increased serious infectious complications. This increased risk should be weighed in light of competing injuries when determining operative management timing. Overall, prolonged antibiotic use does not significantly reduce infection risk and should be reserved for those with delayed intervention, intraventricular catheters, or soft-tissue infection.

Epicardial Fat Is Associated With Duration Of Antiretroviral Therapy And Coronary Atherosclerosis In The Multicenter AIDS Cohort Study

Background: HIV infection and anti-retroviral therapy have been associated with coronary artery disease and changes in body fat distribution like increased visceral adiposity. We sought to determine if HIV infection is associated with larger visceral fat depots – particularly around the heart in the form of epicardial fat – and if epicardial fat is associated with coronary atherosclerosis when measured by coronary artery calcium (CAC) scores.

Methods: We performed a cross-sectional analysis with 484 HIV-infected men and 244 HIV-uninfected men from the Multicenter AIDS Cohort Study (MACS) age 40 to 70 years who all underwent non-contrast computed tomography (CT) to measure epicardial fat volume and CAC. Additional measures of atherosclerosis like total plaque score, and plaque subtype scores (non-calcified, calcified, and mixed plaque) were also obtained by coronary CT angiography in 543 men within the sample population. We evaluated the association between the extent of epicardial fat and HIV serostatus, as well as the association between epicardial fat volume and coronary artery calcium after adjusting for age, race, serostatus and additional cardiovascular risk factors.

Results: HIV-infected men had greater epicardial fat than HIV-uninfected men (median epicardial fat volume with interquartile range: 114.3, 78.5-154.5 cm³ vs. 110.0, 76.3-142.0 cm³, $p = 0.003$); and the extent of epicardial fat in HIV-infected men was positively associated with the duration of use of antiretroviral therapy ($p = 0.004$). Epicardial fat was also associated with presence of underlying coronary artery plaque (OR = 1.10, 95% CI, 1.04-1.17, $p = 0.002$) and non-calcified plaque (OR = 1.06, 95% CI 1.02-1.11, $p = 0.005$) after adjusting for age, race, serostatus, and cardiovascular risk factors.

Conclusion: Epicardial fat is associated with coronary plaque, HIV infection, and duration of antiretroviral therapy. Studies are needed to investigate which aspects of HIV infection or its treatments contribute most to epicardial adiposity, and therefore coronary atherosclerosis.

Rates Of Long-Term Cochlear Implant Use In Children

Background: Despite the significant personal and financial investment associated with pediatric cochlear implantation (CI), there is limited characterization of long-term usage of the cochlear implant. The purpose of this study was to determine the rate of long-term CI use through a large, consecutive case series of children receiving cochlear implants.

Methods: From 1999-2011, 474 patients <18 years received a first cochlear implant at Johns Hopkins Hospital. We successfully contacted and obtained follow-up data on 402 patients (85%) via email, telephone, and postal survey. Regular CI use was defined as wearing the CI for ≥ 8 hours per day averaged over the past 4 weeks. The time from CI to the date of discontinued regular CI use was analyzed using Kaplan-Meier and Cox proportional hazard models.

Results: The cumulative rates of regular CI use were 93.2% (95% confidence interval, 90.0-95.4) at 5 years post-implantation and 87.7% (95% confidence interval, 82.9-91.3) at 10 years post-implantation. The mean hours of use per day was 12.0 ± 4.1 hours. There was a linear association between the risk of discontinuing regular CI use and the age at implantation (18.2% [95% confidence interval, 7.2-30.4] increased risk of discontinuing regular use per year of increasing age at implantation). For patients reporting less than 8 hours of use per day, the most common causes were poor hearing benefit (53.2%), social pressure (21.3%), recurrent electrode disconnection (17.0%) and internal device failure or infection (10.6%).

Conclusion: Long-term rates of regular CI use remain high in pediatric patients. Earlier age at implantation is associated with lower rates of discontinuing regular CI use.

Determining The Role Of Cytotoxic Necrotizing Factor-1 In The Pathogenesis Of Urinary Tract Infections

Background: Bacterial urinary tract infections are common in today's pediatric population. This study's purpose was to determine the role of the toxin CNF-1 in the pathogenesis of urinary tract infections caused by uropathogenic *Escherichia coli*.

Methods: We created a genetic knockout of the CNF-1 toxin in *E. coli* and reintroduced the gene via transformation to create a complement strain. Chloramphenicol and ampicillin resistance cassettes were used to select for the deletion and complement groups respectively. We inoculated 4 groups of 5 mice with different bacterial strains. The first group was infected with a saline control, the second with wild-type *E. coli*, the third with the *cnf1* knockout, and the fourth with the complement. Organ tissues and urine samples were collected 1 week later. We plated all samples on 3 sets of LB media containing either no antibiotics, chloramphenicol, or ampicillin and counted colonies after overnight incubation.

Results: We found higher bacterial counts in samples from mice that received wild-type compared with deletion mutant inoculum, and no growth was present on any control group plates. Surprisingly, the complement group showed similar growth patterns to the deletion group. This suggests that the complement plasmid was spontaneously lost in vivo despite demonstration of successful plasmid transformation and growth on ampicillin plates in vitro.

Conclusion: The experiment will need to be repeated by reintroducing *cnf1* into the complement using a transposon rather than an extrachromosomal plasmid. The control group results suggest that our technique was sterile and contamination-free, and our wild-type and deletion mutant results preliminarily suggest that although CNF-1 plays a role in the pathogenesis of UTIs, it is not necessary for infection. After uncovering the role of CNF-1, we hope to study its mechanism of secretion and apply this information to the development of new prevention and treatment options that circumvent bacterial drug resistance mechanisms.

Autopsy And The Influenza Epidemic At Johns Hopkins Hospital, 1918

Background: Baltimore was hit hard by the influenza pandemic of 1918; 3500 influenza victims died in October alone. Johns Hopkins Hospital admitted more than 300 cases of the disease, and performed over a dozen autopsies on influenza victims. These autopsies were used as evidence in the international debates about the disease's etiology.

Methods: Specimens and autopsy records from the Hopkins pathology department were used to reconstruct the lives of the people behind the hospital's statistics. These were enriched with information from death certificates, census data and maps. Pathological reports were correlated with articles on influenza published by Hopkins medical staff. Comparison of the response to the pandemic in Baltimore and at Hopkins was accomplished through analysis of Baltimore Health Commissioner reports, newspaper articles, patient memoirs, letters, scientific articles and the 1919-1920 Hopkins Bulletins.

Results: Influenza victims at Hopkins had a wide variety of backgrounds, from poor children to the hospital's own nurses and physicians. This project explores how the pathology department's autopsies reduced this diversity of human experience to argue that a virus was the probable pathogenic cause of influenza, and raised awareness of the signs, symptoms, and non-pulmonary manifestations of the disease. Scientific method, rigorous data collection and documentary fastidiousness were conjoined to maintain order in the hospital. This compared favorably to the chaos that reigned in Baltimore and its Health Department.

Conclusion: Autopsies explain much about the nature of medical practice, and the integration of pathological findings with clinical diagnosis and treatment. The 1918 Hopkins influenza autopsies show the patient stories behind the statistics, and provide some of the fundamental information from which the hospital and the wider world came to understand influenza. While Hopkins distanced itself from the city's disarray, it still benefited from it through the admission of local cases, which resulted in autopsies, pathological knowledge and groundbreaking virus research.

Nerve Injury After Total Shoulder Arthroplasty

Background: Previous studies report the neurological complication rate for shoulder arthroplasty to be 4.3% to 5.0%. However, these studies were limited to total shoulder arthroplasty (TSA) and did not include hemiarthroplasty (HA) or reverse shoulder arthroplasty (RSA). Our hypotheses were that the neurological complication incidence after shoulder arthroplasty would vary by type of procedure performed and that the overall incidence would be higher than previously reported in the literature.

Methods: We retrospectively reviewed the charts of 512 consecutive patients who had a total of 604 SA by the same surgeon between June 1995 and August 2012. Only patients with over six months follow up were included. The charts were reviewed for any sensory or motor disturbance postoperatively. Those who had EMG confirmation of nerve injury were placed into the surgical complication group, with a second group composed of patients with neurological symptoms who did not require electromyography. These two groups were statistically compared to those patients without neurological injury using standard statistics software.

Results: Of the 349 procedures currently analyzed, there were 113 HA, 191 TSA and 45 RSA with over 6 month follow up, and there were 10 (10/349; 2.9%) neurological injuries. There was no statistically significant difference in the incidences between the groups (HA: N=3/113, 2.7%; TSA: N=5/191, 2.6%; RSA: N=2/45, 4.4%). There were an additional 34 neurological symptoms after shoulder arthroplasty, and if included with the NI then the total rate of neurological complaints after shoulder arthroplasty was 12.6% (44/349). If the injuries and symptoms are combined, multivariate analysis showed that there was a statistically significant association between the developments of neurological symptoms and revision surgery.

Conclusion: The rate of neurological complications after shoulder arthroplasty was independent of the type of procedure. The incidence of neurological complaints after shoulder arthroplasty is higher than previously reported.

Survey Of Partner Notification Practices For Sexually Transmitted Infections In The United States

Background: Partner notification (PN) is the public health practice of informing the sexual partners of patients newly diagnosed with a sexually transmitted infection (STI) about the need for testing and possible treatment. PN is effective in reducing onward STI transmission and re-infection in patients. The most recent evaluation of PN practices in the US, however, indicated that few patients diagnosed with an STI were offered PN services in high-prevalence areas in 1999. Our objective was to assess the current provision of PN services in STI/HIV testing sites throughout the US and to determine the types of PN services available.

Methods: We randomized a list of current STI/HIV testing sites in the US compiled by the Centers for Disease Control and Prevention and called the first 383 sites to administer a phone survey about their PN practices. Sites were eligible to participate if they provided testing services for STIs or HIV and were not hospitals or Planned Parenthood locations.

Results: Of the 300 eligible sites called, 79 sites were successfully reached, of which 74 agreed to participate, yielding an overall response rate of 26.3% (adjusted for survey eligibility). The proportion of sites offering some form of PN service to chlamydia, gonorrhea, HIV, and syphilis patients was 94.6%, 94.6%, 98.6%, and 95.9%, respectively. Anonymous PN services were available at 66.2%, 70.3%, 74.3%, and 74.3% of sites, respectively. Only 8.1% and 12.2% of sites offered internet-based anonymous PN to patients with chlamydia/gonorrhea and HIV/syphilis, respectively.

Conclusion: Most surveyed testing sites currently offer some type of PN service for chlamydia, gonorrhea, HIV, and syphilis infection, in contrast to 1999. However, approximately 25% to 33% of surveyed sites do not offer anonymous services. Internet-based services are the least offered PN method. Novel, particularly internet-based methods may be warranted to increase the availability of anonymous services.

Perceptions Of Short Term Medical Aid In The Dominican Republic: Voices Of Host Community Members

Background: Many clinicians and trainees from high-income countries participate in short-term global health service programs in low- and middle-income countries. Although the impact of these programs on individuals from sending institutions has been described, a paucity of information exists regarding the perceptions of program recipients. This study examines the perceptions of individuals receiving medical care from Medical Ministry International (MMI), an international non-governmental organization with experience providing short-term and long-term health programs in the Dominican Republic.

Methods: Following approval from the Johns Hopkins Medicine IRB and the Elias Santana Hospital research ethics committee, individual, semi-structured interviews were conducted by one of the researchers with a convenience sample of 47 adults receiving medical or surgical services from MMI in Monte Plata province during July 2012. Interviews occurred in clinical settings. Interviews were conducted in Spanish, audio recorded, transcribed and translated. Transcripts were independently coded by two researchers to identify themes and subthemes. Disagreements were resolved by consensus.

Results: Of the 47 interviews, 20 were able to be analyzed based on completeness, audio quality, and overall comprehensibility of Spanish dialect. Major themes identified included the perceived quality of services (e.g., compared to locally available care); improved access to care (e.g., closer proximity, reduced cost); and meeting of general community needs. Interviewees frequently expressed appreciation for “atender,” understood in the interview context as providers' deep care and compassion. Some interviewees misidentified the interviewer as a health care provider; others were reluctant to discuss ways to improve the MMI program.

Conclusion: Recipients of short-term medical aid in the Dominican Republic expressed satisfaction with both tangible and intangible program benefits. Participants' reluctance to discuss program improvement and difficulty separating the researcher from the provider institution have implications for future program evaluations. Future research should examine these themes in other locales and investigate them quantitatively.

Metastatic Brain Tumor Survival And Recurrence By Primary Tumor

Background: Metastatic brain tumors affect over 30,000 patients yearly in the United States. For these patients, outcomes can be maximized by establishing a thorough profile both of the patient and of the tumor prior to establishing a treatment plan. This study identifies variables that influence overall survival, local recurrence, or distal recurrence and explores how these associations vary by tumor histology.

Methods: 708 patients who underwent surgery for intracranial metastases (1997-2011) were reviewed. Primary outcomes evaluated were overall survival, local recurrence, and distal recurrence. Univariate analysis was performed on each primary tumor to evaluate associations between radiographic, preoperative, operative, perioperative, and pathologic variables associated with primary outcomes. Step-wise multivariate proportional hazards regression models were constructed for each primary outcome. Kaplan-Meier curves were plotted for overall survival, local progression free survival, and distal progression free survival. Log-rank tests compared Kaplan-Meier plots between each histology type and all patients.

Results: Patients with non-small cell carcinomas had longer median survival times than patients with other types of primary cancers ($p < 0.0001$). Breast cancer patients had longer median survival times than patients with GI cancers ($p = 0.005$) and melanomas ($p = 0.04$). There were no significant statistical differences in survival between primary cancers for a solitary brain metastasis. Renal cell cancer patients had longer local recurrence-free survival rates than patients with non-small cell lung carcinomas ($p = 0.02$), breast cancer ($p = 0.004$), and GI cancer ($p = 0.02$). Additionally, other types of cancers had significantly longer local progression-free survival rates than breast cancers ($p = 0.05$). Patients with non-small cell carcinomas had significantly longer distal recurrence-free survival rates than patients with breast ($p = 0.03$) and melanoma ($p = 0.002$).

Conclusion: Primary cancer origin, pre-operative patient demographics, tumor histology, and patterns of metastatic development can predict overall survival of a metastatic brain tumor and guide surgical and non-surgical treatment in order to minimize recurrence and maximize patient outcomes.

Using Commercial Activity Monitors To Measure Gait In Patients With Suspected Inph: Implications for Ambulatory Monitoring

Background: Patients with idiopathic normal pressure hydrocephalus (iNPH) may not be diagnosed until late in the disease course because of blunt clinical tools that fail to detect early gait disturbances. Ideally we would be able to sense minute symptomatic changes in the ambulatory setting, using inexpensive and user-friendly technologies, so that these patients may be treated before they develop more serious hydrocephalus. In this pilot study we assessed the accuracy of four widely available activity monitors in patients with suspected or confirmed iNPH.

Methods: Following JHU IRB approval of our prospective pilot study, we recruited 17 patients with suspected or confirmed iNPH to each perform two 10-meter walks while wearing four activity monitors: the Omron Step Counter HJ-113, New Lifestyles (NL) 2000, Nike Fuelband, and Fitbit Ultra. We compared the counts recorded by the activity monitors to manual counts from video-recordings of the patients' gaits.

Results: Our elderly patient population (69.7 +/- 12.1 years) required an average of 25.9 +/- 12.9 steps to walk 10-meters. We calculated the mean, standard deviation, and correlation coefficient of the absolute difference between the manual- and device-step counts: Omron (10.4 +/- 14.7; R2 = 0.05), NL (15.3 +/- 15; R2 = 0.12), Nike (14.9 +/- 11.3; R2 = 0.09), and Fitbit (5.1 +/- 7.3; R2 = 0.57). The Fitbit Ultra's MEMS tri-axial accelerometer and algorithm was the most accurate.

Conclusion: We found one activity monitor to be clearly more accurate and intuitive to use in measuring steps taken by iNPH patients. We are currently monitoring patients in the ambulatory setting to determine if clinically relevant data may be collected. The transition to ambulatory monitoring and early detection has the potential to greatly affect management of iNPH in patients.

Tumor DNA detection to monitor the response of BRCA-less tumors to PARP1 (poly ADP ribose polymerase) inhibitors

Background: The BRCA enzymes are functionally important in homologous recombination (HR). BRCA-mutant cancers are often sensitive to targeted therapies known as PARP1 inhibitors (PARPis), which rely on synthetic lethality to shut down high fidelity repair mechanisms. Plasma tumor DNA (ptDNA) technology has been utilized in vivo to detect tumor burden of specific tumors; the technology relies on amplification of mutated DNA sequences that uniquely identify tumors. The goals of our research include (1) developing a protocol that translates the concept of ptDNA detection to an in vitro model, (2) determining if tumor burden as measured by this protocol correlates with more conventional measurements of cell proliferation, (3) and using this protocol to measure the early response of BRCA-less tumors to PARPis.

Methods: HCC1937 (homozygous for the BRCA1 5382C mutation) tumor cells and MCF10A (immortalized breast) cells were seeded at a density of 2,000 cells/ well into 96-well plates. Cells were subject to various PARPi concentrations. At 7 and 9 days, supernatant from wells was extracted and concentrated; tDNA was amplified using qPCR. At 9 days cells were fixed and proliferation was quantified using a sulforhodamine B (SRB) assay.

Results: Within the specified therapeutic windows, HCC1937 tumor cells were differentially killed by both PARPis (ABT-888 and AZD2281) relative to control MCF10A cells. Tumor killing was also seen to be concentration dependent. However, the ptDNA levels appeared to be elevated in all experimental groups, indicating no clear correlation between tumor burden and ptDNA levels as of yet.

Conclusion: We found that PARPis selectively target HCC1937 BRCA-less cells for killing, leaving immortalized MCF10a breast cells relatively unharmed. Initial findings suggest no clear correlation between tumor burden and tDNA levels, however. Further studies are needed to determine if tDNA can be accurately and replicably isolated from supernatant and shown to correlate with cell proliferation.

Oral Presenter, Public Health and Community Service

Multi-Level Influences On Environmental Health In Public Housing

Background: Public housing communities are disproportionately affected by health disparities. Using an ecologic framework, we aimed to identify environmental factors influencing the health of public housing residents.

Methods: We conducted focus groups with Baltimore public housing residents between 6/2011-11/2011, which were recorded and transcribed verbatim. Two investigators independently coded transcripts for thematic content using editing style analysis.

Results: 28 residents participated in 6 focus groups. All were black. Mean age was 51 years (SD 12); 79% were women. We identified 3 themes related to environmental health:

1: Environmental conditions influence the health of residents. Participants expressed concerns about rodents, litter, inadequate cooling/heating, and crime leading to negative health consequences: “[With] the infestation of rats...you scared your kids might get bit.”

2: Community lacks a voice to advocate for environmental change. Local leaders are polarizing figures. One resident considered the local resident council president “an important person in this community... he look out for the little kids,” while another stated that, “He don’t belong there.” These varied opinions of the local leader results in mistrust and skepticism about his ability to bring about environmental change: “The people downtown in the main [housing authority] office - they’re not going to listen to [the resident council president].”

3: Residents report no influence on city policy that directly affects their community’s resources. “[The city] get ready to close [the recreation center] down...and [kids] won’t have no good place to go or nothing to do.” No residents communicated their dissatisfaction about these policies with local leaders or city council representatives.

Conclusion: Environmental health is a concern for public housing residents; however, residents perceive that they have little influence on housing or city policies to improve these conditions. Future interventions targeting the public housing environment should take into account these multilevel influences.

Endocarditis Is Significantly Associated With Patent Foramen Ovale In Patients With Left Heart Valve Procedures

Background: Patent foramen ovale (PFO) has a documented prevalence of 27% in the general population; however, its prevalence in the cardiac surgical population is currently undefined. Additionally, PFO has been associated with an increased risk of left heart valve endocarditis, though its exact contribution has also not been clarified. Therefore, we evaluated the prevalence of PFO in patients undergoing left heart valve procedures and determined the association of PFO with endocarditis.

Methods: We retrospectively reviewed our prospectively maintained cardiac surgery database for patients who underwent a left heart valve procedure from 2001 to 2011. From this database, we abstracted patient demographics, co-morbidities, and operative characteristics. Primary stratification was by the presence of a PFO, and the primary outcome was a positive endocarditis history. Secondary outcomes included postoperative complications (atrial fibrillation, stroke, etc.). Kaplan Meier and multivariate cox analysis were used to assess survival and mortality, respectively.

Results: Of the 1,028 patients, 357 (35%) had a PFO. PFO patients were significantly more likely to have endocarditis (46/357 [13%] vs. 52/658 [8%]; $p=0.01$), but had significantly lower rate of postoperative complications, including atrial fibrillation, stroke, sepsis, wound infection, renal failure, and bleeding ($p<0.001$ for all). Kaplan Meier analysis revealed that patients with PFO had better survival at 5 years ($p<0.001$) and PFO was found to be a protective factor in 1 and 5-year multivariate cox analysis (HR=0.61 [0.39-0.95]; $p=0.03$ and 0.58 [0.41-0.82]; $p=0.002$, respectively).

Conclusion: In the largest study examining this topic, PFO prevalence was higher in patients with left heart valve procedures (35%) compared to the general population (27%) and PFO was significantly associated with endocarditis, suggesting that a potential benefit to preemptively closing these anomalies during unrelated cardiac procedures may exist. PFO was also found to be protective against mortality and complications, but further study is necessary to determine the cause of these associations.

Lysosomal Degradation Of HIF-1alpha Represents A Novel Therapeutic Target

Background: Hypoxia Inducible Factor-1 (HIF-1) is a heterodimeric transcription factor boasting the shortest half-life of any known protein. The alpha subunit is normally regulated by oxygen-dependent hydroxylation and proteasomal degradation. During hypoxia, proteasomal degradation is blocked, leading to an increase in HIF-1alpha levels within minutes. This triggers adaptive changes in angiogenesis, erythropoiesis, metabolism, and cell cycle arrest. Given the importance of HIF-1 activity, the regulation of HIF-1alpha degradation has been intensively studied by molecular biologists over the past decade. However, non-proteasomal methods of regulating HIF-1alpha levels have not been identified. This study examined regulation of HIF-1 by chaperone-mediated autophagy (CMA), a pathway for selective lysosomal degradation of proteins.

Methods: We conducted binding assays with HIF-1alpha and the key CMA effectors Hsc70 and Lamp2. We further examined the effect on HIF-1alpha levels and activity upon manipulation of the CMA pathway using pharmacologic and genetic approaches.

Results: Interaction of HIF-1alpha with endogenous Hsc70 and Lamp2 was readily detectable as was colocalization of HIF-1alpha with lysosomes. Overexpression of Hsc70, Lamp2, or TFEB led to a decrease in HIF-1alpha levels and activity, whereas knockdown of these proteins had the converse effect. Pharmacological activation of CMA also led to a decrease in HIF-1alpha levels and activity. Similarly, inhibitors of lysosomal degradation led to an increase in HIF-1alpha levels and activity, including a potent cell cycle arrest in cancer cell lines that was HIF-1alpha - dependent.

Conclusion: This study delineates a novel pathway for HIF-1 α degradation. Selective targeting of HIF-1 α for lysosomal degradation may serve as a mechanism coupling HIF-1 activity to various physiological stimuli, just as proteasomal degradation couples HIF-1 activity to oxygen levels. We further demonstrated that several known anti-cancer drugs that block lysosomal degradation regulate this pathway and induce a HIF-1alpha dependent cell cycle arrest, indicating that this represents a potential therapeutic target.

Oral Presenter, Public Health and Community Service

Overutilization Of Chlamydia Tests Among Older Women In An Urban, High Prevalence City

Background: Baltimore City ranks in the top half among major US cities for rates of chlamydia infections, 80% of which were from women < 26 years of age. Research has shown that younger women who are at the highest risk for chlamydia are being undertested while older women are being overtested. The purpose of this study was to determine the prevalence of chlamydia infection in women ≥ 26 who are at increased risk of infection (e.g. history of an sexually transmitted infection [STI]) and to determine factors associated with a positive test..

Methods: We conducted a retrospective chart review of medical records for all Medicaid-insured women aged 26 and older who were seen for a gynecology visit at an academic medical institution in Baltimore, MD from January 2009 to December 2010 and tested for chlamydia. Pregnant women and those who desired an IUD were excluded.

Results: Of the 553 women that were included in the study, 92.4% were African American (n=511) and 7.6% were of other ethnicities (n=42). The median age was 35 years with a range of 26-69 years. 90.2% were unmarried (n=497) and 93.5% (n=517) had a previous pregnancy. Of these women, 1.27% (n=7) tested positive for chlamydia. Of these 7 women, 3 denied genitourinary symptoms (43%) and 4 reported symptoms (57%). 71% (n=5) of the positive tests were among women who did not report a history of an STI.

Conclusion: There remains a low prevalence of chlamydia in older women, regardless of risk factors.. This result is magnified even further among asymptomatic women, with less than 1% of this population testing positive for chlamydia. This research demonstrates the need for improved adherence to and rethinking of chlamydia guidelines in older women.

The Shapes Of Proteus: Mental Illness In English Case Literature Of The 17th And 18th Centuries

Background: This paper examines the intersection of two historical literatures, that of mental illness and of medical genres. The late 17th and early 18th centuries are considered a dark age in the history of mental illness in England, and historians often lament the silence of its 'mad doctors.' However, the period is also the infancy of English medical case writing. Here I examine the early English case literature on mental illness and use the case history as a window into these physicians' struggles to write about the protean diseases of the mind.

Methods: 75 cases of mental illness published in English from 1666 to 1769 were characterized by patient gender, narrative format, expressed compassion, and the epistemological significance attributed to the case.

Results: The published cases of this period took several forms, ranging from detailed narrative to a few terse lines. Additionally, the epistemological value of the individual case varied from text to text. This difference in epistemological value is indicated by the form through which the author chose to present his medical experience: as compilations of discrete cases or as an amalgamation of individual patient traits into a composite picture of the 'mad patient'.

Conclusion: Out of the cacophony of individual cases of mental illness—these innumerable 'shapes of Proteus'—the authors struggled to illustrate an order that might guide the practice of their physician-readers. The rich variety of interpretations of the case literature genre and of the epistemological value of the case itself illustrates a disagreement amongst physicians over how one may best transmit knowledge of mental illness. Each author is strongly influenced by the early modern passion for observation, but lingering throughout the period is a necessary reliance upon the explanatory mechanisms of a unifying medical theory, without which a proper 'cure' cannot be determined.

Importance Of Environmental Conditions In Lusaka, Zambia's Seasonal Cholera: A Mathematical Analysis

Background: Cholera incidence in Lusaka, Zambia shows distinctly seasonal patterns, with incidence peaking in January in most years. As a waterborne pathogen, it is natural to assume that cholera seasonality is driven by rainfall. However, in Lusaka and throughout East Africa if and how precipitation drives cholera incidence remains unknown.

Methods: Using generalized additive models, we modeled weekly cholera incidence from 2003-2011 as a function of time of year, precipitation and other climatic factors. Mediation analysis was applied as in the social science fields to determine the extent to which rainfall explains the seasonal nature of cholera.

Results: Results indicated that cumulative rainfall over the prior 8 weeks was the best climatic predictor of cholera incidence, and was a significant predictor even after adjusting for week of year. The relationship between 8 week cumulative rainfall and log-cholera incidence follows an approximately logarithmic form, with a plateau effect beyond 8 inches of rain. Mediation analysis showed that a significant percentage of the variation in cholera incidence by season could be explained by 8 week cumulative rainfall.

Conclusion: The dependence of Cholera incidence on 8 week cumulative rainfall in Lusaka Zambia suggests that wet conditions play a central role in driving cholera transmission in this context. The relevance of the previous 8 weeks may reflect the length over which rainfall influences transmission conditions, or the requirement for sustained conditions that promote transmission to achieve a large epidemic. Regardless, our model of the relationship between rainfall and incidence provides an important tool for those fighting cholera in Lusaka and throughout East Africa.

Oral Presenter, Medical Humanities, Bioethics, and the Healing Arts

"Am I cut out for this?:" A Qualitative Analysis Of Doubt Among First Year Medical Students

Background: Research on medical student wellbeing shows high rates of distress, yet doubt as a distinct phenomenon remains poorly understood. The purpose of our study was to examine how first year medical students experience and respond to doubt, and how doubt relates to other aspects of student distress.

Methods: As part of a larger study, we conducted four 90 minute focus groups with a convenience sample of first year medical students. Focus group questions were written and revised by the authors, then pilot-tested and revised prior to use. Audiotapes were transcribed, independently coded, and iteratively reviewed by the authors to identify major themes.

Results: 34 students participated in the focus groups. Three major themes were identified: types of doubt, ways of coping with doubt, and impact of doubt. Types of doubt were related to two main questions: (1) Do I want to become a doctor? Subthemes related to this question were concerns about medical education and the healthcare system, the opportunity cost of pursuing medicine, and identity loss. (2) Am I capable of becoming a doctor? Subthemes included concerns about students' ability to succeed, maintaining work-life balance, the financial burden of medical school, and social belonging. Important ways of coping with doubt included relying on supportive relationships and maintaining perspective through extracurricular activities, service, and focusing on long-term goals. Students identified both positive and negative impacts of doubt: the positive impacts of motivation, resilience to uncertainty, and finding a passion, and the negative impacts of burnout, depression, stress, poor academic performance.

Conclusion: Doubt among first-year medical students affects students' sense of confidence, identity, and purpose, and may have both positive and negative consequences. Students also experience other forms of distress, which may be related to doubt. The phenomenon of doubt in medical students merits both awareness and further study, particularly with respect to understanding the magnitude of its effects on students' personal and professional development.

Doubt Among Future Doctors: A Survey Of First Year Medical Students

Background: Research shows high rates of distress in medical students, yet doubt as a distinct phenomenon remains poorly understood. The purpose of our study was to examine how first year medical students experience and respond to doubt, and how doubt relates to other aspects of student distress.

Methods: As part of a larger study, all JHUSOM students completing their first year were asked to answer 14 questions about doubt embedded in an online advising program survey. Survey items were developed and iteratively revised based on literature review, and included four questions from a validated wellbeing index. Results were analyzed by grouping students into four categories based on level of doubt: high, moderate, low, and none. For each doubt item, logistic regression was used to compare the proportion of students who “agreed” among moderate/high doubters to low/no doubters. For wellbeing questions, total doubt scores and total wellbeing scores were correlated with Spearman’s rho.

Results: 114/119 (96%) students completed the survey. 20% had high doubt, 29% moderate doubt, 22% low doubt, and 29% no doubt. Compared to those with low/no doubt, students with moderate/high doubt were 13 times as likely to question their personal purpose, 8 times as likely to question who they were, 4 times as likely to struggle with coping with their doubts, 5 times as likely to think the JHUSOM climate discouraged them from expressing doubts, and 6 times as likely to be unsure of where to find helpful resources. There was a moderate correlation between the total doubt scores and total wellbeing scores ($\rho = 0.36$).

Conclusion: A large percentage of first year medical students experienced moderate/high levels of doubt, were more likely to question their identity and purpose, and had trouble coping with their doubts. The moderate correlation suggests that doubt may be a distinct phenomenon from traditional wellbeing measures.

Mutations In Alström Protein Promote Persistent Postnatal Cardiomyocyte Replication In Multiple Families

Background: Normal mammalian development of the heart requires proliferation of cardiomyocytes followed by a period of cardiomyocyte maturation in the perinatal period, during which cardiomyocytes withdraw from active cell cycle proliferation and become terminally differentiated. The factors regulating terminal differentiation in cardiomyocytes are poorly understood. We identified a pair of infant siblings with persistent postnatal cardiomyocyte replication, and we performed genetic analysis to determine the cause.

Methods: Whole exome DNA sequencing was performed on the proband and each of her parents. After identifying compound heterozygous frameshift mutations in a single gene (ALMS1), we also tested her affected sibling. Five additional cases of cardiomyopathy with persistent postnatal cardiomyocyte replication were previously reported by a group from the Hospital for Sick Children in Toronto, Canada, and we received paraffin-embedded tissue for further analysis. DNA was extracted from the paraffin-fixed tissue samples with a QIAamp DNA FFPE Tissue Kit. ALMS1 specific primers were designed and polymerase chain reactions were utilized to amplify ALMS1 exons. Sequencing of the amplified regions was completed and the results were analyzed.

Results: Whole exome sequencing in the proband demonstrated two ALMS1 mutations (c.1794_1801dup8 and c.11116_11134del19) in the proband and her affected sibling, and both parents were heterozygous for a single ALMS1 mutation. In order to replicate this finding, DNA was obtained from four of the samples from Toronto, and we sequenced ALMS1. We identified novel ALMS1 frameshift mutations in two of these individuals and confirmed recessive inheritance using DNA obtained from their parents. We also identified a homozygous nonsense mutation in the other two affected children, whose parents were consanguineous.

Conclusion: Truncating mutations in ALMS1 cause deficiency of Alström protein, and are associated with delay of terminal differentiation of cardiomyocytes in multiple affected families. Further analysis in cellular and murine models is ongoing to identify the responsible mechanisms.

Tyler Mains, MS2
Oral Presenter, Medical Education

Mentor: Joe Confrancesco, MD MPH; Harry Goldberg, PhD

Isolating The Impact Of Audience Response Systems On Learning

Background: The current literature on the impact of Audience Response Systems (ARS), commonly called “clickers,” on learning includes contradictory results. One potential reason is the multiple confounding factors inherent in most medical education research, such as individual lecture effectiveness, learners’ multiple exposures to the material, and learners’ motivation to study the content independent of the teaching methodology used. Therefore, the authors conducted a randomized controlled trial with the goal of isolating the impact of ARS on learning.

Methods: First-year medical students at Johns Hopkins University volunteered to enter this study (n=92), and were randomly assigned to one of two groups. Group A watched a previously recorded lecture on the treatment of severe burn, a topic outside of the first-year curriculum, and Group B watched an identical lecture except three ARS questions were imbedded throughout the lecture. In Group B, the lecturer was present to explain the correct answer after each ARS question. Students took a survey and quiz immediately after the lecture and a second quiz two weeks later.

Results: Adding ARS questions during the lecture increased students’ immediate quiz scores by an average of 1.34 out of 10 (13.4%, $p<0.001$) and their delayed quiz scores by an average of 1.02 (10.2%, $p=0.005$). The rate of information loss during the two weeks did not significantly differ between the groups. Group A’s scores decreased by a mean of 0.512 out of 10 (5.12%) while Group B’s scores decreased by a mean of 0.684 (6.84%), $p=0.60$.

Conclusion: By using a previously recorded lecture on a topic outside of the first-year medical curriculum, the authors were able to isolate the impact of adding ARS to a lecture. Overall, ARS increased learner knowledge and comprehension, both immediately following a lecture and two weeks later, but did not slow the rate of forgetting.

Patterns Of Post-Operative Spirometry In Lung Transplantation

Background: Spirometric Pulmonary Function Tests (PFTs) allow for quantitative measurement of lung capacity and function, and can therefore be used to measure the recovery and performance of transplanted lungs. We investigated the time to maximum functional recovery in patients undergoing lung transplantation (LTx) due to Idiopathic Pulmonary Fibrosis (IPF), Chronic Obstructive Pulmonary Disease (COPD), or Cystic Fibrosis (CF).

Methods: We performed a retrospective review of patients diagnosed with IPF, COPD, or CF who underwent LTx at JHH between 5/05 and 7/11. Patients were excluded if they did not have at least 1 year of PFT data or a Lung Allocation Score. The primary outcome was time to maximum functional recovery, stratified by diagnosis. Sub-group analysis stratified by functional timeline was also performed. Multivariate Cox and Logistic Regression models were used to assess mortality and functional associated outcomes, respectively.

Results: Of the 74 patients, (19) had IPF, (33) had COPD and (22) had CF. Time to peak PFTs in CF and COPD were 9 months, while IPF peaked at 1 year (p-value). On sub-group analysis, the patients were stratified into 4 categories: PFT values peaked early and were sustained (SEP), PFT values peaked early but fell (NSEP), PFT values never reached maximum (NEVER), and PFT values peaked in average time. 3-year Kaplan-Meier curves show that the SEP group had greater survival than all others (P=0.007). Statistically significant differences existed between demographics across diagnoses, however these may not have been clinically significant and did not predict survival. Interestingly, SEP patients had longer ICU stays compared to NEVER patients.

Conclusion: Patterns of spirometry correlate with long-term patient outcome. PFT recovery time varies across diagnoses and clinicians should take these variations into account when assessing patient outcomes and creating treatment plans.

Oral Presenter, Public Health and Community Service

Establishing A Rural Community Health Worker Training Program In San Juan Sacatepequez, Guatemala

Problem: As compared to other Latin American countries, Guatemala performs quite poorly on a variety of health metrics. As of 2003, Guatemala had the lowest life expectancy (65 years, 12 years below that of nearby Costa Rica), highest rate of infant mortality (153 per 100,000), and highest prevalence of chronically malnourished children (44%) in Central America.

Needs Assessment: In the rural municipality of San Juan Sacatepequez, Guatemala, one of the few options for health care is the Centro de Salud Barbara (CSB), a free clinic run by the medical faculty at Universidad Francisco Marroquín (UFM). Due to limited staffing and high demand, the clinic focuses on treatment of acute illness and obstetrics, but lacks the capacity to adequately educate its patient population on disease prevention measures.

Objectives: We partnered with CSB and UFM to establish a rural community health worker training program in San Juan Sacatepequez. The basis of the curriculum is disease prevention with a particular focus on fulfilling CSB's mandate to improve prenatal care and pediatric health in the first 1000 days of life.

Educational Strategy: Our curriculum creates a three-tiered pyramid of health workers, with the highest achievers in lower tiers selected for further training. The first level educates workers in sanitation and nutrition. The second level teaches prenatal care, midwifery, and early childhood care. The third level trains workers in common medications and basic medical procedures. The curriculum will be evaluated by annual follow up with the students to determine knowledge retention and utilization.

Lessons Learned: A key challenge to implementing health initiatives in foreign countries is ensuring integration with the existing health delivery infrastructure. As such, dependable and like-minded local partners are required to ensure the effectiveness, sustainability, and cultural competency of any intervention.

Quantiferon-TB Gold In-Tube Implementation For Latent Tuberculosis Diagnosis In A Public Health Clinic: A Cost-Effectiveness Analysis

Background: The tuberculin skin test (TST) has limitations for latent tuberculosis infection (LTBI) diagnosis in low-prevalence settings. Previously, all TST-positive individuals referred from the community to Baltimore City Health Department (BCHD) were offered LTBI treatment, after active TB was excluded. In 2010, BCHD introduced adjunctive QuantiFERON-TB Gold In-Tube (QFT-GIT) testing for TST-positive referrals. We evaluated costs and cost-effectiveness of this new diagnostic algorithm.

Methods: A decision-analysis model compared the strategy of treating all TST-positive referrals versus only those with positive results on adjunctive QFT-GIT testing. Cost-effectiveness was represented using Incremental Cost-Effectiveness Ratios (ICER).

Results: QFT-GIT testing at BCHD cost \$43.51 per test. Implementation of QFT-GIT testing was associated with an ICER of \$1,202 per quality-adjusted life-year gained and was considered highly cost-effective. In sensitivity analysis, the QFT-GIT strategy became cost-saving if QFT-GIT sensitivity increased above 92% or if less than 3.5% of individuals with LTBI progress to active TB disease.

Conclusion: LTBI screening with TST in low-prevalence settings may lead to overtreatment and increased expenditures. In this public health clinic, additional QFT-GIT testing of individuals referred for a positive TST was cost-effective.

At Ease and Dis-ease: Patient Requests for Reassurance

Background: Reassurance is an important aspect of patient-physician interactions, but little is known about the circumstances under which patients explicitly request it. Our study examined how and when patients request reassurance in routine outpatient encounters.

Methods: We analyzed audio-recorded and transcribed encounters between 45 providers and 418 HIV-infected adult patients. We used the Roter Interaction Analysis System (RIAS) to identify all explicit patient requests for reassurance. We compared characteristics of patients who made versus did not make requests for reassurance, and then qualitatively analyzed these requests within context.

Results: 53 of the 418 encounters contained requests for reassurance, and there were 72 total requests. There were no differences between patients who did versus did not ask for reassurance regarding age, gender, race/ethnicity, education, health literacy or social support. However, patients requesting reassurance reported more depressive symptoms. Our qualitative analysis generated eight categories describing the topics of patient requests: overall health, symptom/illness, physical exam, therapy, testing logistics, interpreting personal data, general information, and administrative. The most common category was interpreting personal data (n=19) such as vital signs and test results (e.g. "So is that good or bad?"), followed by requests regarding therapy (n=12) and symptom/illness (n=10, "Do you all think I might have cancer of my stomach?"). While there were only four requests regarding overall health, these carried a great deal of emotional weight (e.g. "Am I gonna ever have the days again where I just feel good?" and "I just want to know when I can...will I be all right?").

Conclusion: Our study demonstrates that while patients seek reassurance from physicians for a variety of reasons, they do not often request it explicitly. Future studies could examine whether physicians should look for opportunities to offer reassurance even if not requested, particularly when treating patients with depressive symptoms.

IgE-Independent Hypersensitivity Reactions Are Associated With Prolonged Survival In Advanced Pancreatic Cancer Patients Receiving A GM-CSF Cell-Based Vaccine Plus Cyclophosphamide (Cy) And Cetuximab

Background: Combining Cy and GM-CSF secreting irradiated allogeneic pancreatic tumor cells (pancGVAX) has been shown to enhance clinical and vaccine induced anti-tumor immune responses. The mechanism is thought to occur by inhibiting suppressor T-cell activity and promoting a type 1 cytotoxic immune response through dendritic cell (DC) activation.

Methods: Sixty patients with advanced pancreatic cancer who progressed on, or refused, first line standard therapy received six cycles of Cy (day 0), pancGVAX (day 1), and Cetuximab on days 1, 8 and 15 every three weeks. Patients who experienced grade 3 Cetuximab hypersensitivity reactions continued to receive Cy and pancGVAX treatments without further Cetuximab. Serum cytokines and immunoglobulins were analyzed by ELISA and serum cell populations were evaluated using flow cytometry.

Results: Cetuximab hypersensitivity occurred in 12/60 patients. Median survival in the hypersensitivity group was 7.1 versus 4.1 months in the non-hypersensitivity group ($p=0.026$). Interestingly, among hypersensitive patients, higher serum IgE levels at enrollment was associated with increased risk of death (0.019, HR =1.05, 95% CI: 1.009-1.099). The baseline serum IgE level was not predictive of overall survival for non-hypersensitive patients ($p = 0.75$); however, higher serum IgE levels following the first vaccine was associated with increased risk ($p = 0.010$, HR = 1.026, 95% CI: 1.006-1.046). Lower levels of surface IgE bound to plasmacytoid DCs (pDCs) correlated with overall survival both at baseline ($p=0.019$) and after vaccination ($p=0.006$). Overall survival also correlated with lower levels of serum IL-6 ($p=0.031$) and IL-8 ($p=0.043$). This data suggests that a pDC-mediated skewing towards type 2 inflammatory responses is associated with poor prognosis in these patients.

Conclusion: Prolonged survival in advanced pancreatic cancer patients correlated with IgE-independent hypersensitivity to Cetuximab. IgE mediated type 2 inflammatory responses are associated with poor prognosis in patients receiving immunotherapy. Blockade of IgE may enhance the efficacy of immunotherapy in pancreatic cancer patients.

Comorbidities And Causes Of Death In The Management Of Small Renal Masses: A SEER-Medicare Analysis

Background: Recent evidence has demonstrated renal function and cardiovascular disease are closely linked. A non-cancer mortality benefit is touted for partial nephrectomy (PN) versus radical nephrectomy (RN) for small renal masses (SRMs), but controversy persists regarding cardiovascular benefits. We compared SRM management and actual causes of death with an emphasis on cardiovascular comorbidities (CVCs).

Methods: From the SEER-Medicare linked registry (1995-2007), demographic, comorbidity, and death data for patients with T1a SRMs was obtained. Patients were classified as undergoing PN or RN. Patients lacking a code for SRM management within 6 months of diagnosis were classified as non-surgical management (NSM), which is distinct from active surveillance. Subgroup analyses by Charlson comorbidity index and comorbidities assessed causes of death. Cox proportional hazards regression compared patients by CVC status controlling for demographic and patient factors.

Results: A total of 4574 patients underwent RN, 1849 underwent PN, and 754 had NSM. The most prevalent comorbidities included diabetes (20%), COPD (16%), CHF (8%), CKD (5%), history of MI (5%), and PVD (4%), which were all more common in the NSM group ($p<0.001$). Overall survival (OS) was 81% (median 58 months). Mortality was attributed to renal cell carcinoma in 2.5% of the cohort, another malignancy in 5.6%, and cardiovascular-related disease in 7.3%. CVCs significantly decreased OS and cardiovascular-specific survival (CVSS) but not cancer-specific survival (CSS; $p=0.07$). Patients with CHF had the highest mortality with 5-year survival of 57%. Compared to RN, OS and CVSS favored PN for patients regardless of CVCs ($p<0.01$). CSS favored PN for patients without CVCs ($HR 0.34(0.17-0.65), p<0.01$) but not with CVCs ($HR 0.67(0.23-2.01), p=0.48$).

Conclusion: For older patients with SRMs, CVCs are associated with adverse OS, CSS, and CVSS. The data suggest PN confers improved OS and CVSS compared to RN for patients with and without CVCs. PN should be utilized when technically feasible in patients with cardiovascular risk factors.

Racial And Sex Disparities In The Treatment Of Small Renal Masses

Background: Research on healthcare disparities for the management of small renal masses (SRMs) has been inconsistent. Previous work has compared utilization of partial nephrectomy (PN) versus radical nephrectomy (RN), but patients foregoing intervention have not been characterized. The present study characterized associations of race and sex with the management of SRMs recognizing baseline comorbidity as a potential confounder.

Methods: Within the SEER-Medicare linked cancer registry (1995-2007), patients with T1a SRM were included. Procedure codes identified patients undergoing PN or RN, while non-surgical management (NSM) was defined as no SRM intervention within 6 months of diagnosis. Patient demographic and comorbidity data were obtained. Multiple logistic regression models including race, age, sex, and Charlson comorbidity index (CCI) were developed to determine associations with NSM and utilization of PN.

Results: A total of 6,092 Caucasian and 617 African-American patients with SRM undergoing RN(63.9%), PN(25.6%), and NSM(10.6%) were included. African-American patients were older (73.4vs.71.7years, $p<0.001$), had higher proportion of females (50.4%vs.44.4%, $p=0.004$), and higher CCI ($p<0.001$). Five-year overall and cancer-specific survival were 81.3% and 97.4% for Caucasians and 73.5% and 96.9% for African-Americans. The proportion undergoing NSM vs. PN or RN was higher for African-Americans than for Caucasians (16.7% vs. 9.9%, PR 1.68, $p<0.001$) but proportions were similar for PN vs. RN (31.5% vs. 28.3%, $p=0.125$). For NSM, African-Americans had a higher odds of NSM (OR2.00[1.57-2.55], $p<0.001$), but there was no difference for sex ($p=0.904$). For PN, female sex had a lower odds of PN use compared to males (OR0.86[0.77-0.96], $p=0.009$) but no difference by race was observed ($p=0.258$).

Conclusion: Among Medicare beneficiaries, no racial disparities were evident in the use of PN over RN. Underutilization of PN was observed in females, and a significant disparity exists for surgery in African-Americans. Disparities may be even more pronounced in uninsured populations, but healthcare access and socioeconomic factors deserve attention in the future research.

Association Of Uric Acid And Left Ventricular Hypertrophy In Pediatric Hypertension

Background: Uric acid (UA) is associated with elevated blood pressure (BP) in children and cardiovascular disease (CVD) in adults. Left ventricular hypertrophy (LVH) is considered to be an early stage of CVD in children. This study aims to determine if UA is associated with LVH in hypertensive children.

Methods: We conducted a cross-sectional analysis of baseline data from a prospective observational cohort of 43 hypertensive children aged 3-18 yrs. UA norms were used to categorize children as having elevated UA ($\geq 95^{\text{th}}$ ile) or not. Demographics and CVD risk factors were compared between children using Wilcoxon rank-sum tests and chi-squared analyses. Univariate and multivariable logistic regression was used to determine the association between UA and LVH.

Results: Mean age was 15.1 yrs [interquartile range (IQR) 10.7, 17.1], 53% were overweight/obese (BMI $> 85^{\text{th}}$ %ile), and 42% had LVH [left ventricular mass index (LVMI) $> 95^{\text{th}}$ ile]. Median UA was 5.1 mg/dL (IQR 4, 6.4), and 23% had elevated UA. Children with elevated UA were older, with greater markers of obesity, lower HDL, higher hsCRP and greater LVM; median BP and prevalence of LVH was no different between groups. While univariate regression showed a significant relationship between elevated UA and LVH (Odds Ratio (OR) 4.7, 95% confidence interval (CI) 1.01, 21.6), this was no longer present after adjusting for age, sex, race and BMI z-score (OR 3.2, 95%CI 0.45, 23.7). Adjusted analysis of UA as a continuous variable was also nonsignificant.

Conclusion: While children with elevated UA do have increased CVD risk factors, this study does not reveal an independent association of UA with LVH. Further studies are needed to determine if UA is in the causal pathway of hypertension/CVD in children, or rather a marker of other risk factors such as obesity and metabolic syndrome.

Eugene Shenderov, MD/PhD or Student in Residence in research years

Mentor: Jonathan Yewdell, MD PhD

Oral Presenter, Basic Science

Tryptophan Residues In The Hydrophobic Channels Of Human CD1d Molecules Modulate Glycolipid Loading And Presentation To Invariant NKT Cells

Background: CD1d is a non-polymorphic MHC class I family member that presents lipid antigens to Natural Killer T cells (NKT cells). NKT cells recognize a broad range of lipids, and link the innate and adaptive arms of the immune system. However, it remains unclear how human CD1d (hCD1d) molecules stabilize bound lipids into the two hydrophobic channels, known as A' and F'.

Methods: We introduced Tryptophan (Trp) to Phenylalanine (Phe) substitutions of three key residues (Trp 40, 63, and 140) in the hCD1d antigen-binding A' and F' channels that undergo conformational shifts between unliganded (open) and liganded (closed) CD1d molecules. We measured the intracellular stability of mutated hCD1d molecules, their ability to present endogenous and exogenous iNKT cell ligands and the affinity of binding of iNKT T Cell Receptor to mutated hCD1d molecules loaded with a panel of iNKT cell analogs.

Results: We showed that, while mutated hCD1d molecules are stable and expressed at normal levels at the cell surface, they fail to be efficiently loaded by exogenous and endogenous iNKT cell agonists, resulting in suboptimal activation of iNKT cells, despite normal affinity of binding to the iNKT TCR. Of interest, mutated CD1d molecules loaded with exogenous lipids, which fully occupy the A' and F' channels, form long-lived complexes. In contrast, complexes between mutated CD1d molecules and lipids with a shorter phytosphingosine chain are shorter lived as compared with complexes with lipids with a shorter acyl chain.

Conclusion: Since tryptophan 40, 63, and 140 are evolutionarily conserved, our results suggest that a "Tryptophan induced fit" may play a role in regulating groove accessibility and stable binding of a broad range of lipids into the A' and F' channels of CD1d molecules. The findings described may aid the development of pharmacological ligands that allow the fine tuning of iNKT cell immunoregulatory properties.

Frailty Is Associated With An Increased Risk Of Falls In Hemodialysis Patients Of All Ages

Background: Patients with end stage renal disease (ESRD) have a higher fall rate than the general population, which contributes to their high morbidity and mortality. Although frailty has been shown to be an important predictor of falls in older adults, it is unclear whether frailty is associated with an increased risk of falls in patients on hemodialysis of all ages.

Methods: This is a prospective cohort study of 140 hemodialysis patients in a single center in Maryland between 1/2009 and 3/2010. Frailty, defined as having ≥ 3 of 5 domains (shrinking, weakness, exhaustion, low physical activity, and slowed walking), was measured by trained personnel and participants reported whether they had experienced ≥ 1 falls in the six-month period. Logistic regression was used to estimate the association between frailty and ≥ 1 falls adjusted for age, sex, smoking, comorbidity, and disability, which are noted confounders of the association between frailty and falls in this study.

Results: Participant mean age was 60.6 years, 45.7% of participants were female and 83.6% were African American. 25% of the participants had ≥ 1 falls: 17% of nonfrail participants and 43% of frail participants ($P=0.003$). Frailty was associated with a 3.18-fold (95% CI: 1.39-7.27, $P=0.006$) increased odds of ≥ 1 falls adjusted for age, sex, smoking status, comorbidity, and disability. The association of frailty and falls did not differ between older and younger participants (interaction $P=0.57$) or male and female patients (interaction $P=0.21$).

Conclusion: Frail patients undergoing hemodialysis have increased odds of experiencing a fall regardless of age. Frailty may be a useful metric to identify hemodialysis patients of all ages at increased risk for falls.

Oral Presenter, Public Health and Community Service

Risk Factors For Seclusion And Restraint In A Pediatric Psychiatry Day Hospital

Background: The use of seclusion and restraint on psychiatrically hospitalized children and adolescents has been implemented with very specific goals in mind: to prevent harm to the patient or to other patients or staff, to prevent disruption of the treatment program, and/or to prevent physical damage to property. Due to the potential for harmful consequences as a result of seclusion and/or restraint, it is important that their use is kept as limited as possible. However, relatively little data illustrating potential risk factors that may make patients more prone to seclusion and restraint exists. Elucidating this information may be critical if effective strategies aimed at reducing seclusion and restraint use are to be created.

Methods: A retrospective analysis was conducted for 56 patients admitted into the Johns Hopkins Adolescent Psychiatric Day Hospital during FY10 (July 2009- June 2010). Data consisting of clinical and demographic information for patients who experienced an event (seclusion/restraint) at any point in time (cases) and patients who experienced no event (controls) was compared and analyzed. Clinical parameters consisted of adolescent psychiatric disorders (ADHD, mood disorder, etc.). Demographic parameters included: IQ, race, special education requirement status, social economic status, location of residence, sex, age, history of abuse, and GAF score.

Results: Level of education of the patient's mother, history of any abuse, history of physical abuse, diagnosis of an internalizing disorder, and diagnosis of both an internalizing and externalizing disorder were significant risk factors for an event ($p<.05$). Age and GAF score negatively correlated with event susceptibility ($p<.05$). The number of primary diagnoses positively correlated with event susceptibility ($p<.05$).

Conclusion: The results indicate that co-morbidity, history of abuse, and social economic status influence seclusion and restraint vulnerability. Further study is needed to garner a more complete picture of risk factors for seclusion and restraint.

Quantifying The Effect Of Cardiopulmonary Resuscitation Quality On Cardiac Arrest Outcome: A Systematic Review And Meta-Analysis

Background: Evidence has accrued that cardiopulmonary resuscitation (CPR) quality impacts cardiac arrest outcome. However, the relative contributions of chest compression (CC) components (such as rate and depth) to successful resuscitation remain unclear.

Methods: We sought to measure the effect of CPR quality on cardiac arrest outcome through systematic review and meta-analysis. We searched for any clinical study assessing CPR performance on adult cardiac arrest patients where survival was a reported outcome, either return of spontaneous circulation (ROSC) or survival to admission or discharge. Of 603 identified abstracts, ten studies met inclusion criteria. Effect sizes were reported as mean differences. Missing data were resolved by direct author contact. Estimates were segregated by CPR metric (CC rate, depth, no-flow fraction, and ventilation rate), and a random-effects model was applied to estimate an overall pooled effect.

Results: Arrest survivors were significantly more likely to have received deeper CCs than non-survivors (mean difference 2.44 mm, 95% CI 1.19 to 3.69 [$p<0.001$], $n=6$ studies, $I^2=0.0\%$, p for heterogeneity= 0.9). Likewise, survivors were significantly more likely to have received CC rates closer to 85-100 cpm than non-survivors (absolute mean difference from 85 cpm -4.81 cpm, 95% CI -8.19 to -1.43 cpm [$p=0.005$]; from 100 cpm -5.04 cpm, 95% CI -8.44 to -1.65 cpm [$p=0.004$]; $n=6$ studies, $I^2<49\%$, p for heterogeneity >0.2). No significant difference in no-flow fraction ($n=7$ studies) or ventilation rate ($n=4$ studies) was detected between survivors and non-survivors.

Conclusion: Deeper chest compressions and rates closer to 85-100 cpm are significantly associated with improved survival from cardiac arrest.

Inguinal Hernia Repair Using Mesh: The Impact Of International Short-Term Surgical Training In Ghana

Background: Inguinal hernia repair is one of the most frequently performed surgeries worldwide, yet many African countries have limited surgical capacity to address the hernia disease burden. Despite the well-documented advantages of tension-free hernia repair with mesh, over 95% of hernia repairs in Africa are conducted without mesh. This study evaluates whether a 2-day training course on tension-free mesh repair has impacted the practice of training participants.

Methods: A surgical training course on tension-free mesh repair of hernias was provided to a group of 3 Ghanaian surgeons. Follow-up data was collected from the participants. All inguinal hernia surgeries, performed with or without mesh, were recorded over the course of the 14 month period following the training. Demographic variables, diagnoses, and complications were compared between mesh and non-mesh procedures.

Results: The number of surgeries performed with mesh increased significantly, from 10 mesh operations over a period of three years prior to the training, to 89 mesh operations in the 14 months following the training. Non-mesh repair continued to be the predominant practice, accounting for 91.9% of inguinal hernia repair procedures conducted during the same 14 month period. Limited mesh material and infection risk were listed as the main reasons for non-mesh repair. For the most part, mesh repair was reserved for recurrent hernias (95.2%), while most initial hernias were repaired without mesh (97.1%). Of the 2 surgeons who provided charts for complications review, complication rates between mesh and non-mesh procedures were not significantly different ($p=0.53$).

Conclusion: We have demonstrated the value of a 2-day training course to substantially impact the surgical practice of 3 lower-middle income country surgeons, significantly increasing the number of hernia repairs carried out with mesh without increasing complication rates. The present study provides evidence that short-term medical training initiatives can have a substantial impact on local healthcare practice.

Efficacy Of The Orally Delivered, Anti-Parasitic, Mebendazole, In An Intracranial Rodent Gliosarcoma Model

Background: Mebendazole (MBZ), methyl N-[6-9benzoyl]-1H-benzimidazol-2-yl] carbamate is an anti-parasitic approved by the FDA for treating roundworm, common hookworm, American hookworm, pinworm, and whipworm. Its mechanism of action is that it binds to the tubulin subunits in the gut epithelium of the parasite ultimately preventing growth. Mebendazole was previously shown to have survival benefits in two preclinical models of glioblastoma multiforme by the Ludwig Collaborative Laboratory at Johns Hopkins School of Medicine. We hypothesize that Mebendazole will have survival benefits delivered orally in Fisher 344 rats who have been previously implanted with intracranial gliomasarcoma.

Methods: Sixteen rats were divided into 2 groups: 1) Control-no treatment and 2) Daily oral treatment of Mebendazole. All rats were implanted with intracranial 9L gliosarcoma on day 0. On Day 5, the Oral Mebendazole group (n=8) began receiving Mebendazole by daily oral gavage. The control group (n=8) did not receive any treatment. Survival was the primary endpoint.

Results: Control animals had a mean survival of 11 days while the Mebendazole treatment group had a median survival of 15 days ($p=0.0003$ vs. control).

Conclusion: Our results show that daily oral gavage of Mebendazole increased survival in an intracranial gliosarcoma model. Fortuitously, this is an agent that has already been approved by the FDA for anti-parasitic treatment and has an extensive history of use in humans to date. We look forward to the upcoming clinical trial of this anti-parasitic compound.

Aaron Wild, MD/PhD or Student in Residence in research years

Mentor: Phuoc Tran, MD PhD;

Oral Presenter, Basic Science

Joseph Herman, MD MSc

Concurrent Versus Sequential Sorafenib Therapy In Combination With Radiation For Hepatocellular Carcinoma

Background: Background: Sorafenib (SOR) is the only systemic agent known to improve survival for hepatocellular carcinoma (HCC). However, SOR prolongs survival by less than 3 months and does not alter symptomatic progression. To improve outcomes, several phase I-II trials are currently examining SOR with radiation (RT) for HCC utilizing heterogeneous concurrent and sequential treatment regimens. Our study provides the first preclinical data characterizing the effects of concurrent versus sequential RT-SOR on HCC cells.

Aim/Hypothesis: To determine whether treatment with concurrent or sequential RT-SOR is more effective against HCC using both in vitro and in vivo models so as to inform the design of upcoming large-scale trials of RT-SOR for HCC.

Methods: Concurrent and sequential RT-SOR regimens were tested for efficacy among 4 HCC cell lines in vitro by assessment of clonogenic survival, apoptosis, cell cycle distribution, and γ -H2AX foci formation. Results were confirmed in vivo by evaluating tumor growth delay and performing immunohistochemistry in a hind-flank xenograft model.

Results: In vitro, concurrent RT-SOR produced radioprotection in 3 of 4 cell lines, whereas sequential RT-SOR produced decreased clonogenicity among all 4 cell lines. Concurrent RT-SOR did not increase apoptosis compared to RT alone. Sorafenib induced reassortment into less radiosensitive phases of the cell cycle through G1-S delay and cell cycle slowing, providing a mechanistic explanation for the radioprotection observed with concurrent RT-SOR. More double-strand breaks (DSBs; indicated by γ -H2AX foci) were present 24h post-irradiation for RT alone versus concurrent RT-SOR. In vivo, sequential RT-SOR produced the greatest tumor growth delay, while concurrent RT-SOR was similar to RT alone. More DSBs were observed in xenografts treated with RT alone versus concurrent RT-SOR.

Conclusion: Sequential RT-SOR demonstrates greater efficacy against HCC than concurrent RT-SOR both in vitro and in vivo. These results may have implications for clinical decision-making as well as prospective trial design.

Variability In Rates Of Structured Developmental Screening Across A Large Primary Care Organization

Background: Since 2006, The American Academy of Pediatrics (AAP) has recommended standardized developmental screening of all children at 9, 18, and 24-30 months of age, and referral to Early Intervention services for children with concerning results. The aim of this study was to characterize variability in implementation of developmental screening and referrals across a 19-site primary care organization.

Methods: We reviewed retrospective data derived from electronic medical records of patients seen for well-child care at ages when developmental screening was recommended. One-way ANOVA analyses were used to compare screening rates by provider specialty and patient visit volumes.

Results: Developmental screening data were examined from 9,708 visits conducted by 93 primary care providers across 19 sites between 1/2011 - 6/2012. Screening rates varied widely between sites (range 13.0-98.7%). Predictors of higher screening rates included longer duration since developmental screening training (94.1% among sites trained before 7/2010 vs. 47.5% among sites trained after 7/2010 vs. 31.5% among non-trained sites, $p<0.001$), provider specialty (84.23% among pediatric providers vs. 48.24% among medicine-pediatric providers vs. 37.83% among family medicine providers, $p<0.001$), and high or moderate patient volumes (77.3% among providers seeing ≥ 50 patients at target ages per quarter, vs. 78.8% among providers seeing 10-49 patients per quarter vs. 36.5% among providers seeing <10 patients per quarter, $p<0.001$). Rates of documented referral to Early Intervention services were consistently low (7.7% of children with failed screens) across all providers and sites.

Conclusion: In this large primary care organization, rates of structured developmental screening were highest among providers who were pediatricians, saw high or moderate volumes of young patients, and had been conducting screening for longer durations. Future quality improvement efforts should therefore be targeted toward medicine-pediatric providers, family medicine providers, and providers seeing low volumes of young patients. Efforts are required among all providers and sites to improve rates of documented Early Intervention referrals among children with failed screens.

BASIC SCIENCE POSTER ABSTRACTS

Listed Alphabetically

Effect Of Mir141 Expression Modulation On Bladder Cancer Invasive Potential

Background: Due to frequent recurrence and poor prognosis of invasive disease, bladder cancer (BC) requires routine surveillance and high management costs. Currently, there are limitations in BC diagnosis and screening, and no accurate methods exist to assess invasiveness preoperatively. These limitations warrant alternative biomarkers to help evaluate disease progression in a noninvasive, highly specific fashion. MicroRNAs (miRNAs) are small, noncoding RNAs that regulate gene expression by binding to target mRNAs. Aberrant expression of miRNAs can cause gene dysregulation, thus miRNA expression levels can serve as cancer biomarkers. Low-grade, noninvasive and muscle-invasive tumors frequently have distinguishing miRNA dysregulation patterns, thus miRNA expression can help stage cancers. Previous studies have found MicroRNA-141 (miR-141) significantly downregulated in invasive BC cells, and current literature notes correlations of miR-141 with colon, ovarian, and gastric cancer.

Methods: This study investigated the phenotypic effects of miR-141 modulation on the invasive potential of BC cells. miR141 mRNA targets were evaluated using in silico target gene analysis. Using microarray-based global gene expression profiles comparing EJ28 (invasive) cells and RT112 (minimally invasive) cells, we identified putative miR-141 targets. These targets were found upregulated in EJ28 cells. Phenotype assays were conducted with EJ28 cells cultured and transfected with a miR141 mimic, rescuing miR141 levels. Transfection was validated using RT-qPCR to confirm elevated miR141 expression. Changes in cell cycle progression were assessed by flow cytometry. Cellular chemotaxis was measured via migration assays. Invasion assays evaluated changes in the ability of BC cells to cross basement membranes and invade stroma.

Results: Relative to controls, miR141-expressing EJ28 cells had no significant differences in cell cycle distribution and migratory potential. However, miR141-expressing EJ28 cells demonstrated marked reduction in invasive potential.

Conclusion: miR141 is a potential tumor suppressor miRNA; further studies are needed to characterize its role in BC, tumorogenesis, and its role as a biomarker.

Investigating Morpholino Oligonucleotides As A Novel Approach To The Treatment Of Huntington's Disease

Background: Huntington's Disease (HD) is a dominantly inherited, progressive neurodegenerative disorder associated with an expansion of CAG tri-nucleotide repeats in the Huntingtin (HTT) gene. HD demonstrates nearly complete penetrance with anticipation as CAG repeats expand in successive generations. The pathophysiology of HD is thought to be due to the toxicity of soluble mutant Huntingtin protein, protein aggregates, and the RNA transcripts of the mutant Huntingtin (mHTT) gene. Currently, there are no effective therapies for HD. However, there is growing interest in the potential use of antisense oligonucleotides (ASOs) to suppress expression of mHTT. ASOs targeting the expanded CAG repeat region are of particular interest because of their theoretical ability to discriminate between normal and mHTT transcripts. Here we used three different phosphorodiamidate morpholino antisense oligonucleotides (PMOs) that we had previously designed: PMO1, PMO2, and CTRL. PMOs were used because of high stability, high water solubility, neutral charge, and low toxicity compared to other ASOs.

Methods: Toxicity was assessed by LDH assay using HEK293 cells. In all other experiments, a fibroblast cell line that had been previously derived from an HD patient (HD Q109 cells) was used. HD Q109 cells have one normal copy of the Huntingtin gene and one mutant copy containing 109 CAG repeats. The HD Q109 cells were treated with PMOs in Endo-Porter delivery medium for 48 hours. Expression levels of HTT, mHTT, ACTB, ATX2 and ATX3 were assessed by Western Blot. ACTB is a loading control. ATX2 and ATX3 also contain short CAG repeat regions. Expression levels of these genes were used as a measure of specificity of the PMOs.

Results: Morpholinos are not toxic to HEK293 cells at concentrations up to 40uM. Morpholinos targeting mHTT mRNA decrease expression of mHTT in a dose dependent manner over a dose range of 1uM to 20uM. Treatment with 20uM morpholino results in reduction of mHTT expression by 50%. Morpholinos targeting mHTT mRNA do not affect the expression of non-mutant HTT or other genes containing CAG repeats.

Conclusion: Treatment of HD fibroblasts with morpholinos targeting the mHTT transcript can selectively inhibit the expression of mHTT. The extent to which mHTT expression is inhibited may be therapeutically significant.

Investigating The Two-Pronged Role Of HEYL In Breast Cancer Angiogenesis

Background: HEYL is a transcription factor that is over-expressed in breast cancer cells and breast cancer associated endothelial. HEYL regulates the expression of genes involved in angiogenesis and invasion, like secreted CXCL1, 2 and 3. The aim of our study was to define the angiogenic role of HEYL in breast cancer cells and breast cancer associated endothelial cells, and to find a marker of HEYL activity amenable to in vivo imaging.

Methods: Using conditioned media from HS578T breast cancer cell lines +/- HEYL expression, migration assays and tube-forming assays were performed with human umbilical vein (HUVEC) and human mammary microvascular endothelial cells (HMMEC) to determine whether HEYL could stimulate angiogenesis through the upregulation of paracrine signaling molecules like CXCL1, 2 and 3. HMMECs +/- HEYL expression were used in invasion assays and ECM remodeling assays to determine HEYL's effect on the invasion and remodeling abilities of endothelial cells. HEYL knockout mice were created to test the migration ability of neonatal mouse retinal vessels lacking HEYL. Claudin 1 western blot assays were performed in breast cancer cell lines with HEYL siRNA knockdown or HEYL deletion mutants.

Results: Media conditioned by a HEYL overexpressing breast cancer cell line caused increased tube forming and migration of endothelial cells. Migration was decreased when anti-CXCL1/2/3 antibodies or CXCR2 inhibitor were added to the media. HEYL overexpression in HMMECs led to greater invasion and ECM remodeling. In HEYL knockout mice, retinal vessels had decreased migration distance compared to wild type mice. Claudin 1 expression decreased with HEYL siRNA knockdown and with HEYL deletion mutants.

Conclusion: HEYL expression increases the secretion of CXCL1/2/3 by breast cancer cells, which act on the endothelial CXCR2 receptor to increase angiogenic potential. HEYL expression in endothelial cells can increase angiogenic potential in vitro and in vivo. Claudin 1 expression is a marker of HEYL activity.

Quantitative Phosphoproteomic Analysis Of The PTEN Signaling Pathway

Background: The tumor suppressor PTEN (phosphatase and tensin homologue) is a lipid and protein phosphatase that is partially or completely lost in diverse cancers including 40% of breast cancers, resulting in hyperactivation of the PI3K/AKT pathway. This aberrant signaling cascade causes differential protein phosphorylation contributing to tumor oncogenicity, however, the majority of these differentially phosphorylated proteins have not been elucidated. To understand the signaling changes that take place in the absence of PTEN, we aimed to use mass-spectrometry-based phosphoproteomics to quantify differential phosphorylation between two cell lines, the parental MCF10A (a spontaneously immortalized normal mammary epithelial cell line) and the MCF10A PTEN homozygote knockout.

Methods: Optimal growth conditions were determined that would best highlight differential PI3K/AKT pathway activation between the two cell lines. The cell lines were metabolically labeled with SILAC (Stable Optimal growth conditions were determined that would best highlight differential PI3K/AKT pathway activation between the two cell lines. The cell lines were metabolically labeled with SILAC (Stable Isotope Labeling by Amino acids in Cell culture) media, and phospho-Ser/Thr/Tyr peptides were enriched and subjected to LC-MS/MS analysis. Search algorithms were used to analyze the resulting spectra to quantify the relative ratios of phosphoproteins in each cell line. Gene Ontology and gene set enrichment were used to identify activated phosphoproteins and signaling pathways.

Results: We determined the relative ratios of over 3400 phosphopeptides found in both cell lines. Of these, 618 phosphopeptides were hyperphosphorylated (1.5-fold increase) and 358 were hypophosphorylated (1.5-fold decrease) in the PTEN knockout cells. The list of differentially phosphorylated proteins includes a number of protein kinases (particularly those involved in MAPK and tyrosine receptor signaling) as well as proteins involved in cell adhesion and motility.

Conclusion: We identified hundreds of differentially phosphorylated proteins when the PTEN tumor suppressor is lost in a mammary epithelial cell line. This data provides the foundation for further studies to determine the specific roles of these proteins in regulating oncogenicity and to identify druggable targets for treatment of breast cancer and other cancers.

Evaluation Of The Effects Of Sodium Salicylate On Anemia In Aged Mice

Background: Anemia affects greater than 10% of older adults in the United States and is associated with adverse outcomes including physical disability and impaired cognition. The anemia in 1/3 of older adults has features of anemia of chronic disease. Furthermore, data from our group suggested aged C57BL/6 mice have features of anemia of inflammation. The focus of our project was to test whether Sodium Salicylate (SS), an anti-inflammatory drug, would prevent the development of anemia in aged C57BL/6 mice. We hypothesized that SS would inhibit inflammatory cytokines regulated by Nuclear Factor- κ B, such as IL-6, that are elevated in aged mice. We further hypothesized that SS would prevent the decline of hemoglobin and red blood cells in salicylate-treated aged mice compared to placebo-treated, aged-matched controls. We also anticipated that SS would increase the amount of iron available for erythropoiesis in aged mice.

Methods: To test our hypothesis, we collected blood and tissue samples from aged mice that have been treated either with SS (N=10) or placebo (N=11) for 6 months.

Results: Hemoglobin concentration was marginally improved at 24 months in the SS-treated group. Seven out of eleven mice in the placebo group had a hemoglobin drop greater than or equal to 2mg/dL compared to only three out of ten in the salicylate treated group. We then checked the level of erythropoietin in the kidney, a hormone that controls red blood cells production. We found that Epo was high in two mice in the placebo group; these mice also had the lowest level of hemoglobin again confirming that the anemia seen in this setting is independent of the level of Epo.

Conclusion: In conclusion, Sodium Salicylate did not prevent the development of anemia in aged mice even though there was a slight increase in the Hb level. There are a few limitations to our experiment. The concentration of Salicylate in the treated mice was not assessed due to the limited amount of serum that could be collected from the mice. Some of the side effects of Salicylate include bleeding and might have masked the anti-inflammatory effects. In the future, we would do some power calculation to assess feasibility of a larger study.

Helper T Cells Downregulate CD4 Expression Upon Chronic Stimulation

Background: Helper T (TH) cells play a central role in the adaptive immune response by activating cytotoxic T cells and modulating antibody-producing B cells. Their dysfunction can lead to states of immunodeficiency or autoimmunity. TH cells express CD4, a co-receptor that participates in T cell receptor (TCR) signaling and TH cell activation. Changes in CD4 expression could thus disturb regulation of the immune response.

Methods: TH cells isolated from C57BL/6 or TCR-transgenic mice by negative selection were activated with anti-CD3/CD28-coated beads. The cells were cultured for 5 rounds of stimulation, with each round consisting of 4 days of stimulation followed by 3 days of rest. Expression of CD4 and other surface molecules was quantified by FACS analysis. Light microscopy was used to evaluate the cell morphology.

Results: After approximately 4 rounds of anti-CD3/CD28 stimulation, a change in morphology of TH cells was observed: They became larger and more uniformly spherical. Further characterization of these cells by FACS revealed robust expression of CD3 and a lack of CD4 expression. These cells did not express CD8, NK1.1, or B220, produced IFN γ and IL-17, and were dependent on anti-CD3/CD28 stimulation for proliferation and survival. Utilizing TCR-transgenic animals, the expression of the TCR α and β chains during CD4 downregulation will be evaluated to confirm that the T cells remain MHC II-restricted, thus verifying their origin from a CD4⁺ population.

Conclusion: Herein, we report a novel observation that chronic in vitro stimulation leads to downregulation of CD4 expression on murine TH cells. Although used to mimic antigenic response, anti-CD3/CD28 stimulation is supra-physiologic, does not require CD4, and bypasses normal inhibitory signals mediated by CTLA4. Such TH-cell stimulation does not accurately represent normal immunologic response, but could be characteristic of autoimmunity. Further studies of functional implications of chronic stimulation and CD4 downregulation on TH cells are warranted and underway.

Cardiac Function Analysis Using A 4D Motion Estimation Algorithm For Computed Tomography

Background: Treatment of cardiovascular disease, the leading cause of mortality worldwide, demands early detection. While echocardiography remains a routine diagnostic tool, more sensitive imaging modalities such as X-ray computed tomography (CT) and magnetic resonance imaging (MRI) can not only reveal subtle abnormalities but also more accurately measure heart function. In particular, cardiac deformation analysis---calculating myocardial strain and related indices---has demonstrated tremendous prognostic value and has been well described in echocardiography, MRI, and SPECT, but not in CT. Given that CT possesses both high acquisition speed and excellent spatial resolution, it would bring unique advantages to cardiac deformation analysis. This computational project extends our laboratory's four-dimensional CT motion estimation algorithm, a low-dose time-resolved alternative to today's electrocardiogram-gated CT, to characterize cardiac deformation analysis in CT.

Methods: MATLAB software was developed to calculate deformation indices (such as strain, strain rate, and maximal strain) from 4D motion estimation data, which were computed from normal patient CT images. Notably, calculations were done at every grid point pair, in contrast with less precise prior approaches that divided the heart into a small number of segments. To aid interpretation, results were visualized as color maps superimposed on CT slices in orthogonal views of the heart.

Results: In each of the several patients tested, calculated myocardial deformation agreed with normal cardiac physiology. For instance, in each cardiac cycle, calculated radial strain around the left ventricle increased from end-diastole to end-systole before returning to baseline, consistent with the timings and magnitudes of normal myocardial contraction.

Conclusion: This computational approach provides a quantitative, physiologic, and intuitive way to assess cardiac function. Clinical integration will result in a precise and low-dose imaging modality to detect early manifestations of cardiovascular disease, thereby reducing mortality.

Identification Of External Factors That Affect The Fidelity Of Eukaryotic Start Codon Recognition

Background: Many eukaryotic mRNAs possess multiple start codons. The selection of a particular start codon by the ribosome may be modulated by external signals and internal programs to regulate gene expression on a post-transcriptional level. Aberrant start codon recognition is implicated in a variety of diseases; thus, elucidation of the mechanism(s) underlying start codon recognition might reveal avenues for therapeutic intervention. The goal of this project is to identify external stimuli that are capable of altering the fidelity of start codon recognition.

Methods: A yeast dual-luciferase assay was used to assess the fidelity of start codon recognition. The assay employs a plasmid encoding firefly luciferase with a UUG start codon and Renilla luciferase with an AUG start codon, which serves as internal control. To control for effects specific to the firefly luciferase enzyme, a plasmid vector encoding firefly and Renilla luciferase, both with an AUG start codon, was used.

Results: Reduced growth temperature increased the fidelity of start codon recognition. Increased pH of the growth medium decreased the fidelity of start codon recognition. Four compounds out of 55,000 small molecules screened decreased fidelity. Overexpression of eIF1, a eukaryotic translation factor known to increase the fidelity of start codon recognition, partially suppressed these effects. Additional experiments revealed that the effects of these stimuli are partially additive in some instances and mutually exclusive in others.

Conclusion: We identified several external factors and compounds that modulate the fidelity of start-codon recognition in yeast. Rescue of codon recognition by overexpression of eIF1 further suggests that these compounds decrease the fidelity of start codon recognition. The effects of the compounds at different pHs suggest action via two distinct mechanisms. This hypothesis is substantiated by drug competition experiments. Further studies are required to establish modes of action for these agents and identify additional stimuli that alter start codon recognition.

Ian-James Malm, MD/PhD or Student in Residence in research years Mentor: Young J. Kim, MD PhD

Poster Presenter, Basic Science

PD-1 Blockade Combined With TEGVAX (TLR Agonists-Enhanced GVAX) Can Induce Regression Of Established Palpable Tumors

Background: Cell-based vaccines have been developed for several types of tumors, but these vaccines have two critical shortcomings that weaken their clinical efficacy. The first of which is a limited capability to activate antigen presenting cells. Second, they fail to address critical immune checkpoint molecules that dampen the subsequent T-cell response against the established tumor. In order to optimize the activation of antigen presenting cells capable of marshalling both an innate and adaptive immune response against the tumor, we formulated a GM-CSF secreting tumor cell vaccine with multiple TLR agonists. To address the immune checkpoint signaling pathway, we combined our formulated vaccine with a blocking α PD-1 antibody in two mouse models of established tumor – one with melanoma and the other with tongue cancer.

Methods: To optimize in vivo efficacy of anti-tumor T-cell response, we engineered TEGVAX, a GM-CSF secreting cell-based tumor vaccine formulated with GLA (TLR4 agonist) and R848 (TLR7/8 agonists), molecules that are amenable for clinical translation. We then combined TEGVAX with antiPD-1 blocking antibody (G4 clone) in the murine B16 melanoma and SCCFVII tongue cancer model. Furthermore, we studied immunological parameters that correlated with in vivo anti-tumor response.

Results: In both B16 and SCCFVII treatment models, TEGVAX demonstrated statistically significantly ($p < 0.01$) enhanced anti-tumor responses in comparison to the parental cell vaccine in vivo. For tumor bearing mice treated with TEGVAX, these potent anti-tumor responses were correlated with a statistically significant increase in CD4⁺ and CD8⁺ T-cells that secrete IFN γ in the tumor microenvironment. TEGVAX treated mice also had significantly higher levels of tumor antigen p15E-specific cell mediated killing in vivo. Blockade of the PD-1 immune checkpoint pathway further augmented the therapeutic potential of TEGVAX and induced the regression of established B16 and SCCFVII tumors.

Conclusion: When combined with α PD-1 antibody, TEGVAX was able to induce regression of established B16 and SCCFVII tumors. Our results with these combinatorial immunotherapeutic strategies provide preclinical evidence to support the translation of these reagents for HNSCC patients that are refractory to standard treatment modalities.

Matrix Metalloproteinase Expression In Cavity Tissue In A Rabbit Model Of Post-Primary Tuberculosis

Background: Infection with *Mycobacterium tuberculosis* (MTB) kills 1.4 million people annually. Post-primary disease results from reactivation or reinfection, accounts for an estimated 80% of clinical cases and 100% of transmission, and is characterized by pulmonary cavitation, the pathogenesis of which is unclear. Given that the lung is largely extracellular matrix (ECM), we hypothesize that upregulation of ECM-degrading enzymes are important in cavitation. Matrix metalloproteinases (MMPs) are ECM-degrading enzymes which have already been implicated in MTB pathogenesis. MMP-1 is a collagenase which is upregulated in macrophages infected with MTB and has also been found elevated in sputum of patients.

Methods: In a rabbit model of cavitary tuberculosis, we sampled cavity wall and nearby normal lung parenchyma in nine rabbits. Quantitative real time PCR was used to assess expression of 21 genes: MMP-1, 2, 3, 7, 8, 9, 10, 12, 13, 14, 15, 16, 17, 19, 21, 24, and 27, and the tissue inhibitors of MMPs (TIMPs) 1-4. The rabbits were derived three each from separate protocols for infection (CDC1551, H37Rv high dose, H37Rv low dose), and the results were analyzed accordingly. The matched-pair cavity:normal ratio was determined and averaged across rabbit groups.

Results: In H37Rv low dose rabbits, MMP1 was upregulated 10^7 -fold ($p < 0.01$). This group and the CDC1551 group revealed a consistent MMP profile which was characterized by marked but non-significant upregulation of several genes: MMP1 (10^7 fold change), MMP3 (10^6), MMP7 (10^3), MMP8 (10^4), MMP10 (10^6), MMP12 (10^2), and MMP13 (10^3). No gene was downregulated. The H37Rv high dose group showed no changes greater than 10-fold.

Conclusion: MMPs are generally upregulated in tissue at the edge of a cavity. In accordance with in vitro and human data, MMP1 is particularly upregulated and represents a potential therapeutic target. This concordance helps validate this model for assessment of MMP activity.

The Effect Of Fibroblast Identity On Induction Of Keratin 9 Gene In Human Epithelial Keratinocytes

Background: Despite advances in prosthetic design, skin problems such as skin breakdown at the stump site constitute a significant source of morbidity for the 1.6 million amputees in the United States. To address this issue, we propose to change the identity of skin at the stump site to more durable volar (palmo-plantar) skin found on the palms and soles. The goal of this study is to establish that transplanted volar dermal fibroblasts can stimulate target non-volar epidermis (i.e. stump site) to express structural protein keratin 9 (KRT9) and to optimize experimental methods for KRT9 induction.

Methods: Primary human keratinocytes derived from neonatal foreskin were co-incubated with either volar fibroblasts or non-volar fibroblasts obtained from living donors under various conditions. KRT9 induction was compared using quantitative RT-PCR.

Results: Preliminary data suggest that the greatest amount of KRT9 induction was derived with 2.5×10^5 fibroblasts incubated with 2×10^5 keratinocytes in 100 mm cell culture dishes.

Conclusion: We have found that volar dermal fibroblasts can stimulate target non-volar epidermis to express KRT9 under certain conditions. We plan further experiments to optimize the conditions for maximal level of KRT9 induction.

N-Acetylcysteine Enhances Cystic Fibrosis Sputum Penetration And Airway Gene Transfer By Highly Compacted DNA Nanoparticles

Background: For effective airway gene therapy of cystic fibrosis (CF), inhaled gene carriers must first penetrate the hyperviscoelastic sputum covering the epithelium. Whether clinically studied gene carriers can penetrate CF sputum remains unknown. Here, we measured the diffusion of a clinically tested non-viral gene carrier, composed of poly-L-lysine conjugated with a 10 kDa polyethylene glycol (CK30PEG10k) segment.

Methods: To improve gene carrier diffusion across sputum, we tested adjuvant regimens consisting of N-acetylcysteine (NAC), recombinant human DNase (rhDNase) or NAC together with rhDNase. We further tested the adjuvant effects of NAC in the airways of mice with *Pseudomonas aeruginosa* lipopolysaccharide (LPS)-induced mucus hypersecretion.

Results: We found CK30PEG10k/DNA nanoparticles were trapped in CF sputum. While rhDNase alone did not enhance gene carrier diffusion, NAC and NAC+rhDNase increased average effective diffusivities by 6-fold and 13-fold, respectively, leading to markedly greater fractions of gene carriers that may penetrate sputum layers. Intranasal dosing of NAC prior to CK30PEG10k/DNA nanoparticles enhanced gene expression by up to ~12-fold compared to saline control, reaching levels observed in the lungs of mice without LPS challenge.

Conclusion: Our findings suggest that a promising synthetic nanoparticle gene carrier may transfer genes substantially more effectively to lungs of CF patients if administered following adjuvant mucolytic therapy with NAC or NAC+rhDNase.

Pelvic Nerve Injury Leads To Marked Changes In Adrenergic And Cholinergic Signaling In The Vagina And Bladder

Background: Radical hysterectomy (RH) is effective for the management of cervical cancer; however, damage to the neurovascular bundle and pelvic plexus following RH can lead to bladder and sexual dysfunctions. The purpose of this study was to characterize the pathophysiological changes that occur in the bladder and vagina following bilateral pelvic nerve injury (BPNI).

Methods: Female Sprague-Dawley rats underwent BPNI (n=32) or sham (n=8) surgery and were sacrificed 7, 14, 30, and 60 days post-surgery. Vagina and bladder were excised, weighed and mounted in the myograph. Adrenergic contractions to norepinephrine and electrical field stimulation (EFS), and relaxation to EFS and nitric oxide donor (NONOate) was measured in the vagina. Bladder cholinergic contractions were examined with carbachol and EFS. Gene expression of rho-kinase (ROCK1, ROCK2) and RhoA in the vagina and muscarinic type 2 (MR2) and 3 (MR3) receptors in the bladder were assessed by qPCR. Vaginal segments were formalin-fixed and stained with Masson's trichrome to assess fibrosis.

Results: Vaginal adrenergic-mediated contractions were greater at 7 and 14 days following BPNI ($p<0.05$). Gene expression of RhoA, ROCK1 and ROCK2 was elevated, indicating increased rho-kinase expression may contribute to enhanced adrenergic signaling ($p<0.05$). Non-adrenergic, non-cholinergic (NANC) relaxation was impaired in vaginas from BPNI rats ($p<0.05$). Furthermore, vaginal fibrosis was increased 14 days following BPNI. Following BPNI, bladder weights were higher and cholinergic contractions by carbachol and EFS were significantly reduced ($p<0.05$). Gene expression of MR2 was 60% less following BPNI while MR3 expression was unchanged.

Conclusion: These findings demonstrate that neuropraxia leads to increased rho-kinase-mediated adrenergic contraction, impaired NANC-mediated relaxation and fibrosis in the vagina contributing to sexual dysfunction. Additionally, BPNI increased the weight of the bladder and impaired cholinergic-mediated contractions. These findings suggest that this model can be used to study the mechanisms of neuropraxia-induced sexual and voiding dysfunctions.

Behavioral Effects Of Cocaine Are Mediated By Nitric Oxide-GAPDH Transcriptional Signaling

Background: The behavioral stimulant effects of cocaine are thought to be elicited by the potentiation of synaptic dopamine activity leading to the activation of a number of transcription factors such as CREB and DfosB. To date, mechanisms connecting neurotransmitter-receptor interactions to these transcriptional systems upon cocaine treatment are not well-characterized. Here, we show that cocaine signals by stimulating the nitrosylation and nuclear translocation of GAPDH to alter transcriptional events.

Methods: Mice were treated with 5-50mg/kg cocaine and 0.15mg/kg CGP3466B where applicable. Nitrosylation of GAPDH was detected via the biotin-switch assay and its localization by cytoplasmic/nuclear fractionation. Binding experiments were performed via immunoprecipitation. Transcription was assessed via rtPCR, and transcription factor recruitment to promoters via ChIP. Cocaine-associated behaviors were monitored via open-field and conditioned placed preference tests.

Results: At lower, behavioral-stimulant doses, cocaine elicits nitrosylation/nuclear translocation of GAPDH with Siah1 in a ternary complex with the histone methylating enzyme SUV39H1. Siah1, via its ubiquitin-E3-ligase activity, degrades SUV39H1, and the resultant decreased methylation of histone H3K9 leads to increased transcription of CREB transcriptional targets. By contrast, high, neurotoxic doses of cocaine cause nitrosylated, nuclear GAPDH to associate with p300/CBP, activating p300/CBP acetylation of p53. This elicits p53-mediated transcription of pro-apoptotic genes such as PUMA and Bax. CGP3466B is a small molecule found to prevent the nitrosylation and nuclear localization of GAPDH in sub-nanomolar concentrations. In vivo, CGP3466B prevents both CREB and p53 transcriptional signaling of cocaine and reverses both the behavioral stimuli and the neurotoxic actions of cocaine. Notably, CGP3466B reduces conditioned placed preference in mice.

Conclusion: These results demonstrate that nitrosylation/nuclear localization of GAPDH is indispensable for mediating the behavioral-stimulant and neurotoxic transcriptional responses to cocaine. Through CGP3466B, which reverses the effects of cocaine in vivo, we demonstrate the clinical applicability of targeting GAPDH nitrosylation as a means for treating cocaine addiction and neurotoxicity.

(This work is currently undergoing revision at Neuron. We have a patent pending based on these findings, and are collaborating with NIDA to test CGP3466B in cocaine)

Bioluminescence As A Surrogate Marker Of Functional Decline In Metastatic Disease

Background: Bioluminescence quantitatively correlates with poor functional status in a rat model of metastatic disease.

Methods: Seventeen female athymic rats underwent an anterior laparotomy for implantation of luciferase positive human breast adenocarcinoma (RBC3) in the L6 vertebral body. Functional assessments of locomotion via the Basso, Beattie, and Bresnahan (BBB) score were performed on postoperative day 22. On postoperative day 23, the animals were injected with Luciferin and exposed to IVIS bioluminescence (Xenogen). An unpaired, unequal variance t-test was performed for statistical analysis.

Results: Seven rats demonstrated a robust bioluminescence at day 23 ($>1E6$ photons). Ten animals demonstrated background signal only ($<1E4$ photons). The difference in average bioluminescence was statistically significant between groups ($p=0.02$). Among animals with bioluminescence positivity above the $1E6$ photon threshold at day 23, functional scores were significantly higher at day 22 (average 20.3; $p=0.03$) compared to animals with robust bioluminescence (average 17.7). Higher functional scores correlate with better neurologic function.

Conclusion: Measurement of neurologic status in an animal model is difficult using ambulatory scoring systems alone. In this study, we report the use of bioluminescence imaging as a surrogate marker of functional decline. We demonstrated a statistically significant difference in functional scores for animals with positive bioluminescence in a rat model of spine metastatic disease.

CLINICAL RESEARCH POSTER ABSTRACTS

Listed Alphabetically

Quality Of Life Outcomes Associated With Nipple Sparing Mastectomy And Breast Reconstruction

Background: Post-mastectomy breast reconstruction plays an integral role in patients' overall treatment and survivorship experience. However, loss of the nipple areolar complex can be psychologically and sexually devastating. Although recent literature has shown nipple-sparing mastectomies (NSM) provide robust cosmetic results and are oncologically safe, few studies have investigated quality of life (QOL) outcomes associated with NSM.

Methods: We performed an IRB-approved retrospective chart review of 32 patients who underwent NSM with implant-based or autologous reconstruction and 32 control patients who underwent non-NSM with reconstruction matched by reconstruction type and operative time period. We then compared pre-mastectomy and post-reconstruction responses to the BREAST-Q®, a validated quality of life questionnaire related to breast reconstruction, within and between our study and control populations.

Results: Simple statistics revealed that our NSM and non-NSM groups were statistically similar in terms of age [mean age: NSM=49.9+/-8.5 years (range=36-69), non-NSM=47.7+/-10.3 years (range=26-68)(p=0.29)] and BMI [mean BMI: NSM=24.3+/-3.5 (range=17.9-33.7), non-NSM=25.5+/-5.4 (range=19.2-39.2)(p=0.29)]. There were no significant between-group differences in occurrence of post-reconstruction complications. We found significantly higher post-reconstruction scores in the NSM group within the satisfaction with breasts domain (p=0.039). The relationship between the NSM group and the satisfaction with breasts domain differed by radiation exposure. In addition, we found significantly higher satisfaction with outcome domain scores in the NSM group (p=0.017). There were no other significant differences between NSM and non-NSM on any pre-mastectomy or post-reconstruction dimension of the BREAST-Q®.

Conclusion: Psychological concerns regarding malignancy may negatively impact pre-mastectomy patient QOL. Reconstructive surgery improves patients' post-reconstruction QOL even though it may involve complex surgery, scarring, and discomfort. NSM appears to provide significantly better improvement in post-reconstruction QOL, specifically in the satisfaction with breasts and outcome domains of the BREAST-Q®, when compared with non-nipple sparing mastectomies.

Postoperative Outcomes And Quality Of Life (QOL) Of Planned Vs. Unplanned Vascular Delay (VD) In Free Flap Breast Reconstruction Surgery

Background: Vascular Delay (VD) is a surgical tool, which allows for an increased volume of harvested tissue and improved flap survival through the dilation of choke vessels. At our institution we have planned VD in the presence of subjectively poor perforators on CT angiography or in flaps requiring all 4 Hartrampf Zones. For salvage of flaps with vascular compromise, unplanned VD has been used intraoperatively. Our aims were to quantify and describe differences in postoperative outcomes and QoL in patients undergoing 1) planned vs. unplanned VD for free flap breast reconstruction, and 2) VD (planned and unplanned) vs. non-delayed reconstructions.

Methods: This was a retrospective review (June 2008-Sept 2011) of free flap breast reconstructions with and without VD. We recorded demographics, length of VD, flap weight, reason for VD, and postoperative complications. The BREAST-Q® was administered >6 months postoperatively. Univariate analysis and descriptive statistics were performed to compare QoL and postoperative outcomes respectively.

Results: A total of 39 women had free flap breast reconstruction, 19 with VD (12 planned, 7 unplanned) and 20 randomly selected controls with no VD. Reasons for VD were: larger flap volume need, unfavorable perforator anatomy, venous congestion and intraoperative vascular compromise. Flap weight averaged 603.5 ± 264.5 g (VD) vs. 634.9 ± 284.0 g (control). Average length of VD was 14.2 ± 2.6 days (planned) and 15.3 ± 5.2 days (unplanned). VD didn't work in two patients resulting in total flap loss. Total postoperative complications in VD patients were 64.7% vs. 35% for the control group ($p=0.07$). The incidence of abdominal wound complications was significantly higher in the VD group (47.1% vs. 15%, $p=0.03$). Differences in QoL were not statistically significant among the groups ($p=0.43$).

Conclusion: The decision to delay tissue transfer intraoperatively vs a planned vascular delay does not influence postoperative outcomes and QoL. However, the additional surgery required with the delay phenomenon does increase donor-site morbidity.

Clinical And Neuropathological Correlates Of Apathy In Alzheimer's Disease (AD)

Background: Alzheimer's disease (AD) is the most common dementia in the elderly and hallmarks include neuritic plaques and neurofibrillary tangles. Apathy is highly prevalent in AD and relatively little is known about its relation to AD neuropathology. Clinical and neuropathological correlates of apathy in AD were assessed from participants in the National Alzheimer's Coordinating Center (NACC) dataset. We hypothesized that apathy would be associated with worse AD neuropathology including more neuritic plaques and neurofibrillary tangles.

Methods: Data were obtained from 28 Alzheimer's Disease Centers (ADCs). Clinical diagnoses were healthy controls (HC) (N=146), mild cognitive impairment (MCI) (N=103), or AD with Clinical Dementia Severity (CDR) at the last visit prior to death of <2.0 (excluding participants with moderate or severe AD). AD neuropathology was assessed by a combination of neuritic plaques and neurofibrillary tangle density. There were 123 patients who met the criteria for "clinical AD" and 148 who met the criteria for "pathological AD". There were 86 participants who met both criteria and were classified as "clinical + pathological AD". The severity of the Apathy domain of the Neuropsychiatric Inventory (NPI-Apathy) was modeled with multivariate ordinal logistic regression.

Results: Mean age at death was 85.94 years (SD=9.75). "Clinical AD" patients had a higher severity of apathy and more neuritic plaques and neurofibrillary tangles than MCI and HC patients. Greater severity of apathy was associated with a lower density of neuritic plaques in "clinical AD" and "clinical + pathological AD." Apathy was also associated with depression in "clinical AD" and a lower mini-mental state examination (MMSE) score in "pathological AD".

Conclusion: Apathy severity in AD was associated with a lower density of neuritic plaques, suggesting a previously unobserved heterogeneity in the neuropathologic substrate of apathy in AD.

Long-Term Follow-Up Of Children Treated With The Modified Atkins Diet

Background: The modified Atkins diet (MAD) has been studied since 2003 for children with intractable epilepsy, with over 200 children reported in mostly short-term clinical trials and case series. However, no studies have systematically examined the long-term benefits and side effects beyond 6 months of use. We believed outcomes beyond 6 months on the MAD would be similar to at 6 months or earlier. We also believed that the long-term outcomes (>6 months) would be similar to those reported for the traditional ketogenic diet (KD) after this period of time.

Methods: A total of 54 children who started the MAD (without prior KD use) at Johns Hopkins Hospital were examined retrospectively to assess their long-term outcomes (>6 months MAD duration). Children who had not been seen within the past 2 years were contacted by phone and email for updated information.

Results: At the most recent point during the MAD (mean 19.9 months), 30 out of 54 children (56%) with diet durations of more than 6 months achieved >50% improvement, of which 23/54 (43%) had >90% improvement, and 19/54 (35%) were seizure-free. These results are similar to published data reporting 49% of children responding (>50% improvement) to the MAD after 3-6 months and 43% of children responding to the traditional ketogenic diet after several years. Side effects were mild during the MAD and mostly limited to elevations in lipid profile and gastrointestinal upset.

Conclusion: The MAD appears safe and effective long-term, confirming previous short-term results.

Pediatric Extirpative Renal Surgery: A 12-Year Experience in Maryland

Background: There has been a growing interest in the application of laparoscopy and robot-assisted surgical techniques to extirpative renal surgery in children, yet no population-based analyses of children undergoing extirpative renal surgery have been conducted comparing open and minimally-invasive techniques. Our objective is to report trends and associations with outcomes and hospital charges of children undergoing extirpative renal surgery in the state of Maryland over a 12 year period.

Methods: The Maryland Health Services Cost Review Commission database was queried to identify children undergoing total or partial nephrectomy between 2000 and 2011. Demographic, clinical, outcome, hospital, and charge data were compared between children undergoing open and minimally-invasive renal surgery. Multivariable logistic regression analysis was performed to identify independent predictors of prolonged length of hospital stay and 30-day readmission. Multivariable linear regression was performed to identify independent predictors of increased hospital charges.

Results: The Maryland Health Services Cost Review Commission database was queried to identify children undergoing total or partial nephrectomy between 2000 and 2011. Demographic, clinical, outcome, hospital, and charge data were compared between children undergoing open and minimally-invasive renal surgery. Multivariable logistic regression analysis was performed to identify independent predictors of prolonged length of hospital stay and 30-day readmission. Multivariable linear regression was performed to identify independent predictors of increased hospital charges.

Conclusion: In Maryland hospitals, most extirpative renal surgeries in children are total nephrectomies performed by an open technique by high volume surgeons. Patient complexity and not operative approach dictates post-operative morbidity and hospital charges. Treatment recommendations in children should be made after careful consideration of the child's disease and overall health.

Trends In Renal Surgery: Robotic Technology Is Associated With Increased Utilization Of Partial Nephrectomy

Background: Underutilization of partial compared to radical nephrectomy for renal tumors has been demonstrated in recent population-based analyses. One explanation for this is the learning curve associated with laparoscopic partial nephrectomy. We analyzed state trends in renal surgery and their relationship to the introduction of robotic technology.

Methods: The Maryland Health Services Cost Review Commission (HSCRC) database was used to identify patients who underwent radical nephrectomy, partial nephrectomy, or renal ablation from 2000-2011. Utilization trends and associated patient and hospital factors were analyzed using multivariate logistic regression. ICD-9 robotic modifier codes were established in October 2008.

Results: Of 14,260 patients included, 11,271 (79.0%), 2,622 (18.4%), and 367 (2.6%) underwent radical nephrectomy, partial nephrectomy, and renal ablation, respectively. Partial nephrectomy use increased from 8.6% in 2000 to 27% in 2011. Open radical nephrectomy use decreased by 33% while the utilization of minimally-invasive radical nephrectomy increased by 15%. Robotic-assisted laparoscopic partial nephrectomy use increased from 2008 to 2011, reaching 14% for university and 10% for non-university hospitals ($p=0.03$) and was associated with increased utilization of partial nephrectomy (OR 9.67, $p<0.001$). Younger age, male sex, and low patient complexity predicted partial nephrectomy use on overall analysis, while higher hospital volume and university status were predictors only in earlier years.

Conclusion: Partial nephrectomy use has increased in Maryland from 2001-2011, and this has been facilitated by robotic technology. Associations with hospital factors declined over time. These data suggest robotic technology may enable surgeons across practice settings to more frequently utilize nephron-sparing surgery.

Auditory Force Feedback Substitution Improves Surgical Precision During Simulated Ophthalmic Surgery

Background: Many ophthalmic surgical maneuvers generate forces below human tactile sensation. We tested the impact of auditory force feedback (AFF) substitution during a simulated ophthalmic peeling procedure. We hypothesized that force feedback substitution would improve surgical task performance.

Methods: A 25-gauge force-sensing microforceps was linked to two AFF modes. The “alarm” AFF mode notified the surgeon with a continuous audible tone when the force reached 9 mN. The “warning” AFF mode informed the surgeon with audio beeps that had a frequency proportional to the force being applied. Participants with different surgical experience levels were asked to peel a series of 13 mm bandage strips off a platform as quickly as possible without exceeding 9 mN of force. In study arm A, participants peeled with alarm and warning AFF, the order randomized within experience level. In study arm B, participants first peeled without AFF, then alarm or warning AFF (order randomized within experience level), and once again without AFF.

Results: We enrolled 28 participants, or “surgeons” for this study. Participants included medical students, ophthalmology residents, fellows, and faculty. Regardless of surgical experience, AFF improved membrane peeling performance by reducing average force generated ($p<0.01$), standard deviation of forces ($p<0.05$), and force*time above 9 mN ($p<0.01$). Short training periods with AFF improved subsequent peeling performance when AFF was turned off, with reductions in average force, standard deviation of force, maximum force, time spent above 9 mN, and force*time above 9 mN (all $p<0.001$). Except for maximum force, peeling with AFF reduced all force parameters ($p<0.05$) more than peeling without AFF after completing a training session.

Conclusion: AFF enables the surgeon to reduce the forces generated with improved precision during phantom membrane peeling, regardless of surgical experience. New force-sensing surgical tools combined with AFF offer the potential to enhance surgical training and improve surgical performance.

Facial Reanimation Surgery Restores Affect Display

Background: Previous studies demonstrate that affect, the external display of one's emotions, is diminished in patients with facial paralysis. Ample evidence supports the importance of proper affect display in one's ability to function and thrive in society. Therefore, facial paralysis patients often experience adverse psychological and social outcomes. The primary treatment modality for facial paralysis is facial reanimation surgery. In this randomized, controlled study, we evaluate the impact of reanimation surgery on affect display in patients with facial paralysis.

Methods: Ninety naïve observers completed a survey with pictures of paralyzed faces, smiling and in repose before and after surgery, as well as normal comparison faces. Observers characterized the affect display of each face using eight primary affects from the Derogatis Affects Balance Scale plus one neutral affect. Results were analyzed with latent class analysis and regression using a three-class model representing positive, negative, and neutral affect dimensions.

Results: Preoperatively, paralyzed faces smiling and in repose were most likely to be considered negative. Postoperatively, these same faces smiling and in repose were most often characterized as positive and neutral, respectively. This improvement in affect display approaches the pattern seen in normal faces. The probability of classifying normal faces in repose as neutral is 63%, positive 22%, and negative 15%. For paralyzed faces in repose, reanimation surgery restored affect display to normal levels; changing the probability of neutral classification from 41% to 54%, positive from 3% to 28%, and negative from 56% to 18%. These results were statistically significant. For paralyzed smiling faces, surgery failed to restore affect display to the degree seen in normal smiling faces; however, it still showed improvement by decreasing negative and increasing positive characterization.

Conclusion: Facial reanimation surgery improved affect display in patients with facial paralysis. These results provide evidence to support the importance of facial reconstruction to minimize psychosocial dysfunction.

Efficacy Of Sorafenib Combined With Doxorubicin Eluting Bead-Transarterial Chemoembolization For Patients With Unresectable Hepatocellular Carcinoma

Background: Sorafenib is currently the only systemic therapy to demonstrate survival advantage in patients with unresectable hepatocellular carcinoma (HCC). This study reports the final analysis of a prospective phase II study evaluating the efficacy of sorafenib combined with doxorubicin eluting bead transarterial chemoembolization (DEB-TACE) in patients with unresectable HCC.

Methods: Therapeutic protocol consisted of 6-week cycles of sorafenib at 400mg bid (dosing adjusted based on toxicity) beginning 1-week prior to initial DEB-TACE. Tumor response was assessed by EASL and RECIST criteria using contrast enhanced MRI. Time to untreatable progression (TTUP) and overall survival (OS) were the primary and secondary outcomes.

Results: DEB-TACE in combination with sorafenib was successfully performed in 50 patients: mean 62 yrs (range, 31 - 88 yrs), BCLC staging criteria A/B/C (10%/28%/62%), mean tumor size 7.2cm and mean tumor enhancement of 78%. The median sorafenib dose taken while on study was 318mg/day (range, 100 - 800mg/day). 6-month follow-up showed a mean tumor enhancement reduction of 66.6% ($p<0.001$) and an average reduction in lesion diameter of 25.0% ($p=0.002$). The corresponding disease control rate was 100% using EASL and RECIST criteria. The median TTUP was 11.9 months (95% CI, 6.1-22.9 months) with a significant difference between BCLC A/B (median 22.9 months [95% CI, 8.5-not estimable]) and BCLC C (median 6.2 months [95% CI, 2.8-15.4]) patients ($p=0.01$). The median OS was 24.5 months (95% CI, 12.8-30.9 months) with a significant difference between BCLC A/B (median 33.7 months [95% CI, 16.7-not estimable]) and BCLC C (median 17.1 months [95% CI, 6.9-27.4]) patients ($p<0.001$).

Conclusion: The results of this phase II study confirm treatment safety and suggest a potential benefit to the combination of sorafenib and DEB-TACE therapy. Of note, the addition of DEB-TACE to sorafenib may improve outcomes for advanced stage (BCLC C) unresectable HCC. Future work includes phase III randomized controlled trials.

Using Commercial Activity Monitors To Measure Gait In Patients With Suspected Inph: Implications For Ambulatory Monitoring

Background: Patients with idiopathic normal pressure hydrocephalus (iNPH) may not be diagnosed until late in the disease course because of blunt clinical tools that fail to detect early gait disturbances. Ideally we would be able to sense minute symptomatic changes in the ambulatory setting, using inexpensive and user-friendly technologies, so that these patients may be treated before they develop more serious hydrocephalus. In this pilot study we assessed the accuracy of four widely available activity monitors in patients with suspected or confirmed iNPH.

Methods: Following JHU IRB approval of our prospective pilot study, we recruited 17 patients with suspected or confirmed iNPH to each perform two 10-meter walks while wearing four activity monitors: the Omron Step Counter HJ-113, New Lifestyles (NL) 2000, Nike Fuelband, and Fitbit Ultra. We compared the counts recorded by the activity monitors to manual counts from video-recordings of the patients' gaits.

Results: Our elderly patient population (69.7 +/- 12.1 years) required an average of 25.9 +/- 12.9 steps to walk 10-meters. We calculated the mean, standard deviation, and correlation coefficient of the absolute difference between the manual- and device-step counts: Omron (10.4 +/- 14.7; R2 = 0.05), NL (15.3 +/- 15; R2 = 0.12), Nike (14.9 +/- 11.3; R2 = 0.09), and Fitbit (5.1 +/- 7.3; R2 = 0.57). The Fitbit Ultra's MEMS tri-axial accelerometer and algorithm was the most accurate.

Conclusion: We found one activity monitor to be clearly more accurate and intuitive to use in measuring steps taken by iNPH patients. We are currently monitoring patients in the ambulatory setting to determine if clinically relevant data may be collected. The transition to ambulatory monitoring and early detection has the potential to greatly affect management of iNPH in patients.

Pre-Hospital Rapid Sequence Intubation Is Associated With Decreased Mortality In Pediatric Trauma Patients

Background: Despite theoretical advantages from rapid sequence intubation (RSI) of pediatric patients in the pre-hospital setting, there is no consensus about indications for RSI versus other modes of airway management. We examined if RSI is associated with improved outcomes among pediatric trauma patients.

Methods: A retrospective cohort of pediatric trauma patients who received prehospital intubation since 1999 (n=103) was created from Maryland EMS and Johns Hopkins pediatric trauma databases. Patient data was collected from EMS and hospital charts. Morbidity and mortality were compared between 22 RSI and 81 non-RSI patients using chi-square and unpaired t-test calculations.

Results: There were no statistically significant differences in weight, gender, or Glasgow Coma Scale values between study arms, but RSI patients were slightly older (mean age 9.3 years RSI vs. 7.2 non-RSI, $P=0.05$). On arrival to the hospital, RSI patients were equally likely to have successful tube placement (76.2% vs. 66.2%, $P=0.4$) but did have higher oxygen saturation (99% vs. 91%, $P=0.001$). RSI patients were equally likely to survive to hospital admission (86.4% vs. 81.2%, $P=0.756$) but were more likely than non-RSI patients to survive to hospital discharge (81.8% vs. 35.8%, $P<0.001$). Among survivors, RSI patients were equally likely to require rehabilitation (61.1% vs. 69.0%, $P=0.75$) and had equal hospital lengths of stay (mean of 10.5 days vs. 11.1, $P=0.86$). An unstable systolic blood pressure ($SBP<70 + 2 \times \text{Age}$) independently predicted patient death (36.0% vs. 85.2%, $P<0.001$). Treating hemodynamic instability as a covariate, RSI patients were still more likely to survive to hospital discharge (84.6% vs. 41.7%, $P=0.04$).

Conclusion: Rapid sequence intubation was associated with improved mortality in pediatric trauma patients compared to other methods of endotracheal intubation. These results are encouraging but specific to specially trained paramedics. Further research is needed before suggesting wider implementation.

Generational Difference Between Baby Boomers And Silent Generation: Chronic Diseases, Painful Conditions, And Complementary And Alternative Medicine (CAM) Use

Background: The aging baby boomer generation (adults born 1946-1964) is an unprecedented cohort that will challenge the health care system. More people are supplementing conventional medicine with complementary and alternative medicine (CAM). This project aims to investigate how the incidence of chronic diseases and painful conditions differs between baby boomers and the silent generation (adults born 1925-1945), and to compare the prevalence of CAM use between the two.

Methods: We performed secondary data analysis using data from the 2007 National Health Interview Survey (NHIS) with a supplemental section on CAM. Baby boomers (n=7734) and silent generation (n=4682) were surveyed for chronic diseases including heart disease, lung disease, diabetes, cancer, and stroke as well as painful conditions including joint, neck, low back, facial and head pain. Multivariate logistic regression models and stratified analysis were developed to identify predictors of CAM use.

Results: The baby boomers (BB) are more educated, diverse and obese than the silent generation (SG). Although SG had twice as many chronic diseases (51.3% vs 26.1%, $p<0.01$) and painful conditions (56.1% vs 52.2%, $p<0.01$), BB used significantly more CAM within the past year (43.1% vs 35.4%, $p<0.01$). Pain status, but not chronic disease, is the greatest predictor of CAM use (AOR 2.26 95%CI 2.03-2.52). Comparison of the two generations with the same chronic disease (AOR 1.38 95%CI 1.17-1.63) or painful condition (1.38, 95%CI 1.21-1.57) revealed that CAM use was significantly higher amongst BB.

Conclusion: When the baby boomers are 65, the prevalence of chronic disease and painful conditions will be higher. In order for physicians to implement healthy aging strategies, they need to understand that baby boomers are integrating CAM with conventional medicine.

Involved Field Radiation Therapy For Hodgkin Lymphoma: Treatment Outcomes At The Johns Hopkins Hospital

Background: Hodgkin lymphoma (HL) comprises 6% of pediatric malignancies and radiation therapy remains an integral component of curative therapy. We present clinical outcomes, including patterns of failure, in a cohort of HL patients treated with radiation at Johns Hopkins Hospital.

Methods: Pediatric and adolescent/young adult (AYA) patients 40 years of age or younger with intermediate and high-risk HL who received involved-field radiation therapy (IFRT) at JHH from 1985-2012 were included in this retrospective analysis. Patients were evaluated for overall survival (OS), progression free survival (PFS), and patterns of recurrence. Kaplan-Meier curves and descriptive statistics were used for analysis.

Results: 76 patients with intermediate or high-risk HL (Stage IIA-IVB) were reviewed. Median follow up was 4.4 years, mean age at diagnosis was 21.5 years and 59% patients were male. Patients received chemotherapy followed by consolidative radiation (median dose: 2550cGy). OS and PFS of the entire cohort at 18 years were 92% and 80%, respectively. At last follow up, no second malignancies were reported. All 6 deaths in the cohort were related to recurrent disease. 40 patients received <30 Gy of consolidative radiation and 36 patients received ≥ 30 Gy. The six-year survival of the cohort receiving ≥ 30 Gy was 92%, compared to the 96% six-year survival of the patients who received <30Gy of radiation ($p=0.63$). Among the 15 patients with ≥ 1 recurrence of their HL, 6-year survival was 76%, compared to the 100% 6-year survival in the 61 patients without recurrence ($p=0.0003$). Of the patients who recurred, 33% had in-field recurrences, 33% had out-of-field recurrences, and 33% had local and distant recurrences. The majority of patients with an in-field recurrence alone (80%) received <30Gy of radiation therapy.

Conclusion: This study summarizes the clinical outcomes in intermediate to high-risk pediatric/AYA HL patients at JHH. IFRT led to excellent local control and overall survival in this cohort of patients.

VEGF Secreted by Hypoxic Müller Cells Promotes MMP-2 Expression in Neighboring Endothelial Cells in Proliferative Diabetic Retinopathy

Background: Proliferative diabetic retinopathy (PDR) remains a common cause of severe vision loss in the diabetic population. Current treatment for PDR is limited to inherently destructive procedures with significant visual sequelae, prompting the exploration for other therapeutic options for these patients. In this regard, extracellular proteolysis (ECP) is an early and sustained activity strictly required for retinal neovascularization (NV) in PDR. Here we set out to better understand the role of matrix metalloproteinases (MMPs) in ECP in patients with PDR.

Methods: We used in vitro (retinal Müller and endothelial cells (ECs)) and in vivo (oxygen-induced retinopathy (OIR)) approaches to examine the regulation of MMPs in retinal NV. These data were corroborated by patient samples (i.e., aqueous and serum) from consented patients in which the levels of VEGF and MMP-2 were assessed using an enzyme-linked immunosorbent assay (ELISA).

Results: We found that MMP-2 RNA and protein is increased in the ischemic inner retina in the OIR mouse model. We further demonstrate that this increase indirectly requires the transcriptional enhancer, Hypoxia-Inducible Factor (HIF)-1 α . Accumulation of HIF-1 α in hypoxic Müller cells promotes the transcription of VEGF that, in turn, leads to the upregulation of MMP-2 expression in neighboring ECs. The activity of MMP-2 is further enhanced by the upregulation of membrane-type-1 matrix metalloproteinase (MT1-MMP) in ECs. ELISA analysis of aqueous samples from diabetic patients confirmed an increase in MMP-2 in the eyes of patients with PDR (n=17) compared to controls (n=20; p<0.05). Remarkably, the increase in MMP-2 levels was maintained even after treatment of PDR patients with panretinal photocoagulation (PRP) (p<0.01).

Conclusion: Our findings demonstrate a complex interplay among hypoxic Müller cells and their angiogenic secretions and neighboring ECs in the regulation of MMP-2 expression and activity in PDR patients. Therapies targeting MMP-2 may be an effective approach for the treatment of this vision-threatening disease.

Outcomes For Upper Eyelid Loading For Treatment Of Paralytic Lagophthalmos

Background: Facial paralysis and the inability to close the eye can lead to devastating consequences to the cornea and ultimately blindness. Surgical interventions with upper eyelid loading aim to protect the globe. Adjunctive lower eyelid procedures may be necessary in the treatment of these patients.

Methods: Retrospective review of 95 patients with paralytic lagophthalmos in a single institution over a 6-year period. Implant placement included gold or platinum weights in a pretarsal fashion with fixation. Revision surgery included repositioning, removal and exchange. Adjunctive procedures to the lower eyelid and their revision rates are also described. A modified SF-36 post-operative survey was used to assess patient satisfaction.

Results: Mean follow up was 16 months (range 1 to 62 months). 90.5% of the weights were platinum weights. Revision rate was 22/95 patients (23%), the majority of within the first year after the procedure. Indications for revision included weight extrusion (2/22), prominent implant (3/22), implant migration (3/22), eye ptosis (9/22), persistent lagophthalmos (6/22), facial nerve recovery (2/22) and inability to obtain MRI (1/22). Revision consisted of weight removal (10/22), reposition (1/22), and replacement (11/22). No significant predictors of the need for revision were identified. Adjunctive lower eyelid procedures were used in 41/95 patients (43%). The revision rates for lower eyelid procedures were 12/42 (31%). Increasing age and the use of medial canthopexy was associated with lower eyelid revision ($p=0.003$, $p=0.0004$). Patients subjectively reported 92.3% improvement in eye closure, 88.5% decrease in eye discomfort, and 92.3% aesthetic improvement according to the SF-36 post-operative survey.

Conclusion: Upper eyelid loading is the core treatment in paralytic lagophthalmos. Revision may be required especially within the first year after initial surgery. Adjunctive lower eyelid procedures are required in a large proportion of these patients. High patient satisfaction is achieved in the majority of cases.

Spinal Surgery For Metastatic Epidural Spinal Cord Compression (MESCC) From Breast And Prostate Cancer Provides Functional Benefits Despite Differing Pathology-Specific Characteristics And Prognosis

Background: MESCC is a debilitating disease causing neurological deficits, mechanical instability, and intractable pain. Surgical management, while palliative, may improve quality of life. However, the functional outcomes and selection criteria for patients with metastatic breast and prostate cancers are poorly understood.

Methods: Retrospective chart reviews were performed of all patients undergoing spinal surgery for metastatic cancer from 06/2002-08/2011. Pre- and postoperative neurological status (Frankel scale) and analgesic usage (5-point scale) were compared using the signed-rank test. The Kaplan-Meier method estimated postoperative survival. The Mantel-Cox test assessed preoperative clinical and surgical characteristics for prognostic value.

Results: Forty-three female breast cancer and 27 male prostate cancer patients underwent surgery at a median age of 56 and 65 years, respectively. Within the respective breast and prostate cohorts, 84% and 93% of patients had preserved or improved neurological status after surgery, 56% of non-ambulating patients in both groups recovered ambulation, 60% and 43% of incontinent patients recovered continence, and 26% and 23% experienced complications. Postoperative Frankel grades were significantly improved at 1 month in the prostate cohort ($P=0.033$), and at 6 and 12 months in the breast cohort ($P=0.048$, 0.004). The median analgesic score was significantly lower up to 1 year postoperative in both cohorts ($P=0.006$, 0.04). The median postoperative breast cohort survival (29.3 months) was significantly longer than the prostate median (10.2, $P=0.03$). Patients with castration-resistant prostate cancer (CRPC) had a shorter median survival than hormone-naïve disease (9.8 vs. 40 months, $P=0.015$). Worse preoperative performance status was a predictor of decreased survival in both breast (HR 2.67, $P=0.007$) and CRPC (HR 3.96, $P=0.024$) cohorts.

Conclusion: Spinal surgery for breast and prostate metastases improves neurological function and decreases analgesic requirements. Breast cancer carries a better postoperative survival. Our findings support surgical intervention for carefully selected patients, and preoperative hormone and performance status may help with risk stratification.

Are Hospitals With Poorer Financial Vitality Treating A Larger Proportion Of Minority Patients?

Background: A large body of research over the past decade has shown clear evidence of disparity in health care between subsets of the population. Concurrently, studies have shown that hospital finances can also play a role in the quality of care. This paper focuses on the financial aspect of hospitals in an effort to explain some of this bias. The purpose of this article is to determine if hospitals that treat larger proportions of minority patients have poorer financial vitality.

Methods: Patient demographic data, namely race identifiers, was obtained from the National Inpatient Sample (NIS). We used Operating Margin as a measure of financial vitality as this can be compared between hospitals of different sizes, and has been used in previous studies as a measure of financial strength. This data was collected from the American Hospital Directory, and the Centre for Medicare/Medicaid Services (CMS). A simple analysis of this data was performed by directly comparing the operating margin to the proportion of minority patients treated at each hospital.

Results: The results at a first pass appear to be inconclusive, with the hypothesis holding true only for hospitals that saw between 20 and 30% minority patients. In this group, for every increase in percent minority patients, operating margin decreases by 2.18. Further analysis looking at the insurance status of patients and comparing that to financial vitality also revealed, at best, a minimal trend.

Conclusion: Though the current results remain inconclusive, the fact that this trend holds true for certain hospitals is definitely worth exploring. Further research will involve looking at outcomes in hospitals with poorer financial vitality, namely disproportionate share hospitals. However, at this time we cannot conclusively say that hospital finances, like any other variable, is directly responsible for disparate care. The cause of these unconscious biases remains frustratingly elusive.

Immediate And Follow-Up Results For 44 Consecutive Cases Of Small (<10mm) Internal Carotid Artery Aneurysms Treated With The Pipeline Embolization Device

Background: Background: Endovascular reconstruction of large and giant aneurysms with the Pipeline Embolization Device (PED) has been shown to be effective, durable and safe. However, 80% of all aneurysms found in the general population are less than 10 mm in size. Treatment of small aneurysms (<10 mm) with flow diverters may be advantageous over endosaccular modalities, which inherently carry a high risk of procedural rupture during access of the aneurysm sac or coil placement.

Objective: We present periprocedural outcomes and two- to six-month angiographic follow-up results for a series of 44 consecutive cases with internal carotid artery (ICA) aneurysms less than 10 mm in size that were treated with the PED at a single-center by a single-operator

Methods: Methods: We retrospectively reviewed a prospective, single-center aneurysm database to identify all patients with small (<10mm) ICA aneurysms who underwent endovascular treatment using the PED. Patient demographics, aneurysm characteristics, procedural details, complications, and technical and clinical outcomes were analyzed.

Results: Results: Forty-four cases were performed in 41 patients (age range 31-78 years) with a total of 53 aneurysms. PED was successfully implanted in 42 cases. A single PED was used in 37/42 (88%) cases. Ninety-eight percent of patients were discharged home following the embolization procedure with a mean post-procedure hospital stay of 1.7 ± 0.34 days. A major complication, defined as major stroke or death, occurred in one patient (1/44 cases, 2.3%). This patient died of early SAH. Transient neurological deficit, delayed ICH, and delayed groin infection occurred in one patient each (2.3% each). Of the 49 surviving aneurysms successfully treated, the follow-up rate was 85.7% (42 aneurysms in 33 patients). By post-operative month six, angiographic success was observed in 78.6% with either complete or near complete aneurysm occlusion. Mild, non-flow limiting, in-stenosis was observed at a rate of 5.7% (2/35 cases). Of the 33 patients with follow-up, all remained in good neurological condition.

Conclusion: Conclusion: Treatment of small (<10mm) ICA aneurysms with PED implantation is safe and carries a high rate of angiographic success.

Trainee Application Appraisal: "Just Google It"

Background: The purpose of this study is to evaluate three popular, free, evidence-based applications that early medical trainees are likely to use. We examine their utility compared to a simple Internet search, and additionally, we comment on our experiences as trainees attempting to incorporate new technology into the clinical setting.

Methods: We evaluated three popular, free, evidence-based mobile applications and compared them to a simple web search using Google on both Apple and Android devices. Six medical students at a large academic hospital evaluated each application for a one-week period while on various clinical rotations.

Results: We found that while dedicated healthcare applications were considered to have a better user interface, more reliable sources, and higher search satisfaction than a Google web search, they were utilized much less frequently due to strict search term requirements and limited scope of available resources. Medscape was the most likely mobile medical application to be used repeatedly by medical trainees due to its comprehensive clinical content and appealing user-interface.

Conclusion: While the industry for medical applications continues to grow, the acceptance of such technology in the workplace continues to lag behind. The culture of medicine still presents a barrier to trainees frequently utilizing these resources in clinical settings due to the potential for, and faculty perceived, inappropriate use. As mobile applications continue to evolve, we anticipate that the culture of medicine will embrace the utilization of these resources in both the education and delivery of quality patient care by physicians in all stages of training.

Challenges In Translating Evidence Into Practice: Pulse Oximetry Policy Implementation In The NICU

Background: Recommendations for oxygen supplementation for premature infants have fluctuated due to the competing outcomes of increased mortality at low saturations versus retinopathy of prematurity-induced blindness at high saturations. A cross-sectional audit identified gaps in pulse oximetry policies in the Johns Hopkins Bayview NICU. After a systematic review of the literature, we developed and implemented a policy with stepwise interventions.

Methods: This is a prospective analysis of a quality improvement implementation strategy. Interventions included: education (15-minute presentations outlining current evidence-based recommendations to 54 multi-disciplinary staff), automated EMR orders, and sharing audit results with staff to elicit compliance barriers. We performed 4 monthly cross-sectional audits of alarm limit compliance, and analyzed compliance at each time point using a chi-square test of proportions.

Results: Compliance for pulse oximetry alarm settings was zero in the pre-implementation baseline audit. The low alarm setting compliance peaked at 83%, then dropped precipitously to 33% after one month. With the following two interventions, compliance increased to 40% and then 58% ($P < 0.01$ for baseline vs. all post-audits except #2). High alarm setting compliance peaked at 100%, then decreased to 83% and 53% the next two months, and increased to 74% after the final intervention ($P < 0.001$ for baseline vs. all post-audits). The high alarm settings trended 0.5 points above the high alarm orders and the low alarm settings trended 2.2 points below the low alarm orders.

Conclusion: Policy compliance was highest following the core educational intervention, but dropped precipitously after one month and never reached the level attained with the initial implementation, suggesting that routine rigorous training modules may be more effective than other interventions. The deviation in alarm settings by nurses from EMR orders trended toward decreased likelihood of alarm triggering. Finally, the implementation of a seemingly simple policy change requires cycles of evaluation and education even after a major implementation program.

Outcomes After Early Treatment Of Cauda Equina Syndrome

Background: Cauda equina syndrome is characterized by a constellation of symptoms: bladder dysfunction; back and leg pain, weakness, and numbness; and occasionally bowel or sexual dysfunction. Based on prior studies, the standard of care is emergent surgical decompression within 48 hours. However, there is no guarantee of alleviation of symptoms and outcomes are widely variable. More evidence is needed to determine if a different timeframe is optimal. This study investigated whether intervention within 24 hours correlates with improved outcomes, with a primary focus on bladder function due to its impact on quality of life.

Methods: All patients who underwent operations for cauda equina syndrome at Johns Hopkins Hospital and Bayview Hospital from 1991 to August 2012 were identified. Information from their medical records was extracted, including history of the illness, time of presentation, time to surgery, hospital course, and follow-up course. Analysis was performed using Fisher's test due to the relatively small sample size.

Results: Of the 49 patients, 34 underwent surgery within 24 hours. Within this cohort, 29 (85%) presented with bladder dysfunction; at last follow-up, 14 of the 29 (48%) continued to have bladder dysfunction and 9 (31%) were newly catheterized. Among the 15 patients who underwent surgery after 24 hours, 15 (100%) presented with bladder dysfunction; at last follow-up, 7 of the 15 (47%) continued to have bladder dysfunction and 4 (27%) were newly catheterized. Neither bladder function outcomes ($p=0.25$) nor catheterization outcomes ($p=0.26$) were statistically significant. There were no statistically significant differences in the rates of resolution of any other symptom.

Conclusion: Outcomes based on meaningful symptomatology were not significantly different for patients treated within 24 hours and those treated after 24 hours. Patients with cauda equina syndrome do not appreciably benefit from surgery within 24 hours.

Local Delivery 2-Deoxy-D-Glucose As A Possible Therapeutic Option: A Preclinical Study

Background: The glucose analog, 2-deoxy-D-glucose (2-DG), has been shown to be an effective inhibitor of tumor growth through inhibition of the glycolytic pathway and subsequent halting of glycolytic ATP generation in tumor cells. Previous studies have shown that effective use of 2-DG in cancer treatment requires high systemic doses that can cause dose-limiting side effects. Therefore, clinical trials have been approved for only low dose systemic 2-DG. We postulate that these systemic side effects can largely be avoided by direct intracranial delivery of 2-DG. We implanted 2-DG-impregnated controlled release biopolymer wafers intracranially in rats and assessed efficacy. In this study, we explore the effectiveness of 2-DG as a monotherapy in treating intracranial 9L rat gliosarcoma in vivo.

Methods: Thirty rats were intracranially implanted with 9L rat gliosarcoma on Day 0. Control rats received no treatment. Rats in the 2-DG (Day 0) and 2-DG (Day 5) groups received intracranial 2-DG polymers on Day 0 or Day 5, respectively. Survival was compared across all three groups.

Results: Rats in the control group had a median survival of 11 days, while those in the 2-DG Day 0 and 2-DG Day 5 had median survivals of 18 days ($p < 0.009$ vs. control) and 17 days ($p < 0.0461$ vs. control), respectively.

Conclusion: The results of this study show that 2-DG alone, when delivered locally, can cause a statistically significant increase in survival in rats with intracranial 9L tumors. Additionally, these results suggest that intracranial delivery of 2-DG may further enhance combination therapies that are limited by side effects of systemic 2-DG.

Sacral-Alar-Iliac Fixation In Pediatric Deformity: 2 - 5 Year Follow Up

Background: Challenges in pediatric pelvic fixation include improving anchor strength and corrective potential as well as lowering prominence. We assessed the performance and complication rate of SAI fixation in the pediatric population.

Methods: 94 Patients < 18 yrs with spine surgery including SAI fixation from 2003-2009 having minimum 2 year follow up were reviewed. We studied spinopelvic deformity correction and fusion, as well as implant-related complications.

Results: Pelvic obliquity was corrected from 26 degrees to 5.5 degrees with no loss of correction at latest followup. In total, 91% of patients were corrected to <10 degrees. Patients demonstrated a 3% deep wound infection rate, much lower than other comparable techniques. A total of 5% of all screws broke. This occurred about 3 year postop and only with screws less than or equal to 8mm. There were no revisions for breakage. Lucency also occurred in 5% of all screws. A total of 4 patients received revision surgery, 3 with pseudarthrosis and one with hip pain. There were predisposing factors for pseudarthrosis including prior deformity, shorts screws, and a pre-existing syndrome. With regard to implant density, our study showed no correlation between density and these 3 events.

Conclusion: Our overall complication rate demonstrated that lucency was rare, wound infection rates were low compared to other studies, there was a high rate of pelvic correction and maintenance, and lastly, the ideal screw diameter was 9mm.

Correlation Of Menstrual Cycle Phase And Infection Risk In Women Exposed To N. Gonorrhoeae

Background: Previous studies have shown that a woman is more likely to be diagnosed with gonococcal (GC) infection during the first five days of her menstrual cycle (active menstruation) than during the rest of her cycle. However, no correlation has been established between risk of infection and the day of a women's menstrual cycle at the time of exposure. In this study, risk of GC infection was correlated to female menstrual cycle phase and hormonal contraceptive use (HC) at the time of GC exposure--according to the woman's stated date of last menstrual period and stated date of GC exposure.

Methods: Women who presented to the Baltimore City Health Department STD Clinic as contacts of known GC positive sexual partners were enrolled. Risk of GC infection was compared to calculated phase of menstrual cycle: active menstruation (days 1-5), follicular (days 6-10), periovulatory (days 11-16), and luteal (days 17-30). We used Fisher's exact test to assess differences among groups.

Results: 53 female GC contacts were enrolled. Twenty-two were GC negative and 31 were GC positive. Of the GC negative contacts, 1, 4, 5, and 6 were exposed during active menstruation, follicular, periovulatory and luteal phases, respectively, and 6 used HC. Of the GC positive contacts, 5, 4, 1, and 16 were exposed during active menstruation, follicular, periovulatory and luteal phases respectively, and 5 used HC. During the luteal phase and active menstruation, women were more likely to be infected with GC (7 GC negative, 21 GC positive, $p=0.013$) compared to other times in the cycle.

Conclusion: Increased risk of GC infection during the early and late phases of the menstrual cycle may be, in part, due to lower lactoferrin concentration, lower level of iron sequestration, and higher level of free iron in the female genital tract during these phases.

Single Nucleotide Polymorphisms In Proximity To K-Channel Genes Are Associated With Decreased Qtc Variance

Background: Atrial fibrillation (AF) is the most common form of cardiac arrhythmia. Despite significant progress in identification of predisposing factors, the pathophysiology of AF remains to be elucidated. Previous studies have reported that single nucleotide polymorphisms (SNPs) in several potassium-channel genes associate with AF and the instantaneous corrected QT interval (QTc). The purpose of this study was to examine the association between SNPs in proximity to KCNQ1, KCNH2, KCNE2, and KCNJ2 and longitudinal QTc variations in patients with AF.

Methods: We conducted a retrospective cohort study of 800 electrocardiograms from 93 patients with atrial fibrillation. All patients were Caucasian, with an average age of 61.4 years, and 72% were male. Of all patients, 37% had persistent AF, and 63% had paroxysmal AF. Following DNA extraction from blood, SNPs at the AF-associated loci KCNQ1, KCNH2, KCNE2, and KCNJ2 were genotyped using the Sequenom MassARRAY.

Results: Using a generalized estimating equations method, a decrease in QTc variance was found to associate with SNPs near KCNH2 (rs10240738) and KCNJ2 (rs8079702) when adjusted for patient age, gender, AF type, and anti-arrhythmic medications. Further, we examined a multilevel regression model and found no longitudinal association between presence of SNPs near K-channel genes and changes in QTc.

Conclusion: Polymorphisms near specific potassium-channel genes in AF patients are associated with decreased QTc variance. However, presence of these SNPs is not associated with longitudinal changes in QTc. These results support the hypothesis that effects on myocardial repolarization may mediate the association of these SNPs and AF.

Motor And Cognitive Delay In Duchenne Muscular Dystrophy: Implication For Early Diagnosis

Background: Approximately one third of Duchenne Muscular Dystrophy (DMD) patients have cognitive delay. We hypothesize that in this subset of boys cognitive delay correlates with a developmental delay in walking that, when properly recognized, can lead to substantially earlier diagnosis.

Methods: We retrospectively studied 179 boys with DMD evaluated between 1989 and June 2012 by the senior author. Developmental delay in walking was defined as occurring >16 months of age. Cognitive delay was classified by special education placement or delay in grade level. The age at time of diagnosis was also assessed as well as the age-of-wheelchair-dependence, an indirect measurement of strength and a possible confounder.

Results: We could retrieve all required data elements from the records for 107 of the 179 patients. Of these, 45% were cognitively delayed and 42% were delayed in walking; 30% had both, thus demonstrating a high correlation (chi square 21.6, $p \text{ value} \leq 0.0001$). If cognitively delayed, boys with DMD were 3 times more likely to have a delay in walking. There was no difference in strength as assessed by age-of-wheelchair-dependence ($p=0.9$), or age-of-diagnosis ($p=0.6$, combined average = 5.1 ± 2 years) between those with normal or delayed onset of walking.

Conclusion: Delay in the onset of walking in boys with DMD is likely due more to cognitive delay rather than observable muscle weakness at this early age. Recognition of this association and screening for DMD in those with a delay of both cognitive and motor milestones, but without manifest weakness, will result in an earlier diagnosis for up to one third of boys with DMD, with consequent improvement in therapy and opportunity for meaningful genetic counseling. We suggest that recommended laboratory tests for evaluation of boys with global developmental delay include the inexpensive serum creatine kinase (CK) test.

BMI – Is It Still A Predictor Of Mortality Outcomes In Lung Transplantation Patients Post-Implementation Of The Lung Allocation Score (LAS)?

Background: The effect of BMI on lung transplantation (LTx) outcomes is inconclusive. This study reviews this topic post-implementation of the Lung Allocation Score (LAS), a system established in 2005 to allocate lung organs by need, which has not been performed to date.

Methods: We conducted a retrospective institutional review of all adult (>17 yrs) LTx performed at our institution from 2005-2012, utilizing our prospectively maintained cardiac database. Patients with an LAS score and follow-up data for at least 1 year were stratified by body mass index (BMI) at listing according to the cutoffs designated by the Center for Disease Control (CDC) (BMI<18.5 is underweight, BMI 18.5 – 24.9 is normal, BMI 25.0 – 29.9 is overweight, and BMI>30.0 is obese). Mortality was assessed using a multivariate cox proportional hazards model.

Results: After applying exclusion criteria, our cohort consisted of 98 patients. BMI ranged from 15.47 to 36.42 with a median of 24.1. By BMI groups, 10 (10.2%) were underweight (BMI<18.5), 49 (50.0%) were normal weight (BMI 18.5–24.9), 30 (30.6%) were overweight (BMI 25.0–29.9), and n=9 (9.2%) were obese (BMI>30).

After LTx, patients with BMI>25 did not significantly have increased mortality at 3 years or 5 years. 5 year survival estimates are 100% for BMI<18.5, 79.59% for BMI 18.5-24.9, 73.33% for BMI 25-29.9, and 88.88% for BMI>30 (p<0.402).

After risk adjustment, patients with BMI>25 showed a trend towards increased likelihood of 62% for mortality (HR 1.66. CI 0.53-5.17, p<0.380). Logistic regression yielded a significant correlation between BMI>25 and diagnosis of idiopathic pulmonary fibrosis (IPF) (OR 18.69, CI 1.95-179.11, p<0.011).

Conclusion: LTx patients with BMI>25 do not have statistically significant associations with worse transplantation outcomes. The results of this study suggest that BMI should not be an absolute contraindication in selection criteria for lung transplantation.

Incidence Of Donor Derived Malignancies In Post-Transplantation Cyclophosphamide Treatment During Hematopoietic Stem Cell Transplantation

Background: Cyclophosphamide is a commonly used chemotherapeutic that has also been shown to prevent graft versus host disease and improve survivability in patients receiving hematopoietic stem cell transplantation (HSCT) when given in high doses post-transplant. Due to its carcinogenic nature, there is worry that this could lead to an increased chance of developing malignancy within the donor cells.

Methods: We did a large retrospective analysis of all patients who underwent HSCT at Johns Hopkins Medical Center and determined which of those patients received post-transplant cyclophosphamide. We then went through the medical records of these patients to determine the outcomes and development of any donor derived secondary malignancies (DDM). Variables assessed were the patient and donor age, the preparative and post-transplant regiment of the HSCT, the specific type of HSCT, and the diagnosis of the patient. Outcomes assessed were incidence of graft failure, progression free survival, development of DDM, and overall survival. Incidence of DDM was calculated through competing risk analysis. Competing risks were defined as graft failure, relapse, progression, or death.

Results: 286 of the 779 patients who received post HSCT cyclophosphamide at John Hopkins were analyzed. The cumulative incidence of DDM among those patients was 0.01948 after 2500 days of follow-up. 5 year progression free survival was 30% and overall survival was 39%.

Conclusion: Patients who received post-transplant high dose cyclophosphamide have no significant difference in incidence of DDM when compared to patients who did not receive post-transplant cyclophosphamide.

Increased Flap Weight and Decreased Perforator Number Predicts Fat Necrosis in DIEP Breast Reconstruction

Background: Compromised perfusion in autologous breast reconstruction results in fat necrosis and flap loss. Increased flap weight with fewer perforator vessels may exacerbate imbalances in flap perfusion. We studied deep inferior epigastric perforator (DIEP) and muscle-sparing transverse rectus abdominis myocutaneous (MS-TRAM) flaps to assess this concept.

Methods: Data from patients who underwent reconstruction with DIEP and/or MS-TRAM flaps between Jan. 1, 2010–Dec. 31, 2011 (n=123) were retrospectively reviewed. Patient demographics, comorbidities, intraoperative parameters, and post-operative outcomes were collected, including flap fat necrosis and donor/recipient site complications. Logistic regression analysis was used to examine effects of flap weight and perforator number on breast flap fat necrosis.

Results: One hundred twenty-three patients who underwent 179 flaps (166 DIEP, 13 MS-TRAM) were included. Mean flap weight was 658g \pm 289; 132 (73.7%) were single perforator flaps. Thirteen flaps (7.5%) developed fat necrosis. African American patients had increased odds of fat necrosis (odds ratio, OR 11.58, $p < 0.001$). Odds of developing fat necrosis significantly increased with flap weight (OR 1.5 per 100g increase, $p < 0.001$). In single perforator flaps weighing >1000 g, six (42.9%) developed fat necrosis, compared to 14.3% of large multiple perforator flaps.

Conclusion: Flaps with increasing weight have increased risk of fat necrosis. These data suggest that inclusion of >1 perforator may decrease odds of fat necrosis in large flaps. Perforator flap breast reconstruction can be performed safely, however, considerations concerning race, BMI, staging with tissue expanders, perforator number and flap weight may optimize outcomes.

The Relationship between 25-OH Vitamin D and Peripheral Artery Disease

Background: Low serum 25(OH) D levels are associated with higher prevalence of peripheral arterial disease (PAD). It has been proposed that this inverse relationship is non-linear in that the association diminishes with rising 25(OH) D levels. To test this hypothesis, we examined the relationship between 25 (OH) D and PAD as measured by Ankle-Brachial index (ABI) in healthy adult US population.

Methods: We analyzed data from the continuous National Health and Nutrition Examination Survey for years 2001-2004. ABI was treated as a continuous variable and the minimum of the two reported ABI values was chosen for each individual. To examine the non-linear relationship between 25(OH) D and ABI, we introduced a spline, with a single knot at the median serum levels (21ng/mL) of 25(OH) D. The effect of 25(OH) D was calculated for every 10 ng/mL increase below and above spline. Regression models were adjusted for age, sex, race, body mass index, blood pressure, serum glucose, c-reactive protein, smoking, total cholesterol, and renal function.

Results: Of the 4979 individuals, 48% were females and 58% were Caucasians. The mean (SD) age, 25 (OH) D, c-reactive protein, and ABI was 60.4 (13.22) years, 22.1(8.68) ng/mL, 0.46(0.81) mg/dL and 1.07(0.15), respectively. In both unadjusted and adjusted linear regression models without a spline, we found that 25(OH) D was associated with a significant increase in ABI (0.018, 95% CI: 0.013 to 0.023 and 0.018, 95% CI: 0.012 to 0.024, respectively) for each 10 ng/mL increase in serum 25(OH) D. In the unadjusted linear regression model with spline, any change in ABI with rising serum 25(OH) D was much larger before 21 ng/mL (0.04, 95% CI: 0.03 to 0.05) than after 21 ng/mL (0.01, 95% CI: 0.003 to 0.013), for each 10 ng/mL increase in serum 25(OH) D. In adjusted analysis, the association between ABI and 25(OH) D remained statistically significant before 21 ng/mL (0.04, 95% CI: 0.02 to 0.05) but not after 21 ng/mL (0.008, 95% CI: - 0.0008 to 0.017) for each 10 ng/mL increase in 25(OH) D.

Conclusion: ABI increases as serum 25(OH) D levels increases, however, the change is nonlinear and it appears to plateau after 21 ng/mL of 25(OH) D in healthy adults. It is likely that the benefit of 25(OH) D supplementation for the prevention of PAD may only be seen in individuals with 25(OH) D levels below 21 ng/mL.

Comorbidities And Causes Of Death In The Management Of Small Renal Masses: A SEER-Medicare Analysis

Background: Recent evidence has demonstrated renal function and cardiovascular disease are closely linked. A non-cancer mortality benefit is touted for partial nephrectomy (PN) versus radical nephrectomy (RN) for small renal masses (SRMs), but controversy persists regarding cardiovascular benefits. We compared SRM management and actual causes of death with an emphasis on cardiovascular comorbidities (CVCs).

Methods: From the SEER-Medicare linked registry (1995-2007), demographic, comorbidity, and death data for patients with T1a SRMs was obtained. Patients were classified as undergoing PN or RN. Patients lacking a code for SRM management within 6 months of diagnosis were classified as non-surgical management (NSM), which is distinct from active surveillance. Subgroup analyses by Charlson comorbidity index and comorbidities assessed causes of death. Cox proportional hazards regression compared patients by CVC status controlling for demographic and patient factors.

Results: A total of 4574 patients underwent RN, 1849 underwent PN, and 754 had NSM. The most prevalent comorbidities included diabetes (20%), COPD (16%), CHF (8%), CKD (5%), history of MI (5%), and PVD (4%), which were all more common in the NSM group ($p<0.001$). Overall survival (OS) was 81% (median 58 months). Mortality was attributed to renal cell carcinoma in 2.5% of the cohort, another malignancy in 5.6%, and cardiovascular-related disease in 7.3%. CVCs significantly decreased OS and cardiovascular-specific survival (CVSS) but not cancer-specific survival (CSS; $p=0.07$). Patients with CHF had the highest mortality with 5-year survival of 57%. Compared to RN, OS and CVSS favored PN for patients regardless of CVCs ($p<0.01$). CSS favored PN for patients without CVCs ($HR 0.34(0.17-0.65), p<0.01$) but not with CVCs ($HR 0.67(0.23-2.01), p=0.48$).

Conclusion: For older patients with SRMs, CVCs are associated with adverse OS, CSS, and CVSS. The data suggest PN confers improved OS and CVSS compared to RN for patients with and without CVCs. PN should be utilized when technically feasible in patients with cardiovascular risk factors.

Survivorship After Surgical Resection For Cancer: The Need For Continued Surgical Follow-Up

Background: There is a dearth of follow-up information regarding patients who underwent potentially curative esophageal cancer resection. Though follow-up clinic visits are concentrated on detection of cancer recurrence, other issues arise that require intervention. This study sought to evaluate long-term medical and surgical issues during routine outpatient follow-up in patients who underwent potentially curative surgical resection beyond 2-years after resection.

Methods: This was a retrospective analysis of a prospectively kept esophageal cancer database including patients from 1995-2012 with a primary diagnosis of esophageal cancer and at least 2 years of follow-up after R0 resection. Patient demographics, comorbidities, cancer characteristics, gastrointestinal symptoms, and radiographic findings were abstracted from medical records. Overall survival was analyzed using Cox proportional hazards analysis and Kaplan-Meier estimates. Analysis of the distribution of significant clinicopathologic variables across patient characteristics was performed with chi-squared or Fisher's exact and unpaired t-test.

Results: Overall survival in this cohort of 226 patients at 5 and 10 years was 52% (n=226) and 17% (n=109), respectively. Prevalence of a second primary cancer increased from 6% (n=109) to 16% (n=117) (P=0.02) and gastric dumping syndrome increased from 9% (n=109) to 18% (n=117) (P=0.055) in 2-5 year survivors (n=109) compared with >5 year survivors (n=117). Multivariate hazard analysis revealed that dysphagia conferred a significant survival disadvantage (hazard ratio=1.92, P=0.017). Chi-squared test showed that dysphagia is concurrent with current tobacco use (P=0.039), lower third esophageal malignancy (P=0.004), chemotherapy (P=0.008), radiation (P=0.002), Grade \geq III cancer (P=0.007), and Stage \geq III cancer (P=0.003).

Conclusion: Esophageal cancer survivors >5 years after resection face a nearly tripled prevalence of second primary cancer and doubled prevalence of gastric dumping syndrome as compared with two year survivors. Dysphagia is associated with decreased survival in this cohort. These results underscore the need for surgeons to continue to follow their patients long-term following surgical resection for esophageal cancer.

Three-Dimensional Magnetic Resonance Analysis Of Extraocular Muscles Demonstrates Gaze-Specific Contractile Shape Changes

Background: Purpose: To evaluate whether contractile changes in extraocular muscle (EOM) shape correlate with three-dimensional eye position.

Methods: Methods: Seven normal volunteers were scanned in the supine position with near visual targets placed in nine positions of gaze at 20 degrees eccentricity. Orbits were imaged as targets were viewed through a 3" open surface coil. Magnetic resonance (MR) image sequences consisted of oblique-coronal fast-spin echo T1-weighted MR in 15 coronal sections, with the most anterior slice placed just posterior to the equator (field of view 8 cm, matrix size 256x128, gap 2.0 mm, TR 500 msec, TE 11 msec, echo-train length 6, scan time 39 sec). Images were analyzed using the Medical Image Processing, Analysis, and Visualization platform (MIPAV, National Institutes of Health, Bethesda, MD) for EOM delineation and Matlab (Mathworks, Natick, MA) for assessment of muscle shape.

Results: Results: Individual EOMs displayed characteristic shapes in all subjects: the lateral rectus (LR) was largest in volume, followed in order by the medial rectus (MR), inferior rectus (IR), superior rectus (SR), and superior oblique (SO). Muscle bellies increased in maximal cross-sectional area, and were translated posteriorly upon gaze in its direction of action. Cross-axis thickening occurred within LR in down gaze (25%), MR in up- or down gaze (15%), SR in right- or left gaze (15%), and IR in right- or left gaze (35%). Alterations in slope and eccentricity corresponded with changes in cross-sectional area.

Conclusion: Conclusions: This is the first three-dimensional analysis of position-dependent shape changes in EOMs. Our analysis demonstrates that EOMs exhibit contractile thickening and posterior displacement with gaze in the direction of primary muscle action. Whether quantitative anatomic differences correspond to saccade velocity, accuracy, or acceleration differences are under active investigation. Cross-axis thickening and compartmentalization within horizontal rectus muscles to produce cross-axis forces may account for some of our findings.

Influence Of Battlefield Military Research On Civilian Trauma Practices: A National Survey

Background: Recent US military combat experience has led to the development of new protocols to improve survivability of battlefield injury, but it is unknown the extent to which techniques have been adopted in civilian trauma practice. Our objective was to determine extent of usage for these techniques, stratification of practices between centers of different levels, and barriers to civilian implementation of successful combat medicine techniques by surveying Trauma Medical Directors (TMDs) throughout the US.

Methods: Contact information was obtained by contacting health departments for all 50 states by email and phone. The survey was emailed to TMDs at 630 Level I, II, and III trauma centers in the US. Questions pertained to five aspects of trauma care: damage control resuscitation, tourniquets, hemostatic agents, TBI, and pre-hospital interventions. Participants were asked how often they use these techniques, and the effect of the US military experience on their decision to adopt these guidelines.

Results: Of 630 TMDs contacted, 199 completed the survey. When rating efficacy of battlefield interventions in the civilian setting from 1 to 5 (5: always effective), 60% gave a value of 4 or higher, 32% gave a neutral value, and 8% gave a value of 2 or below. Respondents rated civilian research as adequate for damage control resuscitation and traumatic brain injury, and inadequate for tourniquets and hemostatic agents. Respondents were evenly divided regarding pre-hospital interventions. A majority of respondents stated that lack of civilian research was not a barrier to adopting practices in all areas except hemostatic agents.

Conclusion: Based on responses, lack of civilian research does not appear to be a barrier to adopting battlefield techniques. However, there are still centers which have not adopted these practices. Future analysis of survey responses will help to shed light on the best manner in which to improve translation between military and civilian researchers.

Surgical Treatment of Scoliosis in Osteogenesis Imperfecta Patients May Improve Quality of Life Compared to Non-Surgical Management

Background: Osteogenesis imperfecta (OI) often results in scoliosis secondary to intrinsic structural bone deficits. Due to the decreased biomechanical integrity of bone, there is an increased incidence of fractures and other complications. We compared objective outcomes and quality of life in OI patients who receive surgical treatment with those who did not receive surgical treatment.

Methods: We conducted a retrospective cohort study of 27 total patients (23 non-surgical and 4 surgical) from Shriners' Hospital for Children Chicago and Shriners' Hospital for Children Canada. Data was collected from November 2006 to December 2011 both from routine physical examination and surveys. Radiographic data consisting of Cobb angles, DEXA bone mineral densities, and pulmonary function tests were used to evaluate objective success of treatment. Additionally, SRS-30 and RAND-36 questionnaires were used to evaluate subjective improvement. Two-way t tests were used to determine if there were any significant differences in outcomes between surgical and non-surgical groups, by comparing the post-operative trend with the natural history observed in non-surgical patients.

Results: Our results show that post-operative patients experienced a significant improvement in one subjective parameter measured by the SRS-30 survey. This parameter was Overall Quality of Life, an average of all parameters involved in the questionnaire ($p=0.0079$). This trend of improvement was observed despite the fact that post-operative patients did not have a significantly different progression of scoliosis and other functional parameters as compared to non-surgical patients.

Conclusion: Although surgery may not significantly alter progression of objective functional parameters, it does result in improvement of quality of life in OI patients.

Long-Term Outcomes Of Fractionated Conformational Radiotherapy In Patients With Meningiomas Of The Cavernous Sinus

Background: Surgical resection of cavernous sinus meningiomas (CSM) is associated with significant mortality and morbidity. Fractionated conformational radiotherapy (FCRT) has been considered as a viable treatment option, resulting in better outcomes. Due to the scarcity of data, we evaluated long-term outcomes of CSM following FCRT.

Methods: We retrospectively reviewed medical records for 53 consecutive patients, treated with FCRT for the management of CSM. Tumors were classified as confined or extensive (Cusimano et al., 1995). Clinical outcome and tumor control were assessed by the treating neurosurgeon. An MRI or CT report of change in tumor volume by at least 20% was considered as evidence of radiographic shrinkage or progression. Clinical outcome was determined by the onset of new neurological deficits or improvement/worsening of at least one baseline symptom or sign at last follow-up.

Results: Follow-up was 90 (range, 3-264) months. Extensive lesions were present in 60% of patients. Most patients (n=52) received fractionated radiation to a total dose of 5400 (3500-6500) cGy, with a dose per fraction of 180 (117-500) cGy; one patient received a single dose of 1000 cGy. Radiotherapy was delivered stereotactically for 89% of patients and conformationally for 11%. FCRT was the first-line treatment in 40%, with the remainder having previously received either conventional surgery or radiotherapy. FCRT was an adjuvant treatment for 26%, and 40% had recurrence prior to FCRT. Long-term clinical improvement was achieved in 17% of patients and 34% remained unchanged. Of the 26% of patients who worsened, 13% experienced new cranial neuropathy. Tumor shrinkage was observed in 42% of patients, 17% had stable lesions, and 26% showed tumor progression at last follow-up.

Conclusion: Compared to surgical resection, FCRT offers adequate long-term tumor control and satisfactory functional outcomes for CSM management. Patients may exhibit delayed disease progression, suggesting a need for longer follow-up than the current standard of care.

Increased Inpatient Burden and Neurosurgical Demand in Premature Infants with Intraventricular Hemorrhage

Background: Intraventricular hemorrhage (IVH) in premature infants can lead to post-hemorrhagic hydrocephalus (PHH), often requiring numerous neurosurgical interventions and long-term follow-up by pediatric neurosurgeons. This study aims to provide national estimates of the annual inpatient and neurosurgical burden of PHH and characterize the socioeconomic profile of this patient population.

Methods: We selected infants within 90 days of birth from the 2006 Kids' Inpatient Database, a HCUP database containing a representative national sample of pediatric discharges. Using ICD-9 codes, we identified three groups: non-premature, premature without IVH, and premature with IVH. Demographics, inpatient data, and socioeconomic factors were collected to identify predictors of inpatient procedures, length of stay (LOS), total charges, and mortality.

Results: Of 3.36 million estimated admissions, 1.34% were premature; 0.22% also had IVH. Incidence of IVH in premature infants was 16.3%. Neurosurgical intervention was performed in 340 (4.6%) of the IVH group, compared to < 0.2% of the other groups. Among premature admissions, IVH diagnosis increased mean LOS from 34.0 to 53.1 days ($p<0.0003$) and total charges from \$148,991 to \$248,368 ($p<0.0003$). Neurosurgical intervention for IVH was associated with further increased LOS (80.5 days) and total charges (\$380,914). Inpatient mortality increased dramatically with prematurity (OR 110.4, $p<0.001$) and grade IV IVH (OR 413.7, $p<0.001$). Premature subjects were more likely to be non-white (OR 1.4, $p<0.001$), have public or no insurance (OR 1.4, $p<0.001$), and fall below median household income for zip code (OR 1.2, $p<0.001$) with no significant differences between premature groups.

Conclusion: Premature infants with IVH significantly increase inpatient burden compared to those without IVH by increasing LOS, charges, and mortality for the most severe hemorrhages. A majority of premature babies are minorities with lower socioeconomic status and public or no insurance. These data may help target prevention of prematurity and PHH while also predicting future demands on the neurosurgical workforce.

Assessment Of Skin Color Patterns And Associated Lifestyle Factors In African-Americans Using Tristimulus Colorimetry

Background: Tristimulus colorimetry, which employs the CIE $L^*a^*b^*$ model to quantify color, has been used in the past to analyze human skin. In the Caucasians and Asians, L^* has been indicated as a measure of pigmentation and a^* as a measure of erythema. The purpose of this study was to analyze skin color patterns in African-Americans and compare them to the results of previous studies in the aforementioned ethnic groups.

Methods: Colorimetry readings were taken across three sites: buttock, upper inner arm, and dorsal forearm for African-American volunteers ($n=80$). A survey asking about lifestyle factors, such as sun exposure and cigarette smoking, was also administered to assess whether certain factors contributed to differences in pigmentation. ANOVA, student t-tests, and multiple linear regression models were employed in analysis.

Results: In our study population, we found that the buttock area was generally found to be darker than the upper arm or dorsal forearm, whereas previous studies show that Caucasians and Asians have lighter skin in sun-protected areas. Contrary to previous studies which showed a negative correlation between L^* and a^* values in the reference groups across all sites, a weak positive correlation between the L^* and a^* values was found in the buttock area but lost in the dorsal forearm and upper arm areas. However, similarly to the reference populations, the a^* values were highest in the dorsal forearm, the most sun-exposed area, compared to the other sites.

Conclusion: We conclude that the pattern of pigmentation regarding sun-protected and sun-exposed areas in African-Americans differs from that of Caucasians and Asians. The pattern of a^* values across the three sites suggests that the degree of erythema could be estimated using a^* , but other factors such as the intrinsic pigmentation of the skin in African-Americans may influence a^* as shown by the results in the sun-protected buttock area.

An Efficacy Evaluation Of The Low-Cost Quantum Catch Fundus Camera In Screening For Diabetic Retinopathy

Background: Diabetic retinopathy (DR) is the second most common cause of vision loss in America and the fifth most common worldwide. Early treatment of proliferative diabetic retinopathy (PDR) and clinically significant macular edema (CSME) can dramatically reduce the risk of vision loss; however, DR is often diagnosed late because of poor adherence to recommended routine screening. This may be in part due to the high cost of screening equipment (>\$25,000). Our study assesses the screening capabilities of the more affordable Quantum Catch (QC) fundus camera.

Methods: A convenience sample of 69 subjects was screened at the Wilmer Eye Institute using both QC and Zeiss cameras. Image sets were graded by a certified grader in a masked fashion using the Early Treatment Diabetic Retinopathy Study protocol. Screening time and image quality were noted by the imaging technician and grader, respectively. Agreement between severity level classifications of both cameras was evaluated via a weighted κ statistic.

Results: DR grades of the QC and Zeiss cameras exhibited 47% agreement (weighted κ -value 0.41) with the QC generally underscoring DR relative to the Zeiss. For identifying treatable disease (PDR or CSME), the cameras showed 75% agreement (κ -value 0.50). The QC camera's range of its imaging field and imaging artifacts contributed to its misidentification of PDR and CSME, respectively. Despite these shortcomings, the QC camera had significantly fewer instances of positioning and exposure defects than the Zeiss (p-values <0.001); however, it did also suffer from longer image acquisition times (QC: 23.4 sec/image, Zeiss: 7.8 sec/image).

Conclusion: While the QC camera's affordability and fewer image defects are promising, its current limitations prevent it from qualifying as an adequate replacement for the more established Zeiss camera. Its misidentification of treatable DR and longer acquisition time hinder its effectiveness and must be addressed before it can serve as a screening tool for DR.

Increased Post-Operative Smoking Among Lung Cancer Patients Undergoing Video-Assisted Thoracic Surgery (VATS) Compared To Open Thoracic Surgery

Background: Our objective was to perform a retrospective cross-sectional analysis of smoking behavior and quality of life after lung cancer resection in patients who underwent VATS and open thoracic surgery.

Methods: We surveyed 184 current or former smokers with stage 1A-3B non-small cell lung cancer who underwent either VATS or thoracotomy. We asked about quality of life using the SF-12, and smoking practices at 5 time points: (1) immediately before meeting a surgeon, (2) after meeting a surgeon but before surgery, (3) one month post-operatively, (4) six months post-operatively, and (5) at the time of questionnaire completion. Additional information was obtained from the medical record in compliance with our institution's HIPAA guidelines.

Results: 131 (71%) patients participated, 45 (25%) died, 6 (3%) declined, and 2 (1%) did not respond. At 24 months post-operatively, 9% of thoracotomy patients and 9% of VATS patients returned to smoking ($p = 0.45$). A subgroup analysis of current smokers revealed that 11% of thoracotomy patients and 34% of VATS patients returned to smoking at 24 months ($p = 0.11$). Amongst current smokers, the mean physical quality of life score was 37.2 (95%CI 34.26-40.21) for thoracotomy patients and 36.4 (95%CI 27.74-45.12) for VATS patients. The mean mental quality of life score was 43.76 (95% CI 40.15-47.38) for thoracotomy patients and 36.40 (95% CI 27.74-45.12) for VATS patients.

Conclusion: Lung cancer patients who smoke at the time of surgery and undergo VATS are more likely to smoke post-operatively and have decreased mental quality of life compared to those undergoing thoracotomy.

Factors Associated With Increased Incidence Of Motor And Sensory Deficits In Patients Who Undergo Meningioma Resection

Background: Meningiomas are brain tumors that arise from the arachnoid cap cells of the meninges. They represent about 15% of all primary brain tumors. Although frequently benign, meningiomas often lead to the development of neurological deficits. The purpose of this study was to identify different factors that were associated with the development of motor and sensory deficits in patient who undergo meningioma resection.

Methods: Patients who had undergone meningioma resection by 5 different surgeons between 2007 and 2011 at Johns Hopkins Hospital and Johns Hopkins Bayview Medical Center were identified retrospectively. Different variables such as extent of resection, tumor size, location and invasiveness as well as associated co-morbidities have been collected and multivariate proportional hazards regression analysis will be performed. This will allow us to determine which variables collected are associated with an increased risk of developing neurological deficits in post-operative patients.

Results: Analysis of the data shows that 72% of patients with Karnofsky performance scale (KPS) scores below 70, 55% of patients with hypertension, 55% with headache, 72% with tumor size > 3cm and 42 % with visual deficits developed different motor and sensory deficits post-operatively.

Conclusion: Patients with high KPS scores, hypertension, headaches, tumor size greater than 3 cm and visual deficits are at greater risk of developing post-operative neurological deficits. With this knowledge, the next step will be to attempt to modify these risk factors and study how this will affect the risk of patients developing post-operative neurological deficiencies.

Impact On Seizure Control Of Surgical Resection Or Radiosurgery For Cerebral Arteriovenous Malformations

Background: As a common manifestation of cerebral arteriovenous malformations (AVMs), seizures have a marked impact upon patient quality of life. Although surgical resection or stereotactic radiosurgery are the standard treatment options for selected AVMs, the impact of treatment modalities on seizure control remains unclear. In this study, we compared seizure outcomes after surgical resection or radiosurgery.

Methods: We analyzed retrospectively-collected information for 378 patients with cerebral AVMs treated at our institution from 1990 to 2010. The application of strict inclusion criteria resulted in a study population of 164 patients. Information on patient history, AVM characteristics, treatment strategies, and outcomes was collected. Data was analyzed using Pearson's chi-square test, Student's t test, stepwise multivariate logistic regression, and Kaplan-Meier survival analysis with Cox proportional hazards regression.

Results: A significant interaction was detected between seizure presentation and treatment modality with respect to seizure control after treatment (odds ratio [OR] 0.16, 95% confidence interval [CI] .04–.66, $p=.011$) and was explored with subgroup analyses. Of the 49 patients (30%) presenting with seizures, 60.4% experienced seizure persistence after treatment. For these patients, radiosurgery was associated with seizure recurrence (OR 4.32, 95% CI 1.24–15.02, $p=.021$). In contrast, for patients presenting without seizures, 18.4% experienced de novo seizures after treatment, for which surgical resection was identified as an independent risk factor (hazard ratio [HR] 8.65, 95% CI 3.05–24.5, $p<.001$).

Conclusion: While our data suggest that achieving seizure freedom should not be the primary goal of AVM treatment, surgical resection results in improved seizure control as compared to radiosurgery for patients who present with seizures. Conversely, in patients without presenting seizures, surgical resection increases the risk for new-onset seizures compared to radiosurgery, but primarily within the early post-treatment period. AVM management should include consideration of pre-treatment seizure status and the divergent effects of surgical resection and radiosurgery on seizure control.

HISTORY OF MEDICINE

POSTER ABSTRACTS

Listed Alphabetically

“Too frankly human and not strict science”: A Tale of Psychiatry and Eugenics at Johns Hopkins Hospital

Background: Adolf Meyer, the first director of the Phipps Psychiatric Clinic at the Johns Hopkins Hospital (1913-1941), developed an approach to “scientific psychiatry” that rested upon his theory of psychobiology. Psychobiology held that, in order to understand mental illness, one must consider all domains of a patient’s life, including biology, behaviors, and environment. For Meyer, these domains also included heredity, the focus of the rising American eugenics movement. Although Meyer was an active member of several eugenics organizations, his precise views on eugenics – particularly those concerning birth control, sterilization, and immigration restriction – have never been studied systematically. The aim of my project is to examine Meyer’s views on birth control, sterilization, and immigration restriction, and to understand these in the context of Meyer’s career and the broader American eugenics movement.

Methods: The materials for this study include Meyer’s published work and archival materials from the Chesney Medical Archives (letters, speeches, articles, and working notes). Secondary sources were consulted to gain insight into the history of the American eugenics movement.

Results: My research reveals that Meyer’s views on eugenics were heterogeneous and varied depending on the particular branch of eugenics. For instance, he supported birth control and voluntary sterilization as a means of reducing mental illness and lobbied fiercely to overturn the Comstock laws, which prohibited physicians from giving contraceptive advice. Meyer, however, feared that American eugenic positions on sterilization and immigration restriction were fueled more by xenophobia and dreams of racial purity than by a wish to reduce mental illness.

Conclusion: The present study suggests that Meyer was torn between his support for some domains of eugenics (birth control and sterilization) and his opposition to another (immigration restriction). Ultimately, Meyer distanced himself from eugenics, accusing the movement of using science to justify a field that was “too frankly human and not strict science.”

Cesarean Section Rates and Indications in the Early 20th Century: A Look Through Dr. J. Whitridge Williams' Lens

Background: The popularity of the cesarean section began to increase in the early 20th century as improved pain control and aseptic technique lowered mortality rates. New indications for cesarean section were described frequently, and practitioners were quick to publish case reports claiming low mortality rates. Cesarean section offered a profitable, quick, and convenient way to manage birth compared to the long and uncertain course of natural labor.

Methods: My research examines the changing ideas regarding cesarean section in the U. S. during the pivotal years of 1900-1925. I do so through both an analysis of the scientific literature and a study of Johns Hopkins obstetrician J Whitridge Williams. I am examining such journals as The Transactions of the American Gynecological Society, and The American Journal of Obstetrics and Gynecology, among others, and reading Williams' Obstetrics textbooks and correspondence.

Results: Starting in the 1910s a conservative core of obstetricians, including Williams, began discussing the abuse of the operation. Despite this, Williams in the 1917 edition of his textbook Obstetrics added a series of cesarean section drawings prepared by Mr. Max Brodel. In the subsequent edition, Williams attributes rising maternal mortality to the high rate of cesareans. I analyze Williams' reservations and evolving attitude toward the operation as a reflection of his desire to bring Obstetrics into the scientific way of thought at Johns Hopkins, his concerns regarding medical education, experience with the operation, and distrust of other practitioners.

Conclusion: Aside from illuminating an important chapter in the history of obstetrics and Johns Hopkins, this project sheds light on a continuing pattern: In the United States today over 30% of all births are cesarean deliveries. The current obstetrical literature also discusses the high cesarean rate and increases in maternal mortality, showing that despite the passage of a century, progress is hard to define.

A History of Hospital Infection Control: The Study on the Efficacy of Nosocomial Infection Control

Background: In 1970 the first International Conference on Nosocomial Infections was held by the Center for Disease Control (CDC). Experts and pioneers in the field called for clear scientific evidence to support the unproven methods and procedures of infection surveillance and control used by hospitals nationwide. Consequently the CDC created the Study on the Efficacy of Nosocomial Infection Control (SENIC). This research provides the first detailed historical account of the origins of SENIC, which sought to tackle one of the most important issues in hospital management.

Methods: This project analyses oral interviews with key figures, conference proceedings, journal articles, newspaper articles and infection control recommendation guidelines in order to evaluate the methods of SENIC, the social dynamics of the research team, and the state of hospital Infection control practices in the U.S. in the 1970s and 80s.

Results: SENIC was split into three phases, a Preliminary Screening Questionnaire, a Hospital Interview Survey, and a review of patient medical records. Published in 1985, the final results provided reliable figures on the burden of nosocomial infections nationwide. SENIC defined individual infection rates and ideal surveillance and infection control programs based on the site of infection. The SENIC project led to the creation of new hospital accreditation guidelines and the distribution of concrete recommendations on how best to monitor and prevent nosocomial infections in hospitals.

Conclusion: SENIC was thought to be so significant that an entire issue of a 1980 American Journal of Epidemiology was devoted to it. SENIC had a substantial impact on how hospital infections are dealt with today. However, SENIC encountered a number of obstacles that were surmounted only by the ingenuity of the team members, the exploitation of social connections and the effective use of CDC resources.

An Historical Look at Rex Morgan, MD, a Comic Strip that has Won Readers Over for its Entertainment and Medical Education

Background: In 1948, the comic strip Rex Morgan, MD was published in its first of over 300 newspapers in the United States. The creator, psychiatrist Nicholas P. Dallis, maintained the strip for over 40 years until he passed it along to writer Woody Wilson. The essence of this soap-opera style comic strip is the human ethos, yet it weaves in contemporary and practical medical information useful to the masses. This paper examines the strip from the early 1950's to the late 1990's, and attempts to understand why readers became invested in the story. Was it the drama and intrigue of character development or was it the reliance on health information?

Methods: King Features Syndicate provided a near comprehensive archive of the published strips, which was analyzed for plot development and medical themes. Interviews with Dallis' youngest daughter, Carolyn Uchman provided a personal insight to the story, while conversations with Woody Wilson added substance to the intent and creative process of the strip. Wilson contributed an archive of Dallis' original files from 1950-1990, including correspondence, and letters to and from readers.

Results: In the collection of letters to Dallis, expressions of investment in the personal stories outnumbered - in quantity, but not enthusiasm - the words of praise and gratitude for the medical education.

Conclusion: While these results suggest readers tuned in for the medicine and drama both, perhaps the education was a secondary bonus to the primary entertainment of the character development and storyline. Interestingly, the dynamics of the comic strip (topics covered, plot development, management of conflict and resolution) remained nearly formulaic for the duration of Dallis' career. This dedicated readership continued - and still continues today - under the creativity of Wilson, even during a time when the future of newspaper comics remains uncertain.

The Use of Illustrations in 13th and 14th Centuries Medieval Surgical Manuscripts

Background: It is only in the middle ages that surgery became an occupation distinct from medicine and surgeons began to write manuals of surgery. By the late 1200s, we begin to see the first surgical manuscript with illustrations. My project explores the multiple roles played by these illustrations as surgery came to define itself as distinct body of knowledge.

Methods: After locating digital copies of illustrations belonging to medieval surgical manuscripts, I analyzed the images using the framework provided by Peter Murray Jones. I asked questions such as: what kind of social relations are depicted between doctor and patient, doctor and other doctors, and doctors and students/assistants? How is the role of the surgeon modeled? What are the functions of illustrations in these manuscripts? Do they provide detailed how-to instruction? In doing so, I explored larger questions regarding the origin of the illustrations, their purpose, and their content in relation to the emergence of surgery as specific form of medical knowledge.

Results: I was able to locate images in half a dozen libraries within the US and Europe. I analyzed medieval surgical manuscripts written by most of the major medieval surgeons: Roger Frugard, Roland of Parma, Teodorico dei Borgognoni, Bruno Longobucco, Guglielmo da Saliceto, Lanfranc of Milan, and Henri de Mondeville.

Conclusion: These images served multiple roles in medieval surgical manuscripts. Many provided specific visual instructions on how to perform a procedure, as in the case today, but others functioned organizationally or referentially as headings or index subjects. Still others were used as a mnemonic aids to facilitate memorization. Unusually, Mondeville used the images to illustrate human anatomy. Finally, all these images taken together give us a rare glimpse into what and who a surgeon was at the beginning of a distinct surgical profession.

Physician-Explorers And The Maturation Of The Field Of Polar Medicine During The Heroic Age Of Antarctic Exploration (1897-1920).

Background: During the Heroic Age of Antarctic Exploration, the southern continent offered nations unknown scientific and geopolitical potential and sparked a fervid pursuit of its pole to amass cartographic, geologic, and biologic data. On these expeditions, no crewmember was more important to the well-being of the expedition than the ship's surgeon. Responsibilities of the polar physician were unprecedented and would help establish the emerging field of polar medicine. This paper examines this set of responsibilities and attempts to determine to what extent their experiences shaped their contributions to the body of polar medical knowledge.

Methods: Memoirs and personal accounts of expedition leaders and physician-explorers were used to highlight the responsibilities of polar physicians. The diary of Dr. Alexander Macklin, chronicling the Endeavor expedition, was used to characterize their workload and reveal if physicians were cognizant of their medical legacy. A review of their published journal articles revealed their contributions to medical knowledge.

Results: Working in a resource-limited environment, leaders were compelled to select multidimensional crewmembers. Physicians readily accepted a variety of nonmedical duties including service as dog keepers, veterinarians, meat inspectors, and sledge drivers. Their roles as medical officers were equally diverse and they often served simultaneously as a generalist, nutritionist, dentist, anesthetist, surgeon, psychiatrist, and ophthalmologist.

Conclusion: The majority of these physicians retreated to their homeland, shying away from their polar experiences and returning to their own interests in medicine and science. But an inspired few would return to practice, embracing their experiences as medical professionals. A significant collection of work, published upon their return, addresses several medically relevant polar topics including scurvy, snow-blindness, frostbite, and hygiene. However, while these topics were not new to medicine, the context and fanfare with which they were presented established a unique lens upon which future physicians could rely to build the field of polar medicine.

The History Of Women In Orthopaedic Surgery And Their Impact On The Field

Background: Currently, the percentage of female orthopaedic surgeons in the US is below 5%, making it one of the most gender imbalanced areas of medicine. Since the 1970s, orthopaedics has been one of the least able to recruit women in comparison to other surgical specialties.

Methods: Through a close reading of the medical and historical literature, oral history interviews with female orthopaedic surgeons, and a preliminary survey of female orthopaedic surgeons who are members of the Ruth Jackson Orthopaedic Society, this project characterizes the social and cultural trends that have shaped the history of women in orthopaedic surgery.

Results: Women were gradually excluded from Western medicine starting in the seventeenth century. Medicine became a male-dominated field and, even when women began to overcome these barriers, surgery retained an “old-boys network” that perpetuated the exclusion of women. While the percentage of women in most surgical subspecialties increased dramatically from 1970, orthopaedic surgery has fallen behind. Research reveals that recruitment into orthopaedic surgery is hindered for a number of reasons. Firstly, women find it difficult to identify female mentors in orthopaedic surgery. Secondly, orthopaedics has a reputation for: (1) great physical strength as a prerequisite for success; (2) a “jock/frat” culture geared toward strong, but boorish male athletes; and, (3) an “uncontrollable” lifestyle with a poor work-life balance. Today, strength is no longer required, orthopaedic surgeons are not unintellectual, and the field has a relatively controllable lifestyle; yet, these perceptions continue to deter female applicants. Thirdly, historically, females lacked exposure to orthopaedics prior to medical school; however, exposure has increased over the past few decades as American culture shifted to encourage female participation in athletics from young ages.

Conclusion: This paper uses historical and contemporary evidence to understand the current gender imbalance in orthopaedics, building a platform for devising policy strategies that improve recruitment of females.

How Did Care For Intimate Partner Violence (IPV) Victims Evolve Into An Orthopaedic Medical Issue? Historical Perspective On The Medicalization Of IPV In Orthopaedic Surgery

Background: What society defines as a medical issue changes over time. Medicalization of numerous behaviors and social problems was a characteristic of the twentieth century in the United States, expanding the scope of healthcare. Medicalization transforms healthcare by redefining expectations of and practices by medical professionals. This paper aims to understand how care for Intimate Partner Violence (IPV) victims evolved into an orthopaedic medical issue.

Methods: Oral history interviews with orthopaedic surgeons who have led efforts to improve IPV awareness, response, and advocacy in their specialty were combined with primary and secondary literature reviews and analyses and with research in the historical archive at the Futures without Violence foundation in San Francisco, California.

Results: Until the 1970s, IPV was a nonmedical issue. Starting in the 1970s, “wife battering” (thereafter termed “domestic violence” and then “intimate partner violence”) emerged as a major public health issue through a medicalization process. This paradigm shift set the stage for individual orthopaedic surgeons who took up this cause as an opportunity to improve patient care. Their efforts shaped medical culture, establishing the current expectation that orthopaedic surgeons should screen for and respond to IPV as part of standard patient care. This emergence story illustrates a medicalization pattern: (1) cultural awareness of IPV as a social issue; (2) followed by recognition of IPV as a health issue; (3) followed by creation of specialty-specific patient care policies and practices. Throughout this history, individual healthcare leaders determined that IPV is an issue that affects people’s health significantly and thus is a human condition that warrants response in medical settings, including orthopaedic surgery.

Conclusion: This IPV medicalization history illustrates the close interrelationship between medicine and society and how particular health problems gain recognition and then shape medical policies and practices, as occurred in orthopaedic surgery.

**MEDICAL HUMANITIES, BIOETHICS,
and the HEALING ARTS
POSTER ABSTRACTS**

Listed Alphabetically

First Response for the Austere Medical Environment (FRAME)

The Problem: Few low and middle-income countries (LMICs) have an established Emergency Medical System (EMS). In LMICs, prehospital transport takes place by whatever means possible, often by untrained bystanders. For certain health emergencies, time to intervention is the major variable that determines morbidity and mortality. There is increasing evidence that in these settings layperson training can be used to mitigate poor outcomes. FRAME was created to address this problem.

Needs Assessment: The former FRAME curriculum was only focused on trauma care, and was a single powerpoint presentation designed to be taught in one day. After conducting a needs assessment, the course was expanded to cover a wider variety of medical and trauma care. The curriculum was also converted into a modular format, so that the course could be adapted to fit specific needs of the students and their community.

Objectives: The objective for the course is to teach basic prehospital care to those who live in LMICs without established EMS systems.

Educational Strategy: The course is designed to be administered as a powerpoint presentation, and has been broken up into modules. There are hands-on skill sessions scattered throughout the course that are designed to teach practical components.

Content: 16 new modules were created; airway, burns, cervical spine, choking, circulation, disaster assessment, emergency childbirth, fractures, gender-based violence, mass casualty incidents, medical emergencies, patient extrication, penetrating trauma, psychological first-aid, rescue breathing, and scene safety.

Future Curriculum Evaluation: The future goals for the FRAME curriculum involve teaching it in communities of LMICs and measuring the course efficacy. Our hope is to measure knowledge of the students before the course, after the course, and later on in the future to see what information they retain. We also hope to assess the effect of the course on prehospital care, morbidity, and mortality in the region.

Collaboration in Pre-Clinical Medical Education: Crowdsourced Test Content and User-Friendly Software

Background: Pre-clinical medical education involves substantial memorization and recall. An innovative approach utilized technology and informatics to facilitate learning and improved test performance through “crowdsourcing” and collaboration.

Methods: The approach utilized a simple to use information management system that required student collaboration to create flashcards. Students decreased individual test preparation by sharing the effort of generating concise, high-yield study materials. Students did not have to learn new tools and were able to use familiar software including spreadsheets and slides.

Results: Through sharing of simple tools for development, dissemination, and display of flashcards medical students of the class of 2014 at Johns Hopkins University created a database of over 16,000 questions. Analysis of test scores demonstrated that performance on tests trended toward improvement after introduction of our flashcard tools. A survey indicated approval and perceived value.

Conclusion: Utilizing simple, shared information management and display resources allowed generation of high-yield, valuable study materials in a collaborative fashion that was linked to improved test scores.

Medical Vignettes: The Experience of a Medical Student

Background: Medical school is difficult not only from a factual terrain, but also from an emotional standpoint. Though most people inevitably visit a physician during their lifetimes, very little is understood about the training and personal growth doctors travel through, specifically during medical school. The purpose of this project was to give the reader an insider's view of a single student's emotions and experiences throughout the intricate journey of medical school.

Methods: I free wrote on 15 significant topics experiences thus far with no writing guidelines in order to flesh out these medical experiences and the accompanying emotions. The top five narratives were then chosen based on: relevance to the medical education, ability for the reader to generalize the experience to their own lives, and ease of story telling. A vignette style was chosen so the pieces to be read either separately as stand alone works or together as a cohesive manuscript.

Results: The reader is invited to journey with the author through five separate moments in order to understand the emotional growth one individual has gone through in the first two years of medical school, with the aim of taking unique situations and relating them to experiences and emotions a non-physician reader could relate to. The situations chosen were: an interview with a cancer patient, dissecting a human cadaver, saving a relative's life, a difficult ethics discussion, and finally a moment of questioning one's role in society.

Conclusion: Though the end product is a compilation of vignettes from a single medical student, the collection is meant to augment existing knowledge on the physical tasks and emotional growth a physician goes through on their path to becoming a doctor, inviting the reader to travel along and relate to these experiences as well.

Portrayal Of The Pregnant Woman In Popular U.S. Media: A Content Analysis

Background: Portrayal of pregnancy in the US media is understudied. One question is to what extent media portrayal matches the actual experience of pregnant women. We conducted a study assessing how pregnancy is portrayed in the popular press.

Methods: A search for print articles from popular magazines containing the key words *pregnant* or *pregnancy* was performed using Proquest spanning four quarters of one year: September 2011, December 2011, March 2012, and June 2012. Magazines specializing in pregnancy or parenting were eliminated as were articles using pregnancy as a statement of fact or inclusion in a medical discussion. A content analysis was performed, and findings were organized into thematic categories.

Results: 96 articles were analyzed. Seven major themes were identified: (1) **Body image** including extreme weight loss after pregnancy, negative opinions about weight gain, and increase in beauty. (2) **Lifestyle change** including discontinuation of the party lifestyle and limitation of sex life. (3) **Gender roles** including expectant father as protector and pregnancy as proof of sexuality. (4) **Motherhood role** including and expectant mother as natural and ideal of domesticity. (5) **Emotional reactions** including happiness of couple, lacking emotional control as negative, and fear motivating negative behaviors. (6) **Work-life balance** including absence from work without consequence, prioritizing pregnancy over work, and exhaustion. (7) **Fascination with celebrity** including baby bump as fashion accessory and speculation into possible celebrity pregnancy.

Conclusions: Pregnancy was frequently portrayed idealistically as a time that is happy, innate, and easy for both the woman and partner. On the other hand, few articles addressed the difficulties of pregnancy such as unwanted pregnancies, nausea, and broken relationships. Other studies have shown that many pregnant women feel bodily dissatisfaction, prejudice in the workplace, and judgment of her behavior by peers which is infrequently addressed in media's idealized image of pregnancy experiences.

Megan Hosein, MS2

Mentor: Larry Chang, MD MPH

Poster Presenter, Medical Humanities, Bioethics, and the Healing Arts

Peer Health Workers And HIV Care: How Can Phws Help Reach And Influence At-Risk HIV Patients In Rural Uganda?

Background: To assess the impact of a peer health worker program on the behaviors of people living with HIV (PLHIV) who have not yet started antiretroviral therapy (ART).

Participants: Eligible subjects for the study were people recently diagnosed with HIV in the Rakai Health Sciences Program (RHSP) system, either as walk-in patients or participants in the Rakai Community Cohort Study (RCCS).

Methods: 450 participants were randomized to either control or intervention arms, with intervention patients visited monthly by their assigned PeerCARE peer health worker (PHW). A baseline questionnaire detailing demographic, health status, and behavioral information was administered to control and intervention study participants and all subjects are scheduled to receive an End of Study questionnaire a year after enrollment.

Main Outcome Measures: Appointment adherence, utilization of a basic care package from the RHSP clinic (bednet, water jug, co-trimoxazole prophylaxis), and condom use.

Results: At this point in the study it is too early to describe preliminary findings, as the End of Study questionnaire has been administered to less than 20% of the participants.

Conclusion: It is too early to draw conclusions regarding the impact of peer health workers on patient behavior, as captured in the baseline and end of study questionnaire. The end of study questionnaire will be fully administered by June 2013, at which point conclusions will be available.

Challenges: Transportation and communication problems were noted as the biggest obstacles for peer health workers in accessing their patients. For the study coordinators, technological difficulties with the data management system were a significant challenge.

Future studies: These may analyze baseline questionnaire responses and investigate similarities or differences between the three patient populations—cohort, walk-ins, or fishing villages—particularly focusing on their behavioral motivations.

Poster Presenter, Medical Humanities, Bioethics, and the Healing Arts

Effective Interventions For Obesity Prevention Across Settings: An Overview Of Federal Guidelines And Current Evidence Base

Background: Obesity is a national epidemic with enormous medical, psychosocial, and economic burdens. To advise professional societies and inform policy, federal guidelines should be thorough and based on best available evidence. We examined how closely federal guidelines on obesity prevention reflect best available evidence, and identified gaps in available evidence.

Methods: Federal obesity prevention guidelines were evaluated for 4 settings: clinic, school, workplace, and community. Literature was examined using PubMed searches for obesity prevention and site type (e.g., "schools"). A total of 26 systemic reviews, meta-analyses, and general reviews were analyzed.

Results: 5 sets of federal guidelines were identified. Reviews and meta-analyses were identified for schools (15), clinics (1), workplace (3), and community (7). Guidelines for prevention in schools, communities, and workplace focus primarily on multi-component interventions promoting healthy eating, physical activity, and community partnerships. Guidelines closely match best available evidence, but new developments in research, especially in the school setting, highlight the need for updated guidelines. Specifically, research since 2009 suggests successful school-based interventions last ≥ 1 year and increase participant confidence in ability to translate knowledge to behavior change. For the clinic, evidence and detailed federal guidelines addressing effective prevention strategies are lacking. Of the 26 meta-analyses and reviews identified, none described the impact of interventions on specific demographic subgroups or high risk populations.

Conclusion: Quantity and quality of evidence and guidelines on effective interventions varies across settings and is notably absent for clinical settings. Federal guidelines for obesity prevention strategies in community and worksite settings line up well with current evidence. Federal guidelines in the school setting need to be updated to reflect recent research. Across settings, most interventions appear to be effective when they are multi-component, combining promotion of healthy eating and physical exercise with a decrease in sedentary behavior.

T.H.E. GooseMan: A Simulator for Transhiatal Esophagectomy

Background: Esophageal cancer is the fastest growing cancer in the US and the seventh leading cause of cancer-related death worldwide. The gold-standard therapy is surgical resection, commonly performed as a trans-hiatal esophagectomy (THE), which involves blindly dissecting the esophagus in the mediastinum through an abdominal incision. While it is difficult to perform, THE is also difficult to teach because limited space and lack of visualization in the mediastinum precludes the possibility of careful supervision. Additionally, learning opportunities may be limited as many surgeons perform TTE or laparoscopic esophagectomy instead. Our objective was to develop and assess the utility of a novel biosimulation model of transhiatal esophagectomy (THE) in thoracic surgical training.

Methods: Program directors and surgeons invited to teach at the Thoracic Surgery Directors Association Boot Camp were asked to evaluate the THE GooseMan, a novel surgical simulator designed to simulate transhiatal esophageal mobilization. THE GooseMan consists of a porcine organ block (esophagus, aorta, trachea, and stomach) in a plastic torso with artificial lungs, heart and diaphragm. Participants were walked through the use of the simulator, and given the opportunity to attempt the esophagectomy. On 5-point Likert scales, they were asked to rate the model on its visual realism, tactile realism, emphasis on important skills, similarity to the operating room, quality as a method of skills training, and whether or not they would use the simulator at their home institutions. Participants were also asked to rate the importance of various modifications to the model, such as the ability to use a Sweetheart retractor or laparoscope.

Results: A total of 16 thoracic surgeons and program directors assessed the THE Gooseman and provided written feedback. The simulator was given an average score of 3.6/5 for both visual and tactile realism, 3.7/5 for its emphasis on important skills, 3.3/5 for its similarity to the OR, 4.3/5 for its usefulness as a method of skills training, and 3.6/5 on whether they would use the model at their institutions. In the analysis of potential modifications to the model, no change was rated significantly higher than the others. There was no significant correlation between survey responses and the number of esophagectomies or THEs performed by the respondents.

Conclusion: Thoracic surgery program directors and surgical educators expressed an interest in using simulation to teach transhiatal esophageal mobilization. Variation in surgeons' technical preferences highlights the importance of flexibility in simulator design.

Asking Awkward Questions: A Survey Of Knowledge, Skills, Attitudes, And Practice Of Sexual History Taking In Johns Hopkins Faculty And Medical Students

Background: Few aspects of the medical interview offer as much potential for discomfort as the sexual history despite its importance to both the patient's health and the physician-patient relationship. Medical educators' knowledge and skills in this domain not only impact patient care but also teaching. This study aimed to identify gaps in knowledge and skills among faculty in sexual history taking and compare faculty and students views of their knowledge and skills.

Methods: An anonymous survey was emailed to selected Johns Hopkins faculty (N=57) and medical students entering second through fourth years (N=333). Those surveyed responded to statements about knowledge, skills, attitudes, and practice of sexual history taking on a 4 point Likert-scale. Limited demographic information was collected. Data was analyzed in aggregate; comparisons were made between students and faculty, and between medical student cohorts.

Results: Overall response was 50% for students (166/333) and 56% for faculty (32/57). The majority of respondents (92%) agreed that taking a sexual history was an important element in the clinical vignette; gender/sexual orientation of the patient did not impact this finding. Medical student cohorts demonstrated increased confidence and competency as students progressed through medical school. Significant gaps were identified in knowledge and skills for both students and faculty, particularly working with special populations. Almost half (43%) of respondents self-described as a minority in various categories; however, there was no statistically significant difference in their answers.

Conclusion: The results demonstrate a progressive development of sexual history taking over the course of medical school, yet gaps in knowledge of and skills were noted for both students and faculty. These findings should inform not only targeted faculty development but also potential overall curricular changes. Furthermore, helping students understand the inherent developmental accumulation of skills at the outset of sexual history teaching may be a helpful explicit frame.

PUBLIC HEALTH and COMMUNITY SERVICE

POSTER ABSTRACTS

Listed Alphabetically

Mortality Among Marathon Runners in the United States, 2000-2009

Background: Background: As participation in marathon running has increased, there has also been concern regarding its safety.

Aim: To determine if the increase in marathon participation from 2000 to 2009 has affected mortality and overall performance.

Methods: Methods: We used publicly available racing and news databases to analyze the number of marathon races, finishing race times, and deaths from 2000 to 2009 in marathons in the United States.

Results: Results: The total number of marathon finishers has increased over this decade from 299,018 in 2000 to 473,354 in 2009. The average overall marathon finishing time has remained unchanged from 2000 to 2009 (4:34:47 vs 4:35:28; $P = .85$). Of 3,718,336 total marathon participants over the 10-year study period, we identified 28 people (6 women and 22 men) who died during the marathon race and up to 24 hours after finishing. The overall, male, and female death rates for the 10-year period were 0.75 (95% confidence interval [CI], 0.38-1.13), 0.98 (95% CI, 0.48-1.36), and 0.41 (95% CI, 0.21-0.79) deaths per 100,000 finishers, respectively. There was no change in the death rate during this time period for overall, male, or female groups ($P = .860$, $.533$, and $.238$, respectively). The median age among deaths was 41.5 years (interquartile range, 25.5 years). Fifty percent (14/28) of deaths occurred in participants less than 45 years old. Myocardial infarction/atherosclerotic heart disease caused 93% (13/14) of deaths in those 45 years and older. A variety of conditions caused death in younger racers, the most common being cardiac arrest not otherwise specified (21%, $n = 3$).

Conclusion: Conclusion: Participation in marathons has increased without any change in mortality or average overall performance from 2000 to 2009.

Integration of environmental assessments into a Mass Active Case Finding program in Klerksdorp, South Africa.

Background: Respirable pollutants impair lung function, potentially increasing the risk of acquiring tuberculosis (TB) or activating latent infection. The purpose of this project is to assess environmental exposures in homes of TB patients.

Methods: The Mass Active Case Finding initiative is an effort to increase identification of undiagnosed TB and HIV. Households of newly diagnosed TB patients from the initiative were recruited for participation. Surveys were administered to record fuel use, cigarette exposure and household living conditions. Ambient air and individual expired-breath carbon monoxide, air nicotine, hair nicotine and particulate matter levels inside and outside of the home were objectively measured.

Results: 51 homes and their household members were enrolled in the study. 7 (14%) of the households that were included were classified as shacks, which are constructed with corrugated metal, often poorly ventilated and overcrowded. Reported cooking fuel types included electricity (78%), paraffin or kerosene (16%), and wood (6%). Most households (98%) cooked for less than 2 hours each day and most reported cooking inside more than outside the house (46% and 4%, respectively). The majority of households who heated their homes used electricity (29 of 51; 57%) and 5 (10%) used traditional mbawula and wood ; 17 (33%) reported not using heat. Among those that used a source of heat, the majority reported heating for 1-3 hours per day (n=23, 77%). A burning smell was noted at 10 (19%) of the homes, indicating exposure to outdoor air pollution from burning materials in the area.

Conclusion: Preliminary analysis of collected data suggests that households in the study area may be exposed to environmental pollutants that may increase risk for TB disease. Further analysis of individual and household measurements will help better explore the environmental difference in households where TB transmission exists.

Improving Emergency Department Throughput by Reducing Unnecessary Orthopedics Consultations

Background: The primary contributor to emergency department (ED) overcrowding is ED length-of-stay (LOS). Eliminating unnecessary consultations is one potential solution to reduce LOS and improve throughput. A portion of orthopedic consultations previously done in the Bayview ED was solely for obtaining clinic follow-up, as an orthopedic was required to authorize follow-up. In 2011 an online database (Sharepoint) was implemented, allowing ED providers to request appointments without consultations for patients with simple orthopedic injuries. The purpose of this study is to evaluate this change, as well as the characteristics of the patients in Sharepoint. Our hypothesis is that patients referred through Sharepoint will have shorter LOS than similar patients under the old system. We hope the results will validate the usefulness of this change, and provide insight into improving ED efficiency at Bayview and other hospitals.

Methods: We conducted a retrospective quality improvement analysis of ED LOS before and after the initiation of Sharepoint. This was done by collecting demographic, visit and LOS information from the EMR on patients entered into Sharepoint between June 2011 and July 2012. A comparison group was established of patients with similar orthopedic injuries in the year prior to June 2011. The average LOS was compared between the two groups.

Results: Comparison results are pending final data analysis. Sixty-four patients were included in the final group of Sharepoint patients. The overall average LOS was 167 minutes and the LOS varied by season and location of injury. Further results are displayed on the poster.

Conclusion: Limitations include human error and inherent variability of throughput time.

Ethnic Disparities Persist In The Field Of Plastic And Reconstructive Surgery: An Analysis Of A Large Post-Mastectomy Prospective Cohort

Background: Purpose: Although ethnic disparities have been widely reported in breast cancer patients, analyses have tended to focus on the early stages of management. We hypothesized that undue disparities also permeate into the operating room in the field of plastic and reconstructive surgery. This analysis examined the association between a patient's ethnicity and 30-day post-surgical morbidity within three treatments: mastectomy alone, immediate reconstruction, and delayed reconstruction.

Methods: Methods: The cohort under study is a subset of a nationwide, random sample of patients prospectively followed by the American College of Surgeons (via ACS NSQIP®). A total of 50,045 women observed between 2008 and 2010 were grouped into one of three surgical categories based upon respective CPT coding in the medical record: 1) mastectomy only, 2) immediate reconstruction with concurrent mastectomy, and 3) delayed reconstruction. Pearson chi-square tests were used to detect differences in treatment utilization by ethnicity. Multivariable logistic regression models were then used to estimate the odds of post-operative surgical and medical morbidity reflecting risk of infections, wound disruption, graft failure, return to OR, and other serious medical complications.

Results: Results: Our analysis exposed a differential pattern of use of the breast surgeries by ethnicity; Pearson's chi square (d.f.10)= 388.8157; $p < 0.001$). The fraction of Non-Hispanic Blacks electing to undergo mastectomy without reconstruction was higher than the pooled proportion (82.4% vs. 73.7%). Only 14.7% of Non-Hispanic Black patients underwent immediate reconstruction, compared to 21.9% of Non-Hispanic Whites. Adjusted odds ratios showed that Asian patients are least likely to develop surgical complications compared to all other ethnic groups (OR_BLACK=1.45, $p < 0.005$; OR_HISPANIC=1.38, $p < 0.05$; OR_WHITE=1.52, $p < 0.001$). Ethnicity was a significant predictor of morbidity in the combined cohort as well as in those undergoing mastectomy alone and immediate reconstruction.

Conclusion: Conclusions: We present the analysis of large sample of patients (n=50,045) to show that undue ethnic disparities are present among breast cancer patients treated surgically. First, despite the established benefits of some breast procedures over others, the patterns of treatment utilization differ significantly between ethnic groups. Second, Asian patients enjoy a better profile of post-surgical complications compared to all other ethnic groups. Characterizing the nature of such a protective association could lead to interventions that reduce the morbidity gap between people of different ethnicities in the United States.

Outcomes of patients with eloquent glioblastoma

Background: Patients with glioblastoma multiforme (GBM) who undergo more complete surgical resections have better outcomes, and patients who have worse post-operative deficits have worse outcomes. Surgical approaches to patients who have eloquent GBMs (GBMs that affect language, motor, or sensory areas of the brain) remain unclear, because the greater the extent of resection, the larger the post-operative deficit may be. The purpose of our study was to perform a retrospective analysis of patients with eloquent GBM and to determine the factors that predict survival.

Methods: We constructed a database of 355 patients with eloquent GBM who underwent 425 operations (surgical resections and/or biopsies) performed at Johns Hopkins Hospital and Bayview Medical Center over 5 years. We used statistical analysis to identify factors that predict survival in these patients.

Results: Final results pending analysis. The following are preliminary statistics from 83 patients with eloquent GBM who underwent 94 operations. Mean age at time of surgery was 59.0 years. 61.7% of patients were male. 85.2% of patients were white, 7.4% were black, and 7.4% were other. The most common pre-operative symptoms were deficits in language (54.3%), cognition (39.4%), and motor function (38.3%). Mean pre-operative Karnofsky performance status was 70.3. 14.9% of patients had a prior lower grade glioma. Mean tumor size via imaging was 3.0 cm. Operations included gross total resection (14.9%), near total resection (10.6%), subtotal resection (67.0%), and stereotactic biopsies (7.4%). New post-operative deficits occurred in language (10.6%), motor (19.1%), visual (4.3%), sensory (5.3%), and cognitive (11.7%) function. Mean hospital stay was 8.4 days. Patients were discharged to home (66.0%), rehabilitation (27.7%), or hospice (4.3%). Pre-operative therapies included radiation (9.6%) and chemotherapy (12.8%). Post-operative therapies included radiation (44.7%) and chemotherapy (58.5%). 40.4% of operations were followed by recurrence after a mean of 3.6 months.

Conclusion: Conclusions pending analysis.

The Epidemiology and Ecology of Cholera in Bangladesh: A Reflection

During the summer of 2012, I joined the study "The Epidemiology and Ecology of Cholera in Bangladesh", begun in 1997, which aims to create a predictive model for cholera outbreaks in Bangladesh. As part of this study, clinicians administer diarrheal patients questionnaires about their diarrhea and collect rectal swabs for analysis while ecological specialists sample the local ground water in order to correlate environmental conditions with the occurrence of cholera in the population.

My goal in joining this project was to gain a better understanding of how public health work is done in developing nations. Throughout my time working with the clinical team, I made daily journal entries that helped me process what I was experiencing.

The poster I will present about my summer experience will include the following sections: the objectives of the poster; the burden of cholera disease in Bangladesh; the overall context (political, economical, social) in which this study is being conducted; the methods used by this research study; my goals in participating with this study; an excerpt from my reflective piece; and overall conclusions.

I aim to convey that public health work is significantly impacted by the context in which it is done. The realities of a location's economic status, cultural norms, and political climate (among other factors) go a long way in determining the progress and ultimate success of public health initiatives.

Development and Cost Implications of Quality of Care Indicators for Occupational Injuries

Background: Clinical practice guidelines should maximize clinical outcome while minimizing unnecessary expenditure. Few studies address cost impact of guideline non-adherence in the United States, and there are no published studies of guideline care in occupational injuries. In 2010, there were approximately 2.9 million injuries in the private industry alone. This study looked at the cost of guideline-adherent shoulder and back workplace injury care at the patient level and its impact on time to return to work (RTW).

Methods: Data was acquired from claimants listed in the AIG Chartis dataset from 2001 to 2010. Shoulder (61,748) and back (115,197) injuries accounted for approximately 50% of total spending on worker's compensation. Clinical flags were developed from guidelines promoted by the American College of Occupational and Environmental Medicine (ACOEM) and the Office of Disability Guidelines (ODG) and the professional opinion of an expert multidisciplinary panel of healthcare providers. Clinical flags were defined as strong indicators of quality of care if they met the following criteria: many patients received treatment inconsistent with these flags, non-adherence highlighted the flags as unnecessary, excessive, or inappropriate, and adherence led to higher overall spending and slower RTW.

Results: For shoulder injuries, five clinical flags have presented as strong indicators of quality of care: unnecessary home care, inappropriate steroid injections, excessive time on opioids, inappropriate bracing, and excessive surgeries. Criteria for these indicators are as follows: many patients received treatment inconsistent with these flags, and this non-adherence highlighted the flags as unnecessary, excessive, or inappropriate. These flags were also linked with higher overall spending and slower RTW.

Conclusion: Preliminary findings show that guideline non-adherence is not consistently linked with higher cost and slower RTW. There is much variability between the different clinical flags, but these findings are especially compelling given the lack of existing literature on the efficacy of guideline adherence.

Pilot Study of "The Evergreen Project," an Attempt to Create Systematic Healthcare Change

Background: Our current health care infrastructure suffers from a lack of care coordination, taking away from quality of care and de-valuing preventive practice. The Evergreen Health Cooperative (EHC), a consumer operated and oriented health insurance plan created under the guidance of Section 1322 of the Patient Protection and Affordable Care Act, has been designed to address this issue by including health coaches and social workers as part of an integrated primary care practice targeted at Maryland residents with incomes under 400% of the FPL. Prior to official launch of EHC in 2014, preliminary testing must identify logistical barriers in the model's execution and ensure the numerous interactions within each teamlet are well choreographed.

Methods: The Family Medicine Clinic at MedStar Franklin Square Hospital served as a pilot site for the model from December 2012 through April 2013. After a Grand Rounds instructive symposium, the Clinical care team used the "teamlet" approach for primary care visits during a specified weekly four-hour block. During this period, a research coordinator observed teamlet and patient interactions and obtained consent from patients to participate in flow analyses. Following appointments, a phone interview was conducted with each patient participant to gather feedback. Pre- and post-implementation surveys were administered to nurses and physician participants before and after the five-month study period.

Results: Quantitative results will include those based upon patient flow analyses, pre- and post-surveys from health professionals, and post-appointment interviews. Qualitative results will include observations of Clinic flow and feedback obtained from patients and health professionals.

Conclusion: The short-term goals of this study are to evaluate the EHC teamlet care model and to propose changes to improve its efficacy. We hope to substantiate this innovative model, with the potential of creating drastic change in state healthcare.

Impact of Surgical Video Review in Resident Cataract Surgery

Background: Several endeavors have been undertaken in recent years to address issues of ophthalmology resident training to minimize errors and enhance efficiency. Simulation and wet-lab training modules have been integrated into programs nationwide. In this study, we explore a novel intervention and approach to standardizing cataract surgery through practical teaching video libraries. We predict surgical video libraries will increase rates of skill acquisition for residents.

Methods: Retrospective review of 2nd and 3rd yr ophthalmology residents' cataract surgery assessments pre-intervention without video libraries during 2011-2012. Prospective review of 2nd and 3rd yr ophthalmology residents' cataract surgery assessments post-intervention with video libraries during 2012-2013. 3rd yr residents in post-intervention were the only participants to have pre-intervention data. Statistical improvement was assessed amongst resident groups.

Results: As of November 2012, two 3rd yr residents (A,B) and one 2nd yr resident (A*) had complete post-intervention assessments. Resident A's pre-intervention median assessment score of 3.22 and post-intervention of 4.33 revealed a statistically significant improvement ($p < 0.0001$). Resident B's pre-intervention median assessment score of 4.25 and post-intervention of 5.00 also revealed a statistically significant improvement ($p < 0.0001$). There was a statistically significant improvement when comparing cumulative resident A,B pre- and post-intervention assessments ($p < 0.0001$). There was no statistically significant improvement ($p = .9379$) when comparing post-intervention 3rd yr residents' assessments to total pre-intervention 3rd yr assessments. There was no statistically significant improvement ($p = .8506$) when comparing post-intervention 2nd yr resident's assessment to total pre-intervention 2nd yr assessments.

Conclusion: Though data is currently limited, practical video teaching libraries did provide an improvement in cataract surgery assessments between a resident's 2nd and 3rd year performance. Accurate comparison of total 2nd and 3rd year improvements is restricted due to current low sample size. It is our belief that practical video teaching libraries will serve as an accessible and viable way of standardizing cataract surgery for residents.

Factors Associated with Survival and Recurrence for Patients Undergoing Surgery of Cerebellar Metastases

Background: Patients with cerebellar and non-cerebellar metastases are often included into the same study populations, even though posterior fossa lesions typically have different presenting symptoms, clinical outcomes, and complications than their supratentorial counterparts. This study aims to determine the effect of tumor location on outcomes for metastatic lesions and determine factors independently associated with survival and recurrence.

Methods: Adult patients who underwent surgery for an intracranial metastasis between 2007 and 2011 were retrospectively reviewed. Stepwise multivariate proportional hazards regression analysis was used to identify an association between cerebellar location with survival and recurrence. This same analysis was used to identify factors associated with survival and recurrence for only patients with cerebellar metastases.

Results: 140 (19.8%) of 708 patients who underwent intracranial metastatic surgery had surgery for a cerebellar metastasis. Patients with cerebellar metastases present more commonly with hydrocephalus and headaches ($p=0.0001$), and may present with vision deficits, language deficits, and/or seizures. In multivariate analysis, a cerebellar location was associated with poorer survival ($p=0.04$) and increased spinal recurrence ($p=0.002$). In multivariate analysis, the factors independently associated with prolonged survival were: decreasing number of intracranial metastases ($p=0.0002$), decreasing tumor size ($p=0.002$), and postoperative radiation ($p=0.0006$). The factors independently associated with prolonged local progression free survival were: decreasing tumor size ($p=0.0009$), non-small cell lung cancer (NSCLC) ($p=0.006$), non-bladder cancer ($p=0.0005$), and postoperative radiation therapy ($p=0.02$). The factors independently associated with prolonged distal progression free survival were: age > 40 years ($p=0.02$), surgical resection ($p=0.01$), and whole brain radiation therapy ($p=0.02$).

Conclusion: This study identifies clinical differences between patients with cerebellar and non-cerebellar metastases and identifies factors independently associated with survival and recurrence for patients who undergo surgical resection of their cerebellar lesion. These factors can help risk stratify patients and guide therapeutic regimens aimed at optimizing outcomes for patients with cerebellar metastases.

Eating Habits of Adults in Samborondon, Ecuador

Background: In 2010, 7% of Ecuadorians had hypertension and 6.5% had diabetes. 40% of those diabetics live in the Guayas province (which includes Samborondon). The purpose of this study was to characterize the eating habits of Samborondonians in order to assess the extent to which they may be contributing to increased risk of chronic disease there.

Methods: Adult patients who were waiting to be seen by a doctor at two public Samborondon clinics were randomly approached and asked a series of questions about their eating and smoking habits, and their demographics.

Results: 170 individuals were interviewed. 83% were female. Only 3 people (0.02%) were smokers. People ate fish and chicken more often than steak and most did not fry their foods. Approximately 60% of people reported not eating either fruit or vegetables on a daily basis, 92% reported drinking juice daily (2.5 glasses/day) and 87% reported drinking soda daily or weekly (1.76 glasses/day). 56% of people reported eating jello weekly.

Women ate more jello than men, but ate vegetables daily nearly twice as often and drank juice and soda less often. Eating habits were better among those with secondary versus primary school education. Interestingly, more people without cardiovascular disease or equivalent drank whole milk. Finally, people who showed evidence of knowing about what constitutes healthy eating ate more fruits and vegetables, drank less juice daily and ate jello less frequently than those who did not.

Conclusion: The most unhealthy eating habits among Samborondonians include infrequent consumption of fruit and vegetables and frequent consumption of juice, soda and jello. Eating habits were not healthier among those without than those with cardiovascular disease or equivalent, but were somewhat better among those who had completed more schooling and seemed more knowledgeable about healthy eating, suggesting that nutritional education may be of benefit.

Modeling the Impact of Alternative Strategies for Rapid Molecular Diagnosis of Tuberculosis in Southeast Asia

Background: Development and scale-up of novel diagnostic tests has been advocated as a strategy for tuberculosis (TB) control, but the population-level impact of this approach remains uncertain.

Methods: We developed a transmission model of TB in Southeast Asia to evaluate the potential impact of novel TB diagnostics under idealized scenarios of implementation. We defined diagnostics by their sensitivity for smear-negative TB and “proximity” to patients (proportion of patients testing positive who initiate therapy). Specifically, we considered a “district-level molecular” test with 70% smear-negative sensitivity facilitating 85% treatment initiation among positive testers, a “peripheral-level molecular” test with 50% smear-negative sensitivity facilitating 95% treatment initiation, and a “dipstick” with 40% smear-negative sensitivity facilitating 100% treatment initiation. We projected ten-year impact on TB incidence and mortality when deployed in the public sector (35% of diagnostic attempts), private sector (65% of attempts, with poorer outcomes), or both. We also compared the maximum impact of tests implemented only for passive diagnosis against those that could also be deployed for active case-finding.

Results: Implemented in the public sector, the “district-level molecular” test reduced TB incidence by 8.9% (90% uncertainty range, UR: 5.4%-15.5%) and mortality by 22.3% (90% UR: 15.6%-23.5%) after ten years. Impact was similar for the “peripheral-level molecular” (10.0% incidence and 24.4% mortality reduction) and “dipstick” tests (10.2% and 24.8%). If deployed in both sectors, these tests reduced incidence by a projected 15.6–17.8%, and a perfect test (100% sensitivity and treatment initiation) reduced incidence by 21.6%. Annually detecting 20% of prevalent TB cases through household contact investigation (70% smear-negative sensitivity and 85% treatment initiation) reduced incidence by 22.0%.

Conclusion: Novel diagnostic tests can substantially reduce TB incidence and mortality in Southeast Asia but are unlikely to transform TB control unless deployed both actively and in the private sector.

Effectiveness of a Multicomponent Care Coordination Intervention on Dementia Caregivers in the Community - a Randomized Control Trial

Background: Caring for someone with dementia has significant psychological, physical and financial consequences for the caregiver, and previous interventions have had limited results. The purpose of this research is to examine the benefits of a community-based, multicomponent, individualized, care coordination intervention on improving outcomes for community living caregivers of persons with dementia. This intervention has previously been shown to significantly benefit care recipients.

Methods: 18-month RCT of informal caregivers (n=289) and care recipients aged 70+ with cognitive disorders living at home in Baltimore. All caregivers received results of an initial in-home needs assessment and intervention recommendations. Intervention participant (n=106) and care recipient dyads received multicomponent care coordination by interdisciplinary team of trained paraprofessionals, psychiatric nurse, and geriatric psychiatrist to address unmet needs. Primary outcome measured was percent of unmet caregiver needs. Secondary outcomes included caregiver quality of life, burden, and depression.

Results: Unmet caregiver needs declined over time in both intervention and augmented control groups in 3 of 4 need domains: caregiver education, resource referral, and mental health care. There was no difference in the relative rate of decline between groups. Caregivers in the intervention group reported a significantly greater decrease in the number of hours spent per week with the care recipients and a notable decrease in caregiver burden relative to the control group. There were no differences between groups in caregiver ratings of depression, quality of life, or other outcomes.

Conclusion: The effect of the intervention in reducing hours spent with care recipients and caregiver burden suggests that the intervention was effective. The significant decrease in unmet needs overtime in both groups suggests a benefit from providing the one-time caregiver needs assessment and intervention recommendations to both groups. Such an assessment could prove a low cost alternative to full care coordination and help a larger number of caregivers.

Hospital Recommendations to Reduce the Infant Mortality Rate in South Los Angeles

Background: In 2014, the Martin Luther King, Jr. (MLK) Hospital will re-open in South Los Angeles, a region with the second-highest Infant Mortality Rate (IMR) in the county. The purpose of this study is to identify strategies specific for South LA risk factors that we will recommend as hospital interventions to reduce the IMR. In particular, we investigate whether or not funding a Neonatal Intensive Care Unit (NICU) would be an effective strategy.

Methods: We used LA County Public Health statistics and Maternal and Child Health surveys to identify risk factors specific to South LA. We applied the Perinatal Periods of Risk (PPOR) analysis to highlight the areas of excess mortality contributing to the high IMR. Additionally, we hosted a one-time focus group that included an OB/GYN, neonatologist, prenatal case specialist, and 2 CNMs for their evaluation of the potential impact of a NICU and other community interventions in lowering the IMR.

Results: A comparison of risk factors demonstrated that South LA had the highest rates of preterm births, very low birth weights, teenage mothers, and smoking mothers in LA County. The PPOR analysis revealed that the area of Maternal Health and Prematurity contributed most to excess deaths. 80% of the focus group specialists did not recommend a NICU due to concerns of low-volume and the need to use resources for preventative care, such as bolstering preconception and interconception care, and implementing group prenatal care, which has been shown to reduce preterm births by 33%.

Conclusion: Risk factors contributing to Maternal Health and Prematurity are the leading causes of the high IMR in South LA, and are the most important targets for interventions. Consequently, we do not recommend funding a NICU at MLK Hospital, but rather using resources for preventative care strategies, such as improving preconception, interconception, and group prenatal care.

Medicare Advantage Chronic Special Needs Plan Effect on Long-Term Nursing Home Utilization

Background: Chronic Condition Special Needs Plans (C-SNPs), created with the enactment of the 2003 Medicare Modernization Act, are a subset of traditional Medicare Advantage (Part C) plans that exclusively serve a subpopulation of Medicare beneficiaries who have specific disabling chronic diseases. Disabilities associated with chronic conditions have shown to increase the likelihood of long-term nursing home use. For instance, chronic obstructive pulmonary disease (COPD) is one of the most common diagnoses among nursing home residents at admission. With a targeted and more coordinated model of care, C-SNPs may delay or prevent long-term nursing home placement. However, few studies to date have evaluated the outcomes of C-SNPs. One recent study demonstrated that beneficiaries enrolled in a specific C-SNP, Care Improvement Plus (CIP), experienced lower hospitalization and readmission rates than Medicare fee-for-service (FFS) beneficiaries'. In this study, we seek to address whether a specific C-SNP, CIP, can reduce long-term nursing home use and spenddown to Medicaid in beneficiaries with COPD compared to traditional FFS plans.

Methods: We looked at health outcomes for Medicare beneficiaries with COPD enrolled continuously in the C-SNP or Medicare FFS for at least twelve-months during 2008 and 2009. Exact and propensity score matching were performed on control and C-SNP populations to ensure similar cohorts at baseline. Multiple linear and logistic regression were used to assess mean difference in length of long-term nursing home utilization and adjust odds ratio of Medicaid spenddown, respectively.

Results: The Medicare dataset for those enrolled in 2008 and 2009 has been cleaned and analytic files have been prepared to create matched groups. Long-term nursing home flag variable for the Medicare dataset has been created and COPD severity and COPD-associated hospitalization variables for the C-SNP dataset have been created. Progress is currently being made to clear the C-SNP dataset and to prepare analytic files for matching.

Conclusion: Results that yield a statistically significant reduction in the length of long-term nursing home use in the C-SNP population substantiate the argument that the model of care espoused by C-SNPs offer potential services that delay or prevent patients with COPD from entering into long-term nursing home care.

Using Stories to Improve Patient Health Education in a Patient-Centered Medical Home Setting

Background: This study uses a qualitative, phenomenological approach to investigate the nature of expected outcomes after an educational intervention in a community health clinic.

Methods: Six participants were interviewed using questions formulated to elicit narratives about the participant's education experience. Interviews were thematically coded in terms of knowledge, skills, attitude, and stages of behavioral change, acquired by the participant as a result of the intervention (n=6). The study sought to identify which stage of behavioral change (pre-contemplative, contemplative, determination, action plan, maintenance) the patient belonged to before the interview and investigate whether the patient moved forwards after their participation in the educational intervention.

Results: All six patient's expressed changes in attitudes, knowledge, or skills, which they anticipated would help them to progress the stages of change.

Conclusion: More research should be dedicated to the most effective model of patient educations and acquiring patient feedback.

Health care Utilization Among Reservation-Based American Indians: Findings from the Family Spirit RCT

Background: The “Family Spirit” Intervention (FSI) aims to promote family-based protective factors and reduce health disparities among American Indian teen parents and their children. This intervention was evaluated by a randomized controlled trial.

Methods: FSI + Optimized Standard Care (OSC) or OSC alone was delivered to teen mothers from 28 weeks gestation through three years postpartum. Medical charts were coded using Excel. Associations between dependent variables (acute and primary care utilization) and independent variables (baseline characteristics of mother or child) were examined using multivariate linear regression in STATA 9.0.

Results: Infection was the most common reason for child ED visits (41%), child hospitalizations (46%), and child sick visits (37%) and a leading cause of maternal ED visits (15%) and maternal hospitalizations (13%). 4% of maternal and 14% of child hospitalizations lacked reasons due to incomplete medical records. The least common reasons (<4%) for visits include neurologic/ cardiac, metabolic/ hematologic, illegible, left without being seen/ didn’t keep appointment, and animal bite/ sting. Reasons for and types of health visits were significantly correlated to baseline measures of maternal age, social support, home stability, socioeconomic status, education level, and family planning ($p<0.05$).

Conclusion: The statistically significant correlations between baseline characteristics and health care utilization suggest socioeconomic and environmental indices that are associated with acute and primary care utilization up to three years postpartum.

