51st

MEDICAL STUDENT

RESEARCH FORUM

January 22, 2013

D1.602, 3-6 PM

Guest Speaker: James Malter, M.D.

Chairman, Department of Pathology

University of Texas Southwestern Medical Center

51ᵗʰ Medical Student Research Forum

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**THE UNIVERSITY OF TEXAS
SOUTHWESTERN MEDICAL CENTER AT DALLAS**

**FIFTY-FIRST ANNUAL
MEDICAL STUDENT RESEARCH FORUM**

**TUESDAY, JANUARY 22, 2013
3pm, D1.602**

PROGRAM DIRECTOR: Rene Galindo, M.D., Ph.D.

THE UNIVERSITY OF TEXAS SOUTHWESTERN MEDICAL CENTER
51st ANNUAL MEDICAL STUDENT RESEARCH FORUM

JANUARY 22, 2013
D1.602, 3-6 PM

LIST OF ORAL PRESENTATIONS

Sara Cooper
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Christopher Molina
"Low Dialysate Sodium reduced Systolic blood pressure in Patients with intradialytic hypertension"

Christopher Straka
"Parameters that Predict for High Grade Rectal Toxicity in Prostate Cancer (Pca) Patients Undergoing Stereotactic Body Radiation Therapy (SBRT) – Analysis of Phase I/II Study at UT Southwestern (UTSW)."

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Joel Sun
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Lan Chi Vo
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PRESENTATION OF GUEST SPEAKER

James Malter, M.D.
Chairman, Department of Pathology
University of Texas Southwestern Medical Center

RECEPTION AND POSTER SESSION IMMEDIATELY FOLLOWING
A.W. HARRIS FACULTY CLUB

Doris Duke Fellows

Akshay Goel (University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School)
Mentor: Ronald Peshock, M.D., Division of Radiology and Internal Medicine

Perry Dubin (Tulane University School of Medicine)
Mentor: William M. Lee, M.D., Division of Liver and Digestive Diseases

Salman Hirani (UT Southwestern)
Mentor: Eric Mortensen, M.D., MSc, Division of Internal Medicine

Susan Wu (UT Southwestern)
Mentor: Daniel C. Bowers, M.D., Division of Pediatrics

Frank Xing (University of Missouri Kansas City School of Medicine)
Mentor: Darren McGuire, M.D., Division of Internal Medicine, Cardiology

Clinical Research Scholar
Keerthan Somanath (University of Texas Southwestern Medical School).
Mentor: Ted Mau, M.D., Ph.D., Division of Otolaryngology-Head and Neck Surgery

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Basic Research and Disease Models

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† NIDDK Medical Student Research Trainee
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Û UT Summer Research Program Participant
D Doris Duke Fellow

Characterizing Epigenetic Modifications in Bacillus subtilis and V. cholerae

Maria Bacalao

Mentors: Matthew Waldor M.D. and Michael Chao
Harvard University

Epigenetic modifications of the genome are known to govern a wide variety of cellular processes in eukaryotes. However, there is little known about the role epigenetic regulation plays in bacteria. Studies on model bacteria like *E. coli* have shown that DNA methylation, primarily mediated by DNA adenine methylase, plays a role in controlling cell division, gene expression, and DNA repair. My research involved studying epigenetic modifications in *Bacillus subtillis* and the classical *Vibrio cholerae* strain through SMRT sequencing and bacterial mutagenesis.

For the first part of our research, we used a new technology - single molecule real time (SMRT) DNA sequencing - to analyze epigenetic modifications present in *Bacillus subtilis*. In SMRT, phospholabeled nucleotides are incorporated by DNA polymerase, and the fluorescent pulses can be monitored in real time, allowing for information about the kinetics of nucleotide incorporation to be gathered. Since the three main methylated bases in bacteria have distinct "kinetic signatures" it is possible to detect these modifications on a genome wide basis with single nucleotide resolution.   In our research, we isolated DNA from *B. subtilis* spores and vegetative cells and we are currently in the process of working with collaborators to perform the SMRT sequencing. Once this is finished, we will know the sequence of the epigenome of B. subtilis and whether it varies depending on its physiological state.

A second, closely related goal of this research project was to create knockout mutants of the genes involved in epigenetic modifications in both *B. subtilis* and *V. cholerae*. In *B. subtilis*, epigenetic modifications are governed by three genes: MtbP (coding for an orphan methylase) and the YdiRSjA restriction enzyme and YdiOP methylase forming part of a restriction/modification system. In *V. cholerae*, they are governed by HsdM (R/M system), and the orphan methylases C5 and CcrM. Over the course of the nine weeks, a ΔHsdM mutant was made. Phase contrast microscopy and growth competition assays showed that this mutant was phenotypically very similar to wild type. Though this project is still in process, it will help us better understand how these important bacteria utilize epigenetic regulation to adapt to changing environments.

Impact of Donor Age on Endothelium-Descemet Membrane Layer Preparation and Roll Formation

Adam Bennett

Mentors and Collaborators: V. Vinod Mootha M.D., Shahira Rashad M.D., Donna Drury MBA, CEBT, CTBS, H. Dwight Cavanagh M.D., Ph.D., James P. McCulley M.D., W. Matthew Petroll Ph.D.

Purpose: Descemet membrane endothelial keratoplasty (DMEK) is an alternative to Descemet's stripping automated endothelial keratoplasty (DSAEK) to surgically replace diseased corneal endothelium. Although graft rejection incidence has been reported to be drastically lower in DMEK, wide adoption may be limited by two factors. Harvesting the endothelium-Descemet membrane layer (EDM) can be difficult, and tight EDM scrolling can hinder unfolding once inserted into the patient's eye. Anecdotally, surgeons have noticed the use of younger donors has exacerbated these factors. We sought to correlate donor age with EDM stripping difficulty and scroll tightness.

Methods: EDM scrolls were harvested by a cornea-fellowship trained ophthalmologist masked to donor age from 26 corneoscleral buttons. An 11.5 mm partial trephination was used instead of blunt dissection for a consistent and even outer cut. 7.0 to 8.25 mm EDM scrolls were prepared using the SCUBA technique in Optisol GS. VisionBlue® (.06 % trypan blue) staining was used to harvest and assess EDMs. The surgeon subjectively rated stripping difficulty on a 1 to 5 scale (easiest to unable to strip) based upon DM adherence to underlying stroma and radial tear formation. Three different methods were used to characterize scrolling severity: scroll width, normalized scroll surface area (scroll width ✕ scroll length/surface area of EDM), and tendency for EDM scroll formation (referred to as scroll rating). A scroll rating of 1 corresponded to opposite ends of the EDM not touching, 2 when EDM ends touch, 3 when the EDM forms one complete scroll and 4 when more than one scroll formed.

Results: Mean donor age was 59±14 years (15–69 range). Mean diameter of EDM scroll was 7.9±.23 mm (7.0–8.25 range). Stripping difficulty was shown to be inversely correlated with donor age ($p<.05$). The three methods to determine scrolling severity had different results. Inverse relations between donor age was significant for scroll rating ($p<.05$), nearly significant for normalized surface area ($p=.0508$), and not significant for scroll width ($p<.10$).

Conclusions: Our data supports that the use of older corneas should reduce the surgical difficulty of DMEK procedures. The study showed a significant decrease in the subjective category of stripping difficulty with the use of older donors. In addition, there may be a decreased scrolling tendency based on an inverse correlation between age and scroll rating ($p<0.05$) and a positive correlation between age and normalized scroll surface area ($p=0.0508$).

<u>HNF4a is a potential driver oncogene in childhood yolk sac tumors</u>

Matthew E. Campbell

Mentors: Kenneth S. Chen M.D., James F. Amatruda M.D., Ph.D.

Germ cell tumors (GCTs) are neoplasms derived from germ cells in gonadal and extragonadal sites of infants, children, and young adults. These tumors are classified based on histology, with seminomas and yolk sac tumors (YST) being the two most common malignant histologies. Although these distinct histologies are thought to arise from the same cell of origin, they exhibit different levels of differentiation and clinical behavior, and the molecular changes driving these differences are poorly understood. Our single nucleotide polymorphism (SNP) array studies of YST and seminoma samples have identified consistent high-copy gain of chromosomal region 20q13 specific to YST samples. This region contains hepatocyte nuclear factor 4 alpha (HNF4a), a gene that plays an important role in the development of endodermal derivatives such as liver and yolk sac. This finding was validated by quantitative RT-PCR on GCT specimens and cell lines revealing significantly higher expression of HNF4a in YST samples. A gene set enrichment analysis of whole transcriptome sequencing performed on ten GCTs showed that genes whose transcription is activated by HNF4a are highly enriched in YST samples. **Based on these results, we hypothesize that HNF4a is a driver of YST differentiation and may be responsible for the differences in clinical behavior of these tumors.** Our current studies are focusing on understanding how increased HNF4a expression alters signaling pathways to affect cellular growth and differentiation. This will be accomplished by transfecting undifferentiated germ cell tumor cell lines with HNF4a and measuring protein and RNA expression of downstream targets implicated in YST (such as AFP). We will also use immunoblotting and quantitative PCR to test the effects of HNF4a expression on intracellular signaling pathways that our previous work implicates in germ cell tumorigenesis, including Wnt, mTOR and BMP. Future studies will focus on understanding whether increased HNF4a expression affects cell tumorigenicity, chemoresponsiveness or patient prognosis.

NF-kB Mediates Cartilage Degradation Induced by Trauma Injury and IL-1

Kristen Carter and Meghana Kashyap

Mentor: Chris Chen M.D.

Background: IL-1 is one of the major pro-inflammatory cytokines responsible for cartilage degradation. Several studies have shown that IL-1 mediates the upregulation of tissue degradation through the NF-κB and Mitogen-activated protein kinase (MAPK, p38) pathways, but its role in cartilage degradation after blunt trauma injury is not clear. The objective of this study was to determine the roles of NF-κB and p38 in IL-1- induced cell death, proteoglycan (PG) degradation, nitric oxide (NO) production, and related gene upregulation in cartilage after blunt injury.

Methods: Full-thickness cartilage plugs were obtained from mature bovine knees (>18 mo) and pre-cultured in DMEM. The signaling pathways (p38 and NF-kB) were inhibited by pretreatment with 10μM SB202190 for p38 (p38i) and 50μM BAY117085 for NF-κB (IκBi) for 1 hour. Samples in Injury and Injury+IL-1 groups received impact injury with impact energy of $15J/cm^2$. IL-1 and Injury+IL-1 groups were treated with 1 ng/ml IL-1. Cell viability was assessed using fluorescein diacetate and propidium iodine. The mRNA from cartilage was isolated using Trizol and RNeasy Mini kit (Qiagen), reverse transcribed, and analyzed using qPCR to determine pro-inflammatory cytokine and tissue remodeling genes (IL-6, MMP-3, TIMP-3). All gene expression was normalized to GAPDH. The medium was analyzed for proteoglycan (PG) release/loss and nitric oxide (NO) production using dimethylmethylene blue (DMMB) and Greiss assays, respectively.

Results: Increased cell death was found in the Injury and Injuy+IL-1 groups. Increase of PG loss was found in IL-1, Injury and Injury+IL-1 treated groups (37%, 104% and 126%, respectively). Significant decreases (69-73%) of PG loss were found in all IκBi treated groups, while little or no changes were found in the p38 groups. Results from the qPCR analysis supported the findings. IκBi treatment reduced MMP-3 upregulation induced by IL-1 and Injury, while there was minimal change with the p38 inhibitor. Similarly, NO production was also decreased in the IκBi treated groups.

Discussion and Conclusion: Our study suggests that the NF-κB signaling pathway plays a greater role than p38 in IL-1 mediated PG loss and NO production in cartilage after trauma injury. Future studies are needed to determine the time-course response and specific NF-κB mediators for downstream regulation, as well as the effects in long-term therapeutic treatment to ameliorate the progress of post traumatic osteoarthritis.

Influence of Apolipoprotein E Polymorphism on Postprandial Inflammation

Joshua Hilliard

Mentors: James G. Cash, James E. Heubi, David Y. Hui,
Metabolic Diseases Institute; University of Cincinnati Reading Campus

Background: Apolipoprotein E has a particularly important function in plasma as the facilitator of cholesterol and lipid transport and as a modulator of inflammatory response. There exists three isoforms – ApoE2, ApoE3, and ApoE4 – with E3 being the most common. The less prevalent isoforms are associated with various metabolic diseases including artherosclerosis and diabetes. In particular, ApoE4's inflammation is a result of marophage dysfunction and increased macrophage endoplasmic reticulum stress, possibly due to the misfolding of the ApoE4 protein. Whereas, ApoE2's inflammation is mediated by defective clearance of triglyceride-rich lipoproteins, leading to increased lipid uptake by leukocytes and their resultant activation.

Aims: We wanted to compare the influence of apoE polymorphisms on fasting and postprandial circulating leukocyte levels and activation in humans, and to determine the function of their macrophages *in vitro*.

Methods: Age and weight-matched subjects were recruited from the Princeton Cholesterol Studies. Subjects on lipid-lowering drugs were excluded. Fasting blood samples were drawn then each subject was fed a standardized breakfast of 2 Sausage McMuffins with Egg and a hash brown. Another blood sample was drawn three hours later. Serum triglycerides and cholesterol were measured colorimetrically. Both plasma concentrations and lipid content of monocytes and neutrophils were determined by flow cytometry. Peripheral blood monocytes isolated from each subject were differentiated into macrophages to assess efferocytosis and susceptibility to apoptosis *in vitro*.

Results: Three ApoE3 subjects and three ApoE4 subjects were successfully enrolled. All subjects responded to the high fat meal with elevated postprandial serum triglyceride and unchanged total serum cholesterol; however, the leukocytes of both E3 and E4 subjects did not exhibit significantly increased lipid uptake. All three E4 subjects showed an increase in activated neutrophils and in total monocyte concentrations postprandially; and only one showed an increase in activated monocytes. The E4 subjects' macrophages also tended to be less efficient at efferocytosis and more susceptible to apoptosis.

Conclusion: The impaired macrophage function and viability suggests that the apo E4 polymorphisms have similar effects in humans as in mice. Further testing is needed on a much larger scale in order to cement the mechanism underlying the relationship between ApoE gene polymorphisms and metabolic disease risk.

Regulation of Pyruvate Kinase M2 (PKM2) Expression and Activity in Cardiac Hypertrophy

Victor Hogen

Mentors: Joseph A. Hill M.D., Ph.D., Zhao V. Wang, Bo Wang

Background: Cardiac hypertrophy is characterized by robust structural, metabolic, and signaling events, which include increased myocyte size and width, increased glycolytic flux, aerobic glycolysis, and induction of transcriptional programs governed by such factors as c-Myc, Fos, and Jun. We have noted that this phenotypic profile exhibits similarities to cancer, where c-Myc, HIF-1α and PKM2 contribute to tumorigenesis and enhanced cancer cell survival in the setting of oxidative stress. PKM2, highly expressed in heart, is the sole pyruvate kinase M isoform expressed in a variety of tumors and is thought to participate in shifts between anabolic and catabolic flux in glycolysis.

Methods and Results: First, we set out to determine mechanisms underlying aerobic glycolysis in cardiac hypertrophy. We hypothesized that hypertrophic growth cues, including hypoxia, mediate increases in PKM2 protein levels and oxidation at Cys-358. To test this, we first measured protein levels and activity of glycolytic PKM2 in neonatal rat ventricular myocytes maintained in culture. We evaluated four pro-growth stimuli: phenylephrine, endothelin-1, angiotensin II, and hypoxia. We observed that phenylephrine and angiotensin II did not increase normalized PKM2 protein levels, whereas hypoxia and endothelin-1 did. None of these growth stimuli increased PKM2 fractional oxidation. Further, no change in fractional oxidation of PKM2 was observed in mouse hearts subjected to one week of TAC (thoracic aortic constriction). However, an increase in total normalized PKM2 oxidation was readily detected.

Conclusions: Together, these data suggest that hypoxia increases PKM2 protein levels via mechanisms mediated in part by localized ET-1 signaling. Additionally, these data suggest that TAC triggers an increase in the abundance of oxidized PKM2, mediated in part by increased PKM2 protein production. Finally, as phenylephrine did not increase PKM2 oxidation, this suggests that a non-NOX2-dependent mechanism is involved.

A quantitative study of parathyroid hormone (1-34) and bone morphogenetic protein-2 on spinal fusion outcomes in a rabbit model of lumbar dorsolateral intertransverse process arthrodesis

Lee Hwang

Mentor and Collaborators: Timothy F. Witham M.D., David Santiago-Dieppa B.S., John Lina, Jason Liauw M.D.

Introduction: Lumbar spinal fusion is a common neurosurgical procedure. Over 250,000 lumbar spinal fusion operations are performed annually in the U.S. and, by far, dorsolateral intertransverse process arthrodesis (DIPA) is the most common type of fusion technique performed in the lumbar spine. Unfortunately, the rate of non-fusion (pseudoarthrosis) has been reported to be as high as 35%. Pseudoarthrosis is also one known cause of Failed Back Surgery Syndrome (FBSS), which is characterized by chronic back pain that is often unbearable and debilitating to the patient. In the following study, our goal was to explore methods of improving the rate of fusion by first establishing an accurate animal model – more specifically the New Zealand White rabbit model, which has a pseudoarthrosis rate nearly identical to that of humans as well as similar spinal anatomy. We also aimed to assess the effects of osteoinductive agents PTH (1-34) and rhBMP-2 on bone turnover after DIPA spinal fusion in the rabbit model. We hypothesize that the use of both PTH (1-34) and rhBMP-2 has a synergistic effect on stiffness and composition of the bone fusion mass.

Methods: To elucidate the potential relationship between PTH (1-34) and rhBMP-2, 24 NZW rabbits will be assigned to each of the following 4 groups: spinal fusion with iliac crest autograft and saline-based injections (control); spinal fusion with rhBMP-2 matrix alone; spinal fusion with iliac crest autograft and PTH (1-34) injections alone; spinal fusion with rhBMP-2 matrix and PTH (1-34) injections. Each specimen will undergo manual palpation, radiographic analysis, four-point non-destructive biomechanical testing, and histological analysis.

Preliminary results: Based on the CT reconstructions, the spine fusion rates for the control group (n = 9) and the PTH (1-34) group (n = 5) were 44% and 60%, respectively. Although manual palpation is used as the standard measure of fusion, radiographic analysis proved more effective in differentiating fused masses based on bone, not fibrous tissue. In both the PTH (1-34) and control groups, lateral bending in both the right and left orientations proved to be the stiffest testing orientation.

Conclusions: Preliminary data suggests that PTH (1-34) may enhance both the composition and mechanical properties of L5-L6 fusion in rabbits. As demonstrated by biomechanical testing, the enhanced bone formation in the PTH (1-34) group may be responsible for an increase in stiffness. We expect that data from the additional two groups will allow for further investigation of individual efficacies as well as any synergistic effects of PTH (1-34) and rhBMP-2.

Anti-VEGF induced reduction in microvessel density does not correlate with anti-tumor response in lung cancer xenografts

Antonia Jacob

Mentors: Rolf A. Brekken Ph.D., Laura A. Sullivan
Hamon Center for Therapeutic Oncology Research

Vascular endothelial growth factor-A (VEGF) is a primary stimulant of angiogenesis in pathological conditions including tumor progression. Strategies to block VEGF activity prevent or slow tumor growth in preclinical settings; however, clinical studies with bevacizumab, a monoclonal antibody (mAb) specific for VEGF have resulted in only modest benefit to a subset of patients with lung cancer. Previous studies in our laboratory defined the therapeutic efficacy of bevacizumab and an alternative anti-VEGF mAb (r84) in 12 non-small cell lung cancer (NSCLC) xenografts. Three NSCLC xenografts (Calu-6, A549 and Calu-3) showed intrinsic resistance to bevacizumab therapy. In the present study we evaluated whether microvessel density (MVD) could be used to 1) demonstrate if the anti-VEGF mAbs were effective at reducing VEGF-driven angiogenesis and 2) if MVD changes induced by bevacizumab or r84 correlated with overall therapeutic efficacy as determined by tumor size after chronic therapy. 3-5 tumors from animals bearing NSCLC xenografts treated with a control mAb (XTLl, bevacizumab or r84 were evaluated by immunohistochemistry for endothelial cells as a measure of microvessel density. Two independent endothelial cell markers were used, endomucin and CD31. In 11 of the 12 xenografts treatment with bevaclzumab or r84 significantly reduced MVD compared to XTL treatment, suggesting that bevacizumab and r84 do reduce VEGF-driven angiogenesis. However, the reduction in MVD induced by anti-VEGF therapy did not correlate with overall tumor response to therapy. These results strongly implicate resistance to anti-VEGF therapy is not mediated by activation af alternative angiogenic programs to compensate for VEGF blockade. Further the results suggest that tumor cell adaptation to therapy-induced hypoxia underlies poor therapeutic response to anti-VEGF strategies. Microarray of gene expression analysis of control treated tumors revealed several genes associated with metabolism, proliferation, and metastasis were significantly increased in tumors that displayed intrinsic resistant to bevacizumab. We conclude that response of tumor cells to therapy-induced hypoxia is a critical feature that drives the overall efficacy of anti-VEGF strategies.

Cdk5-dependent regulation of neuronal MEK1

Govind Krishnan

Mentors and Collaborators: James Bibb Ph.D., Tara Tassin, David Benavides

Introduction: Cyclin-dependent protein kinase 5 (Cdk5) is a member of the Cdk family that is implicated in many regulatory pathways in post-mitotic neurons. The kinase plays an important role in neuronal development and synaptic transmission; its disregulation contributes to neurodegenerative diseases such as Alzheimer's disease. Cdk5 is involved in the regulation of the Ras-Raf-MEK-ERK signaling pathway. It is hypothesized that Cdk5 serves a neuroprotective role by preventing the prolonged stimulation of ERK from inducing cell cycle reentry and, hence, neuronal apoptosis.

In order to address whether Cdk5 phosphorylation of MEK1 affects its in vitro kinase activity, we sought to confirm the Cdk5-phosphorylation site of MEK1. Although it has been previously shown that Cdk5 phosphorylates MEK1-T286, our previous unpublished mass spectometry analysis of in vitro kinase reactions identifies the site as T292. We corroborated this data with Western blot analysis of the in vitro Cdk5 phosphorylation of MEK with phosphate-specific antibodies to sites T286 and T292.

Methods: Glutathione S-transferase (GST)-tagged MEK1 was expressed and purified from E.coli. The tagged protein was run through column fractions, with glutathione beads that would attach to the GST tag, such that GST-MEK1 would be purified out of the bacterial lysates. This was then run through gel electrophoresis to confirm that MEK1 had indeed been purified, by comparing the bands seen in the gels to the known molecular weights of GST-MEK1. The protein concentration was determined using a Bradford assay. Non-radioactive and radioactive Cdk5 kinase assays of MEK1 were then performed. MEK1 was incubated in the absence or presence of Cdk5 with Mg2+/ATP or Mg2+/ATP plus trace amounts of [gamma-32P]-ATP, respectively. The non-radiolabeled kinase reactions were subjected to polyacrylamide gel electrophoresis (PAGE) on a 10-20% acrylamide gradient gel, followed by electrophoretic transfer and Western blot analysis with phospho-T286 and phospho-T292 MEK1 antibodies. Phosphorimages of radiolabeled kinase reactions were generated by PAGE, dried gels and standards were exposed to a phosphorimager screen and analyzed on a phosphorimager.

Results: Our results confirm that T292 is indeed the Cdk5 site of MEK1. The identity of this site is important because it is the location at which control can be exercised over the ERK pathway.

The Interaction of Polylysine with Flagella

Matthew McKeever

Mentor: Dong Li

Introduction: Assembly of individual nanomaterials into higher ordered architectures by non-covalent interactions in water is essential for their applications, especially in tissue engineering and regenerative medicine. In this study we have demonstrated self-assembly of nanofibers into ordered bundles induced by polymers. Bacterial flagella are naturally occurring nanofibers that function as an appendage in the locomotion of microorganisms. They are assembled from major protein subunits called flagellin and some other minor protein units. Polylysine is a homopolymer that has positively charged residues. Previous studies have shown that filamentous bionanofibers can be induced to form bundles by exposure to homopolymers. Since a flagellum is a filamentous biopolymer, it is expected the flagella will bundle together and form paracrystal structures when exposed to polylysine.

Methods: *E. coli* bacteria were cultured and collected by centrifugation. The *E. coli* were then vortexed to detach the flagella from the bacteria. The bacteria were removed by centrifugation while the detached flagella remained in the supernatant. Different concentrations of polylysine or Polyethylene Glycol (PEG) were added to the flagella. The degree of aggregation was measured by transmission electron microscope (TEM) and monitored by optical density (OD) at 320 nm.

Results: The bundles of flagella were formed in a polylysine/PEG concentration dependent manner. Higher concentrations of the polylysine/PEG induced more bundle formation of flagella. However, the degree of bundle formation induced by polylysine is much less than that of PEG. High concentration of polylysine induced a higher number of small flagellar bundles. However, high concentration of PEG could induce thicker, more compact bundles which form paracrystal-like structures.

Discussion: PEG and polylysine form bundles by two different mechanisms. PEG is a nonpolar molecule and it acts as an inert crowder molecule. This crowding causes the flagella to form bundles and paracrystal like structures. Polylysine, however, forms bundles in a different manner. Polylysine is a homopolymer with positively charged residues. It forms bundles by interacting with the negatively charged flagella molecules and causes counterion condensation. The difference in mechanism is likely the reason PEG and polylysine formed different types of bundles. The results of this experiment show that both crowder molecules and positively charged homopolymers can be used to induce bundle formation. However, crowder molecules are better at inducing the formation of thicker and more compact bundles while positively charged homopolymers like polylysine are better at inducing the formation of smaller flagella bundles.

Voluntary exercise alters adaptive immunity prior to injury

Angelica McPartlin

Mentor and Collaborators: Anne M. Stowe Ph.D., Katherine Poinsatte, Mariam Mouti, Sarah J. Ireland, Min Li

Objective: Exercise provides a neuroprotective role in the setting of cerebral infarct. However, the exact mechanism for this protection is unclear. This study established an exercise preconditioning protocol to test the hypothesis that exercise mediates protection from stroke by altering the immune profile prior to injury to reduce inflammation post-infarct.

Materials/Methods: In our first trial, a three week exercise preconditioning protocol was established using nine C57 mice that endogenously expressed green fluorescent protein (GFP) under the PLP promoter. This biomarker was used to identify oligodendrocyte precursor cells (OPC) to qualify their relationship with voluntary exercise. Exercise activity was recorded and tissues were collected for histological and serological analysis. Analysis of histological sections acquired through Nanozoomer imaging was performed using an unbiased quantification (Stereo Investigator). Ten Swiss Webster (SW) mice with no endogenous fluorescence were used in the subsequent trial. Following sacrifice of the SW mice, samples of the spleen and peripheral blood were collected and analyzed by flow cytometry and microarray was used to analyze resident B cell expression (IPA software). Standard ELISA analysis of peripheral blood was also used for all trials. Significance was determined using t-test or ANOVA.

Results: Voluntary exercise in PLP-EGFP mice correlated with a trend increase in OPCs as well as a trend increase in cortical angiogenesis (p=0.06). However, voluntary exercise did not increase hippocampal neuron counts. Voluntary exercise in SW mice showed decreases in percent and raw number of splenic neutrophils and CD8+ T cells (both p<0.01), with a concomitant increase in B cell representation (p<0.05). Peripheral blood samples demonstrated a decrease in percent CD4+ T cells (p<0.01) and decrease in CCL2 (p<0.05) and VEGF (p<0.01) protein. Microarray showed a significant upregulation of 1844 genes and significant downregulation of 1333 genes in the resident splenic B cells of SW exercise mice over the sedentary controls.

Conclusion: Three weeks of voluntary exercise in mice results in a change in the immune profile prior to an injury occurring. Downregulation of neutrophils, cytotoxic T cells, and CCL2 suggest that this alteration in immunity is anti-inflammatory. Microarray analysis of isolated B cells showed an upregulation of genes associated with lymphocyte maturation and differentiation, with simultaneous downregulation of genes responsible for apoptosis and B cell death. Further studies will determine the significance of these immune adaptations and their mechanistic role in decreased deficits following neurovascular injury.

Live Imaging of Primordial Germ Cell Migration in the Zebrafish

Danielle Meals

Mentor and Collaborator: James F. Amatruda M.D., Ph.D., and Clayton Boldt

In multicellular organisms, primordial germ cells (PGCs), the gamete precursors, arise distant from the site of gonad development. During embryogenesis, these cells must migrate to the site of the eventual gonad where they will interact with somatic cells to initiate gametogenesis. Aberrant migration may cause gonadal malformations and infertility, and may lead to the development of germ cell tumors (GCTs). GCTs occur in children and adults, and testicular GCT is the most common cancer of young men. In some cases, particularly in children, GCTs occur outside of the ovary or testis. These extragonadal GCTs could originate from PGCs that failed to migrate properly, prompting us to examine the fate of ectopic germ cells using the zebrafish model system.

In order to examine germ cell fate, we utilized a transgenic line created in the lab with robust expression of the green fluorescent protein (GFP) targeted specifically to PGCs. We induced abnormal migration by morpholino knockdown of SDF-1a, the chemokine responsible for guiding PGC migration in zebrafish. Ectopic germ cells were monitored daily by fluorescence microscopy.

We also sought to perform lineage-tracing experiments in order to follow ectopic cell fate in the event of differentiation to an alternate cell type. An additional transgenic line with expression of the red fluorescent protein, DsRED, under control of the Cre-lox recombination system enables us to alternately label PGCs with DsREd by expressing Cre RNA specifically in the PGCs. Incorporation of this line into the experimental system just described allows us to doubly label ectopic germ cells to more thoroughly monitor their fate during later development or following differentiation events.

Our results indicate that ectopic germ cells are not rapidly cleared by apoptosis, as occurs in mice, but persist in their ectopic locations. In several cases, we observed ectopic PGCs that underwent rapid morphologic changes consistent with differentiation and subsequent loss of GFP expression. We are continuing to optimize the lineage-tracing system in order to better characterize these potential differentiation events. Zebrafish provide an excellent model for studying the fate of ectopic germ cells and our future work will elucidate the possible role of these cells in extragonadal germ cell tumor development.

Peptoids: A Novel Platform for Vaccine Development

Ali A. Saherwala

Mentor and Collaborators: Ellen Vitetta Ph.D., Allison Case Ph.D., Angela Desmond

Peptoids, or peptidomimetics with side chains attached to backbone nitrogen atoms rather than α carbons, are endowed with several important properties, including protease resistance and enormous diversity. **Our goal is to develop a peptoid vaccine platform that uses available broadly neutralizing monoclonal antibodies (MAbs) against pathogens or toxins to identify peptoids that mimic B cell epitopes on these pathogens or toxins.** We have shown previously that peptoids act as haptens. Conjugating peptoids to carrier proteins will provide T cell epitopes during vaccination, allowing T cell help for the production of protective IgG antibodies. Our initial vaccine targets include murine norovirus-1 (MNV-1), West Nile virus (WNV), Hepatitis C virus (HCV), human immunodeficiency virus (HIV), and ricin toxin. However, this peptoid vaccine platform could be applied to any disease for which a protective MAb exists, even without knowing what the natural protective epitopes are.

Methods and Results. To identify B cell epitope mimetic peptoids, one-bead-one-compound peptoid libraries are screened in two sequential assays. The first isolates are on-bead peptoids bound by the MAb using magnetic Protein G- dynabeads. A second step verifies binding specificity using enzyme-conjugated species-specific antibodies against IgG. Peptoids are then cleaved from beads and their sequences determined by tandem mass spectrometry. These peptoids are synthesized in bulk, purified by HPLC, lyophilized, conjugated to carrier protein, and tested in enzyme-linked immunosorbent assays (ELISAs) to determine whether they compete for MAb binding with the MAb's native antigen. Since no peptoid-antibody pair was available to develop these assays, we first utilized a FLAG peptide and a commercially available MAb against it. In addition we developed a peptoid-antibody pair by designing, synthesizing, and purifying a peptoid sequence ("R5"), conjugating it to carrier protein, adsorbing it to alum, and immunizing rabbits. Anti-R5 antibody (Ab) titers were monitored by ELISA until they reached approximately 1 mg/mL, at which point the rabbits were exsanguinated. The presence of anti-R5 Ab was assessed by Ouchterlony and ELISA. Affinity purification of anti-R5 Ab is ongoing.

Conclusions. Using a peptoid-antibody pair to optimize our peptoid vaccine platform should help us to identify potential vaccine candidates. Peptoids that compete with the native or recombinant protein for binding to the screening MAb will be conjugated to carrier protein, adsorbed to alum, and used to immunize mice. Sera will be tested for cross-reactivity with the peptoid and native antigen. Cross-reactive sera will then be evaluated for *in vitro* neutralization of the pathogen or toxin. The peptoids that induced neutralizing antibodies will be used as experimental vaccines.

Circadian Regulation of Gene Expression in Peripheral Metabolic Tissue by Neuronal Clocks in *Drosophila Melanogaster*

Rima Shah

Mentor: Amita Sehgal

Introduction: Through evolution, humans often went through periods of restricted eating, making use of the ability to convert glucose into triglycerides to store enough energy for days. However, in today's Western civilization, where food is readily available, obesity and other metabolic disorders have become a widespread problem. There is evidence to suggest that the circadian system plays a role in regulating metabolism and that misregulation of the circadian system can lead to metabolic defects. Here we used *Drosophila Melanogaster,* a well-established model of circadian rhythms, to address the interaction between clocks in the brain and those in metabolic tissues such as the fat body, the fly equivalent of liver and adipose tissue.

Objective: To determine whether neuronal clocks regulate cyclic gene expression in the fat body of *Drosophila Melanogaster*.

Methods: Neuronal clocks were disrupted by expressing a dominant negative form of the CLOCK protein (DN-CLK) under a RU-486 inducible pan neuronal driver (elavGS). Flies were entrained to a 12h:12h light:dark (LD) cycle for at least 48 hours then either maintained in these cycles or transferred to constant darkness for 48 hours, after which cyclic gene expression was assessed. A quantitative PCR (qPCR) approach was used to examine the 24 hour expression of clock genes and genes known to be cyclically expressed in the fat body of wild-type flies.

Results: Preliminary results show that, under conditions of constant darkness, flies in which the neuronal clocks have been ablated display a shift in the phase of *per* gene expression in the fat body compared to cyclic *per* gene expression in the fat body of control flies.

Conclusions: Our preliminary data suggest that neuronal clocks modulate the phase of the fat body clock. Future studies will examine the effect of disrupting neuronal clocks on the cyclic expression of metabolic genes in the fat body that have been shown to cycle independently of the fat body clock. Additionally, the role of insulin-producing cells (IPCs) in the regulation of the fat body clock by neuronal clocks will be examined.

Confirmation of Hypoglycemia in Goat -/- Mice When Total Body Fat Falls Below 2% of Body Weight

Ashish Singh

Mentor and Collaborators: Joseph L. Goldstein M.D., Tongjin Zhao, Michael S. Brown

Ghrelin is an octanoylated peptide hormone first identified in stomach, with the octanoyl group being essential to its biological activity. The enzyme that attaches the octanoyl group to ghrelin is called Ghrelin-Oacyltransferase (GOAT). By studying mice that have the GOAT gene knocked out (GOAT KO mice), we have shown that these mice develop severe hypoglycemia under a 60% calorie restricted diet. In order for this hypoglycemia to occur, depletion of fat deposits is required. Specifically, GOAT knockout mice will not develop severe hypoglycemia until the total fat mass drops to 2% of the total body weight. These observations were made in 8-week-old mice with an average starting fat mass between 8-10% of total body weight. In our present work, we wanted to know whether we could reproduce the results using older mice with a higher percentage of fat mass. The mice used in this study were 32-34 week old male mice (wild type and GOAT knockout mice, n=8/group), and both groups had an average starting fat mass of 17% of total body weight. We then subjected these mice to a 60% calorie restriction and monitored their fat mass and blood glucose level everyone or two days. For the first 7 days of calorie restriction, both wild type and GOAT knockout mice were able to maintain their blood glucose around 60 mg/dl. After that, the GOAT knockout mice start to develop hypoglycemia when their body fat mass dropped below 2% of the body weight. However, the wild type mice were able to maintain their blood glucose level above 40 mg/dl throughout the course even when their fat mass dropped below 2% of their body weight. The results here further confirm that in order to develop hypoglycemia in the GOAT knockout mice, the fat mass needs to be depleted from these mice during calorie restriction , even in older mice (32-34 weeks versus 8 weeks).

Severe Remote Burn Injury Results in Early, Elevated Markers of Alzheimer's Disease

Leyya Suleman

Mentors: Jane Wigginton M.D., Joshua Gatson Ph.D., David Maass BS, Victoria Warren RN, Steven Wolf M.D., Joseph Minei M.D., Paul Pepe M.D., Ahamed Idris M.D.

Background: Prior studies have found that patients with severe burns may suffer neurocognitive decline. While these observations are frequently attributed to psycho-social causes, our lab recently reported that remote burn injury is associated with significant brain changes, including new data revealing a substantial, rapid and sustained (30 min - 45 day) increase in rat brain inflammation following remote burns. Other acute brain injury processes, such as traumatic brain injury and stroke have been associated with an accelerated accumulation of Aβ40, Aβ42, and Tau, and ultimately a clinical picture of early-onset Alzheimer's disease (AD). We hypothesized that similar AD-like processes may be triggered in the brain following remote, severe burn injury.

Methods: In this study, 44 male rats received a 3° 40% TBSA back/flank scald burn by immersion (divided into 6 harvest time points), with an additional 8 receiving a sham burn (immersion in *room temperature* water), totaling 52 rats. Brains of those burned were harvested at 1, 6, 12, 24 hours, 7 days (n=8/each time point) and 45 days (n=4/time point) after injury. Brain tissue IL-6, TNF-α, IL-1β, Aβ40, Aβ42, total Tau and phosphorylated Tau were measured using ELISA methods.

Results: Burned animals had significantly increased markers of inflammation and AD at each time point measured compared with those receiving a sham burn injury (*see table for data at 1 hour and 45 days*).

Conclusions: Severe remote burn injury not only results in early, robust, and sustained neuroinflammation, but also significantly increases brain levels of Aβ40, Aβ42, and Tau. This novel finding may pave the way for future brain-preserving interventional trials in burn patients, as well as provide a more rapid and effective testing-ground for new therapies aimed at slowing and/or preventing AD.

Group	Time Point	Il-6	TNF-α	IL-1β	Aβ40	Aβ42	Tau - Total	Tau - Phos
Sham Burn		136.9	97.9	38.5	342.2	3.4	210.8	51.5
Burn	I Hour	1113.5	230.0	650.8	417.2	97.3	349.9	189.3
Burn	45 Days	996.0	326.0	502.1	941.3	340.4	1353.6	517.5

Folate receptor beta targeting for in vivo optical imaging of head and neck squamous cell carcinoma

Joel Y Sun

Mentor: Joel Thibodeaux M.D.
Contributors: Gang Huang, Yiguang Wang, Jinming Gao, Philip S. Low, Baran D. Sumer

Objective: The folate receptor (FR) is a high-affinity folic acid binding endocytic receptor uncommonly expressed in normal tissues. The α isoform (FR-α) is overexpressed in a variety of epithelial neoplastic cells. In contrast, functional expression of the β isoform (FR-β) is limited to activated macrophages. Importantly, in many malignancies FR serves as a target for the delivery of tumor specific drugs and imaging markers. Folic acid conjugated fluorescent dyes have been used to guide tumor resection in mouse models and humans. However, their potential utility in head and neck squamous cell carcinoma (HNSCC) is unclear due an incomplete characterization of FR expression in such tumors. We hypothesized that tumor infiltrating macrophages expressing FR-β could allow fluorescent visualization of HNSCC tumors using folate conjugated dyes even when FR expression in cancer cells is low.

Subjects and Methods: Immunohistochemistry was performed on a tissue microarray (TMA) containing primary tumor tissue and matched tumor free surgical margins from 22 patients who underwent HNSCC resection. Primary tumor sites included the oral tongue, base of tongue, tonsil, supraglottic larynx, glottic larynx and hypopharynx. We evaluated the expression of FR-α, FR-β, TGF-β, CD68 and arginase-1. To examine the use of folate targeting for image guided surgery, orthotopic xenograft HNSCC tumor models were generated from nude mice. The mice received 0.8 mg/kg intravenous injections of fluorescein isothiocyanate conjugated folate (Folate-FITC) and were imaged for fluorescent emission under 495nm light two hours later.

Results: No FR-α expression was observed in any TMA tumor specimen. All tumor samples demonstrated positive FR-β expression. Cellular morphology and CD68 expression identified the FR-β expressing cells as tumor infiltrating macrophages. No association was observed between FR-β staining and either TGF-β or arginase-1 staining. In tumor xenograft mouse models, tumors showed strong fluorescence in vivo after folate-FITC injection. Normal salivary glands and surrounding neck muscles did not demonstrate significant fluorescence. Histologic examination of the xenografts revealed that fluorescence within the tumors was confined to areas of inflammatory cell infiltration, consistent with our TMA data.

Conclusion: HNSCC tumors contain a significant population of FR-β expressing macrophages. In contrast to many other carcinomas, the HNSCC tumor cells in our TMA did not express FR-α. By targeting tumor infiltrating macrophages, the folate linked delivery of fluorescent dyes can facilitate image guided HNSCC resection even when the tumor cells themselves do not express FR.

Impact of Ethnicity in Upper Gastrointestinal Hemorrhage

Casey S. Wollenman

Mentor: Don C. Rockey M.D.
Contributors: Rebecca Chason, Joan S. Reisch

Background and Aims: Upper gastrointestinal hemorrhage (UGIH) is a serious condition, with considerable morbidity and mortality. Thus, we aimed to examine the role of ethnicity in UGIH outcomes.

Methods: We analyzed 2196 consecutive patients admitted with acute UGIH between January 2006 and February 2012. Data (including complete demographic and clinical data) was gathered prospectively and entered into our GI Bleed Registry, which captures multiple demographic and clinical variables. Results were analyzed using the Chi-square analyses and the analysis of variance techniques with Tukey multiple comparisons.

Results: Among 2196 patients, 620 (28%) were Black, 625 (29%) White, 881 (40%) Hispanic, and 70 (3%) were members of other ethnic groups. Males outnumbered females by approximately 2:1 (p=0.01). ASA (18%; p<0.001) and NSAID (17% p=0.007) use was common across ethnic groups. Smoking and illicit drug use was highest in Whites (63% and 31%), and Blacks (62% and 31%). Alcohol use was highest in Hispanics (63%) and Whites (63%). The most frequently identified causes of UGIH include gastric and duodenal ulcers (25%), esophageal varices (25%), and esophagitis (12%). Among the 3 main ethnicities, Blacks frequently had UGIH due to gastroduodenal ulcers (32%), while Hispanics most commonly bled from esophageal varices (34%). Ulcer disease and esophageal varices in Whites were found equally (25%). Causative bleeding varied with age. More Black (50%) and White patients (44%) bled between 50-64 years, while 40% of Hispanics bled between 35-49. The most common cause of bleeding in patients younger than 35 or older than 65 years was gastroduodenal ulcer disease. Overall, rebleeding rates were significantly lower in Whites (5.8%) than in Hispanics (9.9%) or Blacks (8.7%) (p = 0.02). Looking at outcomes in patients with variceal or gastroduodenal ulcers, Blacks had a higher mortality rate (7% and 11%), while Whites had a lower mortality rate (5% and 5%). Hispanics with varices had higher rebleeding rates (13%) but the lowest mortality (6%).

Conclusions: By examining an ethically large and diverse population, we conclude that the etiology and outcome of UGIH has specific trends across age and ethnic groups. Hispanics were more likely to have esophageal varices and higher rebleeding rates, while Blacks were more likely to have ulcers and the highest mortality overall. Whites were equally likely to have ulcers or varices, but a lower rate of rebleeding. UGIH frequently occurs between the ages of 34-49; however, patients over 65 were more likely to have ulcers.

Aβ1-42 antibody producing plasma cells in DNA Aβ42 trimer immunized mice reside predominantly in the bone marrow.

Tresa Zacharias

Mentor and Collaborators: Doris Lambracht-Washington Ph.D., Suzanna Langworthy, Min Fu, Larry Anderson, Olaf Stüve, Roger Rosenberg

Alzheimer's disease (AD) is the most common form of age-related dementia and affects nearly 40 million people worldwide. Immunotherapy provides a possible avenue for prophylaxis of AD, but a clinical trial (AN1792) in which patients with early AD were immunized with Aβ1-42 peptide was halted after the occurrence of meningoencephalitis in 6% of the immunized people which was attributed to a T cell autoimmune response. DNA vaccination has been shown to have a polarized Th2 immune response that lacks many of the features responsible for inflammation seen in peptide immunizations. In this study, we show a new feature of the DNA Aβ42 trimer elicited B cell immune response and present data for the presence of a long lived plasma cell pool residing within the bone marrow in DNA immunized mice but not in peptide immunized mice. Two groups of mice were analyzed: one group of B6C3F1 mice (n=20) were studied 4 months after the last DNA vaccination, and a second group of BALB/c mice (n=14), which received DNA or peptide immunizations, were analyzed 10 days following the last immunization. The comparison of antibody producing cells in bone marrow and spleen for the DNA and peptide immunized mice with an Antibody Forming Cell (AFC) ELISPOT assay and subsequent ELISAs showed that bone marrow plasma cells from DNA immunized mice produced more anti-Aβ42 IgG producing cells and higher levels of secreted IgG antibodies. In peptide immunized mice, more IgG antibody producing cells were found to reside in the spleen. These data indicate that the bone marrow may be an important reservoir for B cells following DNA Aβ42 immunization and is in line with studies showing that the bone marrow represents an excellent niche for the survival of long lived plasma cells and a lifetime source for antibody producing B cells which are independent of continuous antigen specific stimulation. Further studies are needed to show whether it is possible to define additional phenotypic characteristics for the antigen specific B cell immune response in DNA Aβ42 trimer immunized mice or differences in the T_H subsets directly involved in initial signaling events to B cells in the germinal center reactions.

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Research Design and Methods

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£ R25 NHLBI Research Trainee Award Recipient

Cortical segmentation of neonate brain with diffusion tensor imaging

Junyoung Ahn

Mentor: Hao Huang Ph.D.

Introduction: Segmentation of the white matter, gray matter, and the cerebrospinal fluid from MRI imaging data presents significant clinical potential. The neonatal brain is actively developing and the cortex is not well defined due to limited myelination in the neonate white matter. Because of the differences in myelination between the adult and the neonate brain, the segmentation of neonate brain can be challenging with relaxation based T1-weighted or T2-weighted magnetic resonance image (MRI). To date, semi-automated or automated methodologies have been developed for adult human brain based on T1-weighted MRI. However, no developed technology has been presented for segmenting neonate brains. In this project, we aimed to develop a semi-automated cortical segmentation method by introducing more advanced imaging contrasts from diffusion tensor imaging (DTI).

Methods: The b0 image derived from DTI of neonates' brains was segmented using FSL (fsl.fmrib.ox.ac.uk/fsl/fslwiki/) into gray matter, white matter, and CSF. The segmentation data was manually corrected with ROI editor (mristudio.org) because FSL segments according to tissue contrast for adult brains which is inverted in neonates. The segmentation was co-registered onto a template for neonate brains from Johns Hopkins. By inputting the gray and white matter volumes into the Freesurfer pipeline, the volumes were transformed to 3D surfaces for thickness calculations. The average cortical thickness was calculated from the surfaces by using the representations from the gray and white matter boundary to the pial surface to compute the distance across the cortical mantle.

Results: Segmented cortex of neonate brain was obtained and cortical thickness of neonate brains were calculated based on the cortical segmentation.

Discussion: A viable and unique approach has been developed to segment the neonate cortex and calculate cortical thickness using semi-automated methods and contrasts from DTI. Currently, there are no widely accepted methods to segment neonate brain. A semi-automated approach is advantageous in its convenience, speed, and lower probability of human error. Examining the cortical thickness is a sensitive marker for tracking developmental changes in the neonate brain. In the future, we hope to increase the sensitivity and specificity of neonatal brain segmentation to increase the clinical impact of further understanding the normal anatomy and development of the neonatal brain.

Decreased MIR 122 Levels with HCV Clearance in HIV HCV Co-infection

Perry Dubin

Mentor and Collaborators: Hejun Yuan, Robert Devine, Mamta Jain M.D., Linda S. Hynan Ph.D., William M. Lee M.D.

Background and Aims: Micro RNA-122 (miR-122) is under investigation as a target for direct antiviral agents against the hepatitis C virus (HCV), and as a biomarker for both cancer and acute liver injury. Previous data suggest HCV mono-infection is associated with increased serum miR-122 levels. This study sought to determine outcomes in regard to miR-122 levels following clearance of HCV in human immunodeficiency virus (HIV) co-infected patients.

Methods: Nine HCV-HIV co-infected patients undergoing antiviral therapy were treated with interferon and ribavirin for 48 weeks between January 2009 and March 2011, and had serial miR-122 levels measured in triplicate from serum with mirVana™ PARIS™ kit according to the instructions from the manufacturer (Ambion, AM1556). Values were measured at baseline, 1 week, 4 weeks, end of treatment (EOT; 48 weeks), and at 24 weeks after treatment completion (SVR24). SAS V9.3 was used to analyze these data. Change from baseline (copies/µL) was calculated as Log10 (Baseline)-Log 10(time), where time was 1 week, 4weeks, EOT, and SVR24; a repeated measures ANOVA was used to compare the results over time for the patients. If the ANOVA was found significant, post hoc, pairwise comparisons were used to examine change from baseline across the four time points.

Results: Six of nine achieved SVR24, 1 was undetectable at EOT but relapsed, and 2 patients were non-responders. Among the 6 patients achieving SVR, all showed a decrease in miR-122 levels between 0.16 and 1.46 logs, between baseline and SVR24. The ANOVA confirmed a significant decrease in miR-122 levels from 1 week to SVR24 (p=0.0225). Significant pairwise comparisons for change from baseline were found at 1 week versus SVR24 (p=0.0063), 4 weeks versus SVR24 (p=0.0086), and EOT versus SVR24 (p=0.0458).

Conclusion: Clearance of chronic HCV is associated with decreased miR-122 levels in HIV co-infected patients and was not improved in patients with continued infection who failed to respond to treatment.

<u>**Active Preoperative Anemia management to Reduce Transfusion (APART)**
in patients undergoing cardiac surgery:
Design of a Pilot Study</u>

Jing Liu

Mentor: Philip Greilich M.D.

Introduction: Preoperative anemia is a silent epidemic: it occurs in up to 40% of those scheduled for cardiac surgery and leads to perioperative erythrocyte transfusion in 80% of these patients. Most importantly, it is independently associated with a two-fold increase in postoperative morbidity and mortality. Therefore, interventions aimed at reducing preoperative anemia should improve outcomes following cardiac surgery.

Study Design: We propose a pilot study to test the feasibility and efficacy of using an intermediate course (1-3 weeks) of erythrocyte stimulating agent (ESA) plus iron to increase erythrocyte mass before cardiac surgery. The findings from this pilot, feasibility study will be used to design a phase II/III randomized, controlled trial to determine if a similar treatment (ESA plus iron) can significantly increase nadir hematocrit during cardiopulmonary bypass (CPB), reduce erythrocyte transfusion rates and postoperative complications in anemic patients undergoing cardiac surgery. Forty-four patients scheduled for CABG, valve, or CABG/valve surgery at St. Paul University Hospital will be consented with an anticipated 10% dropout rate. Participants will be randomized to treatment (ESA plus iron) or control (standardized care) and followed from enrollment to up to 30 days post-operatively. Erythrocyte transfusions will be limited to those with hematocrit lower than 24% or clinical evidence of organ dysfunction. We will collect data on hematocrit, reticulocyte count, erythrocyte transfusions, and post-operative complications.

Study End Points: The primary end point of the pilot study is to determine the difference in nadir hematocrit during CPB between the treatment and control groups. The secondary end point is to determine the difference in erythrocyte transfusions between the two groups.

Hypothesis: We hypothesize that the use of the intervention will raise the nadir hematocrit during CPB and lead to fewer erythrocyte transfusions in anemic patients undergoing CABG, valve, and CABG/valve surgeries compared to anemic patients undergoing similar procedures without the intervention.

Evaluating the Efficacy of a Public Health and Community Medicine Program at the University of Texas Southwestern Medical School

Bhavini Patel

Mentor and Collaborators: Nora Gimpel M.D., Neil Murthy; Patti Pagels PA-C, Sunzida Sharmin MBBS, MPH

Introduction: Time devoted to public health education has been gradually decreasing in medical school curricula. In 2000, the CDC and the AAMC established the cooperative agreement calling for increased "collaboration between academic medicine and public health." In 2005, the University of Texas Southwestern Medical School established the Community Action Research Track (CART), in order to address student interests in public health and community medicine. The specific aims of this study were to 1) evaluate the process and impact of the CART program; and 2) assess the student body's interest in expanding public health education and community engagement at UT Southwestern.

Methods: This cross-sectional study consisted of two online student surveys. The All Students Survey analyzed interest in public health and community engagement among the 690 medical students currently enrolled at UT Southwestern. The CART Student Survey analyzed the efficacy of the CART program among 35 students currently enrolled in the program.

Results: Of the 690 students who received the All Students Survey, 292 responded (response rate 42%). Fifty percent of all students were interested in an expanded program that incorporates public health, prevention, and community engagement in the medical school curriculum. Of the 35 enrolled in the CART program, 15 responded (response rate 43%). Although 60% of CART students were satisfied with the program, the majority of the weaknesses identified with the program were attributed to a lack of sustainable funding.

Discussion: Students are interested in incorporating public health and community medicine into the medical school curriculum. Recommendations include establishing an inter-professional collaboration between the UT Southwestern Medical School, the Dallas County Public Health Department, and the UT School of Public Health. Other recommendations include expanding the CART program by integrating core principles of public health and prevention, community based participatory research, and community service learning.

While You Were Sleepwalking: Science and Neurobiology of Sleep Disorders and the Enigma of Legal Responsibility of Violence During Parasomnia

Shreeya Popat

Mentor:William Winslade Ph.D., J.D.

In terms of medical science and legal responsibility, the sleep disorder category of parasomnias, chiefly REM sleep behavior disorder and somnambulism, pose an enigmatic dilemma. During an episode of parasomnia, individuals are neither awake nor aware, but their actions appear completely conscious. As these actions move beyond the innocuous, such as eating and blurting out embarrassing information, and enter the realm of rape and homicide, their degree of importance and relevance increases exponentially. Parasomnias that result in illegal activity, particularly violence, are puzzling phenomena for medicine and the law. Through a survey of pertinent medical literature, I will provide a general overview of the current scientific knowledge of parasomnias.

Even though this knowledge is far from complete, it can provide some neurobiological information about the nature of parasomnia, which can give rise to conclusions about a sleepwalker's level of intention as well as a familiarity with factors that predispose one to such episodes. Although a parasomniac's complete lack of consciousness warrants acquittal from criminal liability, it does not exclude responsibility for subjecting oneself to exacerbating factors that result in these violent parasomnias. Individuals should be held accountable if they could be expected to control these factors. In addition, they should undergo appropriate medical treatment and management plans in order to prevent future parasomnia behaviors. Establishing legal parameters for handling parasomnia will prove difficult due to the strong potential for malingering, so specific criteria derived from scientific knowledge of the disorders must be outlined in order to distinguish between true and fraudulent claims of crimes committed during parasomniac states

Decision Making and Contralateral Prophylactic Mastectomy

Shreeya Popat

Mentor: Dr. Patricia Parker
Behavioral Sciences Department at the UT M.D. Anderson Cancer Center

Recently, there has been an increase in breast cancer patients choosing to undergo contralateral prophylactic mastectomy (CPM) surgery, or preventative removal of the unaffected breast. However, evidence supporting the clinical and psychosocial benefits of this surgery are lacking, especially among patients with sporadic breast cancer, who do not show classic risk factors such as genetic predisposition and family history. Several studies have examined the decision making of high-risk breast cancer patients, who cite the pain and suffering they saw in their family members with breast cancer as a significant factor in their decisions. However, no such study has been done on average-risk patients, who do not have a similar family history of breast cancer. In this study, we are examining the potential factors in the decision making process among average-risk breast cancer patients considering CPM. We are recruiting 60 average-risk breast cancer patients considering CPM and 60 average-risk breast cancer patients not considering CPM. These patients complete a set of questionnaires at up to four points in their treatment that assess factors such as cancer worry, fear of recurrence, knowledge about efficacy of breast cancer treatments, perceptions of risk, body image, and trust in the physician. Their interaction with their surgeons are recorded, and, in addition to this, a portion of them are asked to participate in qualitative interviews regarding their experiences as a cancer patient. I contributed to the qualitative interview process by refining the semi-structured interview script after analyzing a set of eight pilot interviews. In order to evoke more descriptive and informative responses from patients, I created separate pre- and post-surgery interview scripts and rearranged the scripts to encourage the patients to chronologically describe their cancer experience. In addition, I added many probes that will provide insight into each patient's unique situation. This script and suggestions are being utilized in the remainder of qualitative interviews in the study. Hopefully, it will bring to light factors in the patients' decision making that were not addressed in the questionnaires. These results will provide important information to explain the rise in patients choosing CPM and the factors that influence them to do so. It is expected that our findings can be applied to better educate patients and their physicians to make well-informed decisions regarding their medical care.

Field Trial of Hypotensive Resuscitation versus Standard Resuscitation in Patients with Hemorrhagic Shock after Trauma

Max Seiter

Mentor: Joseph Minei M.D.

Hemorrhage accounts for over a third of all prehospital trauma deaths, and forty percent of mortality within the first twenty-four hours, only CNS injury kills more patients in the immediate post-traumatic period. The current standard treatment of an exsanguinating trauma patient includes rapid infusion of large volumes of crystalloid solutes, with the goal of maintaining tissue perfusion and preventing vital end-organ ischemia. This is grounded in the knowledge that there is greater survival with isotonic fluid administration in hemorrhagic shock, evidenced by animal studies in the 1950's and 60's. However these landmark studies were based on models of controlled, rather than uncontrolled, hemorrhage. There is considerable evidence that in uncontrolled hemorrhage aggressive fluid administration leads to increased bleeding through several mechanisms. Increased arterial and venous pressures dislodge nascent hemostatic thrombi and lead to increased rates of bleeding from unclotted sites; acidosis, hemodilution of platelets and clotting factors, and alterations in the viscosity of blood lead to coagulopathy; and decreased oxygen carrying capacity of the blood may result in end-organ ischemia. Three major clinical trials have examined low-volume hypotensive resuscitation vs standard fluid resuscitation and delivered starkly contrasting results; one study of 600 patients showed a significant decrease in mortality in the hypotensive arm, while another study of 110 patients and a UK study of 1300 patients showed no significant difference. The goal of our study was to test the hypothesis that hypotensive resuscitation vs standard resuscitation will result in reduced volumes of saline administration and will lead to increased survival at the twenty-four hour mark. Patients were to be randomized in the field after induction into the study by the opening of a bag with either a 250ml bags of saline (hypotensive arm) or 1000ml bag of saline (standard arm). In the hypotensive arm patients were to receive 250ml bags of saline with a goal SBP of 70mmHg or a radial pulse as an endpoint for fluid resuscitation. Then over the next two hour period, or until hemorrhage control (whichever event came first), boluses of 250ml bags of saline were given if SBP was below 70mmHg or no radial pulse was detected, with the same endpoint in resuscitation. In the standard resuscitation arm, patients were to receive 1000ml bags of saline and be resuscitated to SBP of 110mmHg; over the next two hours (or until hemorrhage control) if the patients SBP dropped below 90mmHg, they would be bolused with 1000ml bags of saline to a goal SBP 110mmHg. Unfortunately we did not induct any patients into the trial at our center, however the technique of hypotensive resuscitation has strong basis in animal research and shows considerable promise. This will be a review of current research in the field of hypotensive resuscitation.

Automated Analysis of Electroglottographic Signal in Adductor Spasmodic Dysphonia

Keerthan Somanath

Mentor: Ted Mau M.D., Ph.D.

Introduction: The human voice can be evaluated by a variety of methods. Electroglottographic (EGG) signal is produced when vocal fold vibrations produce cyclic fluctuation in the electrical impedance across the larynx. The EGG signal thus reflects the degree of contact between the vocal folds during voice production and provides a measure of voice quality based on phonatory physiology. However, the utility of EGG has been limited because existing methods of EGG signal analysis focus on the evaluation of 2-3 parameters in a segment of sustained vowel production, which does not reflect pathologies more apparent in conversational speech. We hypothesize that the EGG signal can capture perceptually relevant information from continuous speech in adductor spasmodic dysphonia (ADSD), an enigmatic speech disorder.

Objectives: 1. To develop an automated computer algorithm to analyze the EGG signal in continuous dysphonic speech. 2. To identify EGG waveform features that correlate with the perceived quality of vocal strain in ADSD.

Methods: A computer program was created and refined in MATLAB to display and analyze EGG data via a graphical user interface (GUI). An automated peak-detection algorithm was developed using the differentiated EGG signal and used to perform simultaneous multi-parameter analysis on the EGG signal from normal speech and speech in patients with ADSD. Between-group comparisons were made using two-tailed Student's t test. Also, intrasubject comparison was made between strained and less-strained syllables in ADSD speech.

Results: A program was successfully written to allow the display and automated analysis of EGG data from samples of continuous dysphonic speech. The program was found to generate data with good internal consistency. Application to normal and ADSD subjects showed that the open quotient parameter was able to distinguish between strained and less-strained syllables with statistical significance (p=0.04).

Discussion/Conclusion: We have developed a method to analyze EGG signal from samples of continuous dysphonic speech. The numerical and graphical data obtained support the utility of EGG as an objective means to clinically highlight the speech differences between normal subjects and subjects with ADSD. Further testing to establish normative values for the analyzed EGG parameters and their subsequent comparison with patient EGG data is required to affirm their utility for routine clinical voice assessment.

Searching for Genes of Host Defense

Jeffrey A. SoRelle

Mentors: He-Xin Shi Ph.D., Ying Wang Ph.D., Bruce Beutler M.D.

Through random mutation of the mouse genome and phenotypic screening of the mutated mice, genes can be identified that are associated with dysfunction in the innate immune system. The strategy proposed works under the knowledge that many genes are involved in the immune system and that random mutation could lead to a change in their genetic code. This mutation can present as a phenotypically abnormal immune system. Once a phenotype is identified, the genome can be analyzed in an attempt to trace the mutated gene responsible for the weakened immune system. One of the elegant aspects of this genetic method is that it does not rely on a hypothesis about how the immune response works. This leads to an unbiased approach where interpretation errors are rarely made.

A forward genetic approach is used to create abnormal phenotypes of the innate immune system and then determine the genetic cause. The normal mutation rate is accelerated by the widely used germline mutagen N-ethyl-N-nitrosourea (ENU) to produce an average of 3,000 single nucleotide changes per host leading to an average of 60 coding changes. To produce homozygotes, males of the G1 generation are bred with normal mice of the same strain to yield the G2 generation. Recessive mutations can be found in the G3 generation by a backcross of G2 females with the G1 father. Screening 6 G3 progeny should capture 50% of the mutations in the homozygous form.

Phenotypic screening was performed on peritoneal macrophages ex vivo by stimulation with the following toll-like receptor agonists: lipopolysaccharide (TLR4), double stranded RNA (TLR3), triacylated lipoprotein (TLR 1/2), diacylated lipoprotein (TLR 2/6), resiquimod (TLR 7), and unmethylated DNA (TLR 9). The inflammasome pathway was probed by lipopolysaccharide priming followed by stimulation with either nigericin (K^+ efflux) or ATP. The secreted TNF-alpha (TLR screen) and IL-1beta (inflammasome screen) were measured by ELISA to determine phenovariance.

This research can lead to a deeper understanding of how we combat infection. The study can lead to the development of mutations involved in both the innate and adaptive immune system so autoimmune diseases can also be studied. A long term goal is to identify genes that would render an individual resistant to infection and to study the interaction of these genes.

NANOPARTICLES FOR DRUG DELIVERY:
Characterization of Particle Surface Density and Macrophage Uptake Mechanisms for   Anti-Tuberculosis Drugs

John J. Squiers

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Nanoparticle technology shows promise for improving the efficacy of drug delivery by increasing the bioavailability of otherwise poorly water-soluble pharmaceutical agents. Flash NanoPrecipitation (FNP) is a novel method of nanoparticle (NP) drug formation. A hydrophobic drug is rapidly mixed with an aqueous solution of amphiphilic block copolymer. The hydrophobic block dives into the drug surface, while the hydrophilic blocks form a protective shell around the drug. The first objective of this study is to quantify the density of protective polymers on the surface of NP drugs generated by FNP as a function of block copolymer architecture. A series of NPs were formulated with monodisperse 200 nm latex spheres and a Baleux assay was implemented to measure the density of PEG protective chains on their surface. This study shows quantitatively that as hydrophobic co-block molecular weight increases, the density of hydrophilic protective chains on the surface of NPs decreases. This relationship provides an assessment of previous studies that have shown in vivo circulation times of NPs decrease with increasing hydrophobic block size.

The second objective of the study is to elucidate the particular uptake pathway by which the J774.E macrophage-like cell line incorporates NP drugs in order to optimize drug delivery for the treatment of Tuberculosis. These cells were incubated with NPs in the presence of various pharmacological blocking agents of cellular endocytosis pathways. Statistical analysis revealed that for neutral NPs stabilized by hydroxyl-terminated polyethylene glycol-b-polystyrene block copolymers as well as cationic nanoparticles, the dominant method of uptake is an unspecified form of pinocytosis. Given that macrophages are professional phagocytes, it is surprising that these nanoparticles seem to be internalized via a mechanism other than phagocytosis. Uptake of nanoparticles with a surface charge is increased compared to nanoparticles with a neutral surface. Finally, inhibiting some forms of endocytosis appears to result in upregulation of other uptake mechanisms. The demonstrated reproducibility of this experiment also suggests its protocol can be informative as research into NP targeting to diseased cells continues. This characterization of NP formulation and uptake is an initial step toward improved delivery and efficacy of anti-tuberculosis drugs.

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¥ NHLBI Medical Student Research Trainee
D Doris Duke
û UT Summer Research Program Participant
£ R25 NHLBI Research Trainee

Are There Any Medical Conditions Associated with Keloids?

Prince Adotama

Mentor: Donald Glass M.D., Ph.D.

Keloids develop as a result of the excess growth of scar tissue. They grow invasively beyond the borders of the wound and rarely regress. Once removed, they can return more aggressively and can negatively impact quality of life. Prior research studies indicate that keloids have a strong genetic component. Keloids can have an autosomal dominant mode of inheritance with incomplete penetrance and have a higher prevalence in twins. Keloids also occur more commonly in those of African descent, with a frequency reported as high as 16%.

It is unclear, however, if keloids are a purely cutaneous event or if they are indicative of underlying systemic aberrancy. We hypothesized that there would be differences in the prevalence of medical conditions found in the keloid population compared to the general population. We administered surveys to those of African descent with keloids enrolled in the Genetic Causes of Keloid Formation Study in order to obtain information on past medical history and family history. Data from the Dallas Heart Study (DHS) was used as a representative sample of the general population. We matched six people in DHS for every person from the keloid registry based on ethnicity, gender, and age. We found a higher prevalence of high cholesterol, hypertension, and obesity in the keloid population compared to the general population cohort.

We then looked within our keloid population to assess for any differences in the prevalence of medical conditions associated with familial keloids compared to sporadic keloids. We hypothesized that there would be differences in the prevalence of medical conditions between sporadic and familial keloids. However, with regards to past medical history, we found no statistically significant differences between the two subgroups. These results suggest that the incidence of keloids in individuals does not correlate with the mode of inheritance of keloids. Our study also suggests that keloids may be indicative of other medical conditions, which could provide insight into the pathogenesis of keloids.

Establishing Long-term Medical Follow-up in an Underserved,High-risk Population Identified at a Local Health Fair

Katherina Avila

Mentor and Collaborators: Nora Gimpel M.D., Sandeep Mehta BA; Rima Shah BS, Krishna Sajja BS

Context: UT Southwestern's Annual Celebration of Health is an effort driven by students with the aid of faculty and staff of UT Southwestern Medical Center. Based on the United To Serve (UTS) volunteer initiative of the UT system, the health fair, established in 2004, attracts about 1000 attendees from the local community. A significant portion of the attendees are overweight with a history of hypercholesterolemia and hypertension. Additionally, many do not have an established medical home. Previously, UTS has focused on health education and screenings. We are interested in establishing a follow-up system to address the overall impact of these activities.

Objective: The objective of this study is to identify a cohort of UTS attendees that meet high-risk criteria for cardiovascular diseases (CVD) and to ensure that they are matched with a medical home to receive continuity of care.

Design: Cohort prospective study. Setting: A local health fair in Dallas, TX. Participants: Adult health fair attendees. Intervention: After an initial assessment using the Framingham score, attendees identified at moderate and high risk will complete clinical measurements (fasting glucose, lipid panel, blood pressure and BMI) and receive information about community clinics. Quarterly follow-up phone calls will determine if attendees established ongoing healthcare management.

Preliminary Results: We identified 105 individuals who meet moderate and/or high-risk criteria for CVD, and we were able to follow-up with 74 participants. We found that 21% (n=16) of those contacted visited a primary care physician (PCP) after United To Serve. Of these individuals, 56% (n=9) were diagnosed with a chronic disease, which include hypertension (26%, n=5), hypercholesterolemia (21%, n=4), and type II diabetes mellitus (11%, n=2). After diagnosis by a PCP, 100% (n=9) are now on appropriate medications. These data suggest that United To Serve has helped individuals at high risk for CVD to establish a medical home and decrease overall health risk factors.

Conclusions: Results of the study will be used to better assess the impact that UTS has on the community it serves annually. Furthermore, these data should allow us to construct an appropriate screening and referral system.

Argon Laser trabeculoplasty (ALT) by Residents: Predictors of failure

Eric Chang

Mentor and Collaborator: Karanjit S. Kooner M.D., Nathan Markel BS

Purpose. ALT is widely used to control intraocular pressure (IOP) in glaucoma. We wished to determine predictive factors for long term success of ALT performed by supervised residents in training on patients at a local VA Hospital in Dallas.

Methods. Charts of patients with primary open angle glaucoma who underwent ALT between 2001 and 2011 were reviewed retrospectively. Those with follow up < 3 months, prior ALT/SLT, filtering procedure or inadequate data were excluded. The dependent variable was time to failure after ALT. Failure was defined as any additional medication, ALT/SLT or glaucoma filtering surgery. All patients were treated with 360 ° ALT. Logistic regression and receiver operating characteristic (ROC) analysis was performed to assess correlation between time to failure after ALT and age, pre-op IOP, C/D ratio, visual field defect, family history, refractive error, hypertension, diabetes, number of medications, laser energy used, central corneal thickness.

Results. Evaluable data was obtained on 206 patients; mean age 65, 98% male, and 61% black. 40.8% (84/206) were classified as ALT failures. Failure and non-failure patients had equal follow-up duration of median 2 yr. Pre-ALT LogMar (mean (SD) 0.25 (.3) vs. 0.35 (.3)), no. of glaucoma medications (2.9 (1.0) vs. 3.3 (1.0)), and myopia (46% vs. 61%) differed, respectively, between ALT failures and non-failures ($p<0.05$). In multivariable logistic regression models, after adjusting for age, hypertension, and diabetes, we found that myopia was protective (odds ratio (OR) =0.39, 95% CI 0.21-0.78, p=0.005) but that higher laser energy ((OR=1.6 for a 20k increase in energy, 95% CI: 1.1-2.4, p=0.005) was associated with increased risk associated for ALT failure; model ROC AUC = 0.70 (95% CI: 0.63-0.78).

Discussion. Our VA patients were mainly males but had good ethnical diversity. Better response in myopia may be related to thickness of trabecular meshwork while poorer response to increased laser energy may be from thermal damage. Patients using more than three meds were on systemic carbonic anhydrase inhibitors

Conclusions. ALT results were better in patients who used more than 3 meds, were myopic and required less laser energy.

1- Year Skill Retention following Proficiency-based Training for Robotic Surgery

Julia Chen

Mentor: Daniel Scott M.D., F.A.C.S.

Introduction: We previously reported face, content, and construct validity as well as high reliability measures and significant performance improvement for 9 inanimate exercises as part of a comprehensive, proficiency-based robotic training curriculum. The purpose of this study was to determine 1-year skill retention for this curriculum.

Methods: Over a 2-year period, novice robotic trainees (n=90: 76 residents, 5 faculty, and 9 fellows) from general surgery (n=34), urology (n=24), and gynecology (n=32) successfully completed a 2-month curriculum which included: 1) online-didactics, 2) half-day hands-on tutorial, and 3) self-practice using 9-inanimate exercises until proficiency levels were achieved. Five exercises used FLS models with modifications and 4 used custom-made components. Each task was scored for time and errors using modified FLS metrics; task scores were normalized to proficiency levels and a composite score equaled the sum of the 9 normalized task scores. Each participant performed a single proctored repetition of each task before (pretest) and after (post-test) their initial training. Available trainees were invited to complete two additional repetitions (Rep1 and Rep2) of all 9 tasks at least six months after initial training to determine skill retention. Questionnaires were completed to document interval robotic experience. Comparisons used ANOVA on ranks; mean ± s.d. reported.

Results: 27 trainees (general surgery (n=7), urology (n=8), and gynecology (n=12)) participated in retention testing 12.5 ± 4.8 months after initial training. All trainees demonstrated significant improvement during initial training: pretest score 550 ± 147 vs. post-test 940 ± 50, p<0.001. A significant amount of skill loss (14.0%) was detected at retention testing (Rep1 809 ± 89, p<0.001 vs. post-test). A non-significant amount of improvement was detected on further retention testing (Rep2 848 ± 9, p=n.s. vs. Rep1). Ultimate skill retention (Rep2 vs. post-test) for the entire cohort was 90.2% and ultimate performance (Rep2) was not significantly different from performance immediately after training (post-test). Individuals who did not perform interval robotic cases had significantly worse retention (81.3%) compared to those with interval experience (90.9%, p=.013). Similarly, individuals who required a large amount of practice (>80 repetitions) during initial training had significantly worse retention (79.7%) compared to those who required less initial practice (89.6%, p=.017).

Conclusions: These data suggest that the proficiency-based curriculum is robust, yielding a very high level of skill retention. However, interval operative experience was associated with the smallest amount of skill loss. Skill also improved with minimal additional practice (i.e. by Rep2). For individuals who do not routinely perform robotic operations, additional simulation-based practice may be beneficial in optimizing skill retention.

Urodymanic Parameter Findings for Middle-aged women with normal study interpretation

Stephen Chiang

Mentors: Dominic Lee M.D., Philippe Zimmern M.D.

Introduction and Objectives: To describe urodynamic study (UDS) findings in women with various lower genito−urinary symptoms (LUTS) who were found to have a normal study.

Methods: Following IRB approval, UDS tracings of non−neurogenic women who were studied for various LUTS and were found to have a normal study were reviewed. Demographic data, indications for UDS, and UDS parameters were extracted. UDS was conducted according to an established protocol using a 6F dual−lumen catheter (ICS guidelines) with a Laborie Aquarius XLT ™ and interpreted with a pre−existing template to standardize the reading. The fill−void study was frequently repeated during the same UDS session to confirm normal findings. Study interpretation was done by a neutral reviewer with UDS expertise.

Results Obtained: From 2000−2012, 43 middle−aged women, who had been coded as having a normal study, were retrospectively reviewed from a database of over 2200 studies. The majority were Caucasian, with mean age 63 (range 42−85), mean BMI 24.5 (20−37), mean parity 2 (0−4), and 67% were post−menopausal. Of the 43 patients, 29 underwent a second fill−void study. UDS findings are reported in Table 1 based on clinical indication for UDS: (1) incontinence, (2) pelvic organ prolapse, or (3) other LUTS symptoms. Very consistent findings were noted between first and second studies (table 1).

Conclusions: UDS parameters from a cohort of middle− aged women with normal findings are now available as reference values when interpreting urodynamic studies or for a better design of an age−matched nomogram.

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Discordance in OR safety attitudes: Does safety lie in the eye of the beholder?

Joshua Clayton
Mentor: Le Chen, M.D., Ph.D.

Background: Efforts to improve operating room (OR) safety can be optimized if we understand the safety attitudes of those who work in the OR. We sought to describe the safety attitudes of current OR personnel.

Methods: <u>Survey:</u> The Safety Attitudes Questionnaire (OR Version) was modified to develop a shorter, 23-item anonymous electronic survey to measure attitudes toward OR safety. Respondents were also asked to rate the quality of their communication with other providers who care for surgical patients.

<u>Participants:</u> Surgeons and proceduralists, anesthesia providers, and nurses who worked in perioperative services and on the surgical wards.

<u>Data:</u> Respondents' demographic information was collected. Survey responses were on a 5-point Likert scale, where a higher score reflected a better safety attitude or higher quality communication, as appropriate.

<u>Analysis:</u> Classical test theory and factor analysis. ANOVA was used to compare responses between surgeons/proceduralists, anesthesia providers and nurses. Results are reported as mean (SD).

Results: <u>Survey:</u> The 23 survey items reliably measured attitudes toward OR safety ($\alpha=0.92$).

<u>Respondents:</u> 170 staff responded to the survey (55 surgeons, 29 anesthesia providers, and 86 nurses). Mean age of respondents was 40.1 (10.9) years. Median duration of experience was 8 years (range: <1 to 42).

<u>Attitudes toward OR safety culture:</u> The mean score on the 23-item survey for all respondents was 3.95(0.68). Scores differed significantly among provider groups ($p=0.0009$). Surgeons' mean score was 0.57 higher than anesthesia providers' ($p<0.05$), and 0.33 higher than nurses' ($p<0.05$).

<u>Quality of communication:</u> The surgeons' perception of the quality of their communication with nurses was higher than the nurses' perception of the quality of their communication with surgeons (3.95 vs. 3.05, $p<0.0001$). Similarly, surgeons' perception of the quality of their communication with anesthesia providers was higher than the anesthesia providers' perception of their communication with surgeons (4.43 vs. 3.81, $p=0.0015$). However, the anesthesia providers' perception of the quality of their communication with nurses did not differ from the nurses' perception of the quality of their communication with anesthesia providers (3.62 vs. 3.68, $p=0.77$).

Conclusion: The abbreviated questionnaire is a reliable measure of OR safety attitudes. Surgeons had the most positive OR safety attitude, but there was consistent discrepancy in the way surgeons rated their communication with other provider groups – surgeons reported that the quality of their communication with anesthesia providers and nurses was better than how these other groups rated their communication with surgeons. This finding calls to question the validity of the surgeons' survey scores, and whether they truly had the best safety attitude.

Nationwide Outcomes of Patients with Myasthenia Gravis Undergoing Elective Surgery in the USA: A Propensity Analysis

Daniel Condie

Mentors: Girish Joshi M.D., Eric Rosero M.D., M.S.

Background: Nationwide outcomes of patients with myasthenia gravis (MG) undergoing surgical procedures in the United States are not well known. The purpose of the study was to investigate the rate of in-hospital postoperative complications and hospital length of stay (LOS) in patients with a diagnosis of MG undergoing major elective operative procedures in relation to a matched cohort of non-myasthenic patients.
Methods: The Nationwide Inpatient Sample was used to identify hospital discharges of patients with a diagnosis of MG undergoing major elective operating room surgical procedures in the United States between 2005 and 2009. Discharges with diagnoses of neurological conditions with clinical presentation similar to MG were excluded. Propensity scores (PS) derived from a logistic regression model were used to assemble a 1:1 matched cohort of patients with and without MG. Covariates in the model for PS included class of surgical procedure, age, sex, comorbidities, type of insurance, and hospital characteristics. The incidence of postoperative myasthenic crisis was assessed in the MG group. Differences in in-hospital postoperative adverse outcomes (death, hemorrhage/hematoma, respiratory failure, pulmonary embolism (PE) or deep vein thrombosis, sepsis, acute renal failure, pneumonia, myocardial infarction, and tracheostomy) as well as hospital LOS were assessed between the matched groups.
Results: Between 2005 and 2009, 18,351 patients with a diagnosis of MG undergoing major elective operating room procedures were identified from the database. The rate of postoperative myasthenic crisis was 3.6% (653/18,351). The PS algorithm produced a matched cohort of 3,695 discharges with a diagnosis of MG and 3,695 discharges without MG, balanced on baseline characteristics. MG patients had significantly higher incidence of postoperative respiratory failure (3.19 vs. 1.14%, P<0.0001) and PE or deep vein thrombosis, (1.24 vs. 0.65%, P=0.008) but similar rates of in-hospital mortality, hemorrhage/hematoma, sepsis, acute renal failure, pneumonia, and tracheostomy. In contrast, myocardial infarction rate was lower among MG patients (0.95 vs. 1.60, P=0.01). In addition, hospital LOS was significantly longer in MG than in non-MG patients (median [interquartile range] = 3 [2–5] vs. 3 [1-5] days, respectively; P<0.0001).
Conclusions: In this propensity-matched national sample, our study reveals that patients with a diagnosis of MG have higher rates of postoperative respiratory failure and PE after elective surgery. Nevertheless, the risk profile for other adverse outcomes seems to be similar to that of patients without MG.

Nationwide Safety of Robotic-assisted vs. Laparoscopic Hysterectomy in the United States

Daniel Condie

Mentor: Eric Rosero M.D., M.S.

Background: Despite its increased use, there is limited evidence supporting the safety of robotic hysterectomy (RAH). The purpose of the study was to investigate the safety of RAH in relation to standard laparoscopic hysterectomy (SLH) using the Agency for Healthcare Research and Quality Patient Safety Indicators (AHRQ-PSIs).

Methods: The 2009 Nationwide Inpatient Sample (NIS) was used to identify women who underwent RAH or SLH in the United States. Univariate analyses were performed to compare the two groups regarding the incidence of postoperative complications, including myocardial infarction, acute renal failure, and eight of the AHRQ-PSIs (death among surgical inpatients; foreign body left during procedure; iatrogenic pneumothorax; postoperative hemorrhage or hematoma; postoperative respiratory failure; postoperative pulmonary embolism or deep vein thrombosis; postoperative sepsis; and accidental puncture or laceration). Multivariate logistic and linear regression models were used to assess differences in postoperative clinical outcomes, length of hospital stay (LOS), and total hospital charges.

Results: A total of 23,713 RAH and 90,972 SLH procedures were identified. Patients undergoing RAH were older, had a higher comorbidity index, had a greater frequency of gynecologic malignancy, and were treated in teaching hospitals and in urban areas at a higher frequency. The overall incidence of complications was 2.95% in the RAH and 2.75% in the SLH group (P=0.42). Of all the clinical outcomes, only the unadjusted incidence of postoperative acute renal failure was significantly higher in the RAH group (0.22 vs. 0.09%, P=0.01). The rate of other postoperative clinical outcomes was similar between the groups (P>0.05 for each). The unadjusted hospital LOS (median [IQR]) was 1 [1-2] and 1 [1-2] days for RAH and SLH, respectively (P=0.97). After adjusting for demographics, comorbidities, presence of a diagnosis of cancer, and hospital characteristics, there were no significant differences in the rates of overall complications or postoperative acute renal failure. Linear regression analyses revealed that the adjusted hospital LOS [mean (SE)] was 0.1 (0.04) days shorter in the RAH group (P=0.003). However, hospital charges [mean (SE)] were $7,902 (2,494) higher in the RAH group (P=0.001).

Conclusions: The in-hospital postoperative safety profile of RAH is similar to that of SLH. Although patients undergoing RAH had a shorter hospital LOS, the hospital charges were disproportionately higher. The cost-effectiveness of RAH under the current conditions of the US health care system remains to be determined.

Evolving Characteristics of HIV Infected Pregnancies at a Single Institution

Sara J. Cooper

Mentors and Collaborators: Robert D. Stewart M.D., Elaine L. Duryea, Donald D. McIntire PH.D., Scott W. Roberts M.D., Barbara McElwee, Jeanne S. Sheffield M.D.

Objective: Over the past 26 years, significant advances have been made in the understanding and management of patients infected with HIV. We sought to determine if these changes in HIV care have had an impact on the characteristics of pregnant women with HIV and their pregnancies in a large cohort of HIV infected women at a single institution.

Study Design: This was a retrospective review of all pregnancies infected with HIV who presented for prenatal care at our institution from January 1986 through November 2012. Medical records were reviewed, and maternal, neonatal, and delivery data were ascertained. The data were divided into three cohorts representing different levels of antiretroviral therapy and analyzed for trends. Cohort 1 (pre-HIV interventions) includes data from 1986-1991, Cohort 2 (introduction of ZDV) includes data from 1992-2002, and Cohort 3 (multi-drug therapy) comprises the remaining data from 2003-2012.

Results: During the 26 year study period 1005 HIV infected pregnancies were identified. The incidence of HIV in pregnancy has remained stable at 0.2 –0.3% of all deliveries. The vast majority of our HIV infected obstetric population receives prenatal care and the number of patients receiving no prenatal care has decreased over time (27% to 6%, $p<0.001$). There has been a significant increase in maternal age and number of prenatal visits during the study period. The estimated gestational age at delivery has remained steady throughout the entire data set and there have been no changes in birthweight, 5-minute APGAR <7, prematurity, stillbirth, or neonatal deaths. The rate of cesarean section doubled (24% to 55%, $p<0.001$) for deliveries after 2000 following the release of guidelines recommending scheduled c-section for patients with viral loads >1000 copies/mL. Median maternal viral load and CD4 count have not changed significantly throughout the cohorts, with HIV viral load usually becoming non-detectable by delivery.

Conclusion: Over the past two decades, HIV infected women have presented for prenatal care at an older age, entered prenatal care earlier with more frequent visits and overall have decreased maternal viral copy number at delivery with antiretroviral therapy. Despite increased maternal age, pregnancy outcomes remain excellent. This study highlights the fact that appropriate prenatal care is associated with excellent pregnancy outcome in this high risk population.

Barbed Sutures and Wound Complications in Plastic Surgery: An Analysis of Outcomes

Roberto Cortez

Mentor: Jeffrey M. Kenkel M.D., F.A.C.S.

Goals: Technological advancements, along with their refinements, have substantially increased the amount of wound closure tools at the disposal of the surgeon. Barbed sutures, with a unique design containing circumferentially located barbs, could potentially decrease operation time and facilitate wound healing by eliminating the need to tie knots and providing even tension distribution across the wound. This study was conducted: 1) to determine whether using a barbed suture device in wound closure showed an increase, decrease, or no difference in wound complication development when compared to conventional non-barbed sutures 2) to analyze complication rates observed within the barbed suture population (Angiotech Quill[TM] SRS vs. Covidien V-Loc[TM]) to test for any significant difference between the two competing brands.

Methods: An IRB-approved retrospective chart review identified 1709 patients undergoing plastic surgery procedures from January of 2008 to January of 2012. In our database, a barbed suture device was used in a total of 372 cases and the type used (Angiotech Quill[TM] SRS vs. Covidien V-Loc[TM]) was recorded in each case. The Quill[TM] SRS device was used in 106 cases, while the V-Loc[TM] device was used in 266 total cases. Outcomes following these procedures were compared to outcomes of the same CPT codes where a barbed suture device was not used. Wound complications were defined as one or more of the following: infection, dehiscence, erythema, necrosis, seroma, hematoma, and delayed wound healing.

Results: Using multivariate analysis, barbed sutures appear to be associated with an increased incidence of wound complications (p=0.012), to include dehiscence (p=0.007), erythema (p=0.008), and necrosis (p=0.03) when compared to their non-barbed counterparts. Further exploration within the barbed suture population found the Covidien brand associated with an increased incidence of wound complications (p=0.03), particularly dehiscence (p=0.009), while the Quill brand was found to have a higher association with erythema (p=0.001) along the incision site.

Conclusions: Barbed sutures appear to be associated with an increased incidence of wound complications in plastic and reconstructive surgery procedures, with the Covidien V-Loc[TM] device showing a higher incidence of wound complication development compared to Angiotech Quill[TM] SRS device.

IbaAcute Effect of High vs Low Dialysate Sodium on Endothelial Cell Function During Hemodialysis

Kristin D'Silva and Christopher Molina

Mentors: Peter van Buren M.D.; Catherine Kim M.D.; Jula Inrig M.D.

Background: Intradialytic hypertension (HTN), a rise in blood pressure that occurs during hemodialysis (HD) treatments in up to 15% of patients, is associated with higher morbidity and mortality. The cause of intradialytic HTN is unknown but may be due to endothelial cell (EC) dysfunction. In vitro exposure of ECs to high sodium (Na^+) concentration promotes EC stiffness and imbalances in vasoconstrictors (endothelin-1 [ET-1]) and vasodilators (nitric oxide [NO]). We hypothesized that, among patients with intradialytic HTN, exposure to high dialysate Na^+ would lead to a decrease in NO and increase in ET-1 during HD.

Methods: We performed a 3-week, 2-arm, randomized crossover study among 16 HD patients with intradialytic HTN and compared the effects of high dialysate-to-serum Na^+ gradients (5 mEq/L above participants' baseline Na^+) vs low dialysate-to-serum Na^+ gradients (5 mEq/L below baseline Na^+ with lower limit of 134 mEq/L) on intradialytic changes in nitrite and ET-1. Differences between treatments were compared with repeated measures mixed linear regression and included randomization arm (high - low Na^+ vs low - high Na^+), treatment effect (high vs low Na^+), subject, time and session.

Results: Study participants (N=16) had an average age of 58.8 years, 38% were black, 56% were Hispanic, and 94% were male. Intradialytic changes in NO and ET-1 with high and low dialysate-to-plasma Na^+ gradients are shown in Figure 1. In the primary comparison of high vs low dialysate-to-serum Na^+ gradient, there were no significant differences in intradialytic levels of NO or ET-1 (Table 1). However, when compared by randomization arm, participants who received the low dialysate-to-serum Na^+ gradient followed by high compared to those who received the high dialysate-to-serum Na^+ gradient followed by low had a significant decrease in ET-1 (parameter estimate -0.49 pg/mL, p=0.04) and significant increase in nitrite during hemodialysis (parameter estimate +0.16 nM, p=0.02) (Table 1).

Conclusions: Patients who received the low dialysate-to-serum Na^+ gradient before the high dialysate-to-serum Na^+ gradient had higher levels of nitrite and lower levels of ET-1 throughout the three week study period compared to patients who received the high dialysate-to-serum Na^+ gradient before the low dialysate-to-serum Na^+ gradient. This suggests that the dialysate Na^+ concentration may have longer-term effects on endothelial cell function.

The Radiation Footprint on the Pediatric Trauma Patient

Zainab Farzal,
Mentors: Anne C. Fischer M.D. Ph.D., Sarah Wilson MSN, CPNP, Erica Brown MSN, CPNP, Lorrie Burkhalter,

Background: Overuse of radiation in patients has recently become an important topic of discussion within the medical community. Pediatric patients are most at risk. A recent study has proven the incidence of 1 brain tumor for every 10,000 head computed tomography (CT) scans among patients under the age of 10 in the ten years following a single scan[1]. Although there have been attempts to limit radiation dosage, there is no published data on the quantity of imaging done on the pediatric trauma patient. The high index of suspicion in trauma has created a paradigm of comprehensive imaging independent of symptoms. Our hypothesis was to identify the current amount of radiation used in a pediatric trauma patient for one visit and correlate the levels of imaging with trauma activation status in order to identify the subset of pediatric trauma patients most at risk for over-radiation.

Methods: This IRB-approved retrospective review of pediatric trauma patients at an ACS verified Level 1 independent children's hospital reviewed three levels of trauma activation (Stats, Alerts, Consults) from June 2010 to January 2011. Charts were analyzed for demographics, mechanism of injury, injury severity score (ISS), imaging modalities, and radiation dosages. Our study included the total number of Stats with representative cohorts from Alerts and Consults. 215 patients (N=1050) met inclusion criteria with complete dosimetry data available. RESULTS: The demographics include: gender (143M, 72F); age range <1-16 years (median 5.5), and activation status with average ISS score (Consults, 7.7 ± 9; Alerts, 8.8 ± 7; and Stats, 17 ± 14, respectively). Non-accidental trauma (NAT) and Stat activations exceeded all others in radiation exposure. Per Stat the number of CTs ranged from 0-10 with 2-3 CTs in 35% and 4-10 CTs in 40% for one admission. The studies most often repeated were head CTs (45%), face/sinus CTs (13.8%) and neck CTs (10%). The majority (66%) of outside CTs delivered more radiation, of which 50.0% of the doses were at least double the dosage delivered at the children's hospital.

Conclusion: This study is the first to correlate the amount of radiation exposure with trauma activation status. Most of the repetitive imaging was utilized in Stat activations and NATs and used 2-3 times as many CT scans. The identified factors associated with the most radiation include suspected NATs, Stat activations, and outside imaging. To minimize the radiation footprint, we may need to change the current practice of imaging to identify all possible injuries regardless of symptoms.

[1] Pearce, MS, Ph.D.. Lancet. 2012;380:499-505.

Activation Status	N (#)	Avg # CT/pt	CT Av Dose (mSv)	Avg # X-rays/pt	X-ray Av Dose (mSv)	Total dose (mSv)
Consults	61	0.3	0.79 ± 2.2	5.5	0.27 ± 0.5	1.06 ± 2.4
Alerts	83	1.6	5.34 ± 6.6	8.4	0.83 ± 0.6	6.07 ± 6.6
Stats	48	2.4	8.00 ± 8.4	13.7	0.91 ± 0.8	8.89 ± 8.8
NAT Consults	9	1.2	2.83 ± 1.8	28.0	2.03 ± 0.2	4.86 ± 1.7
NAT Alerts	2	1.0	3.28 ± 1.5	27.5	2.4 ± 0.0	5.68 ± 0.6
NAT Stats	12	3.0	9.19 ± 5.0	38.7	2.55 ± 1.8	11.74 ± 6.5

The Diagnostic Dilemma of Identifying Perforated Appendicitis

Zehra. Farzal

Mentors: Anne C. Fischer M.D., Ph.D., Nudrat Khan

Background: Despite 61 clinical trials on pediatric appendicitis in the Cochrane database over the last decade, a defined best clinical pathway for acute versus complicated appendicitis remains lacking. The lack of accuracy in the classification of appendicitis can affect the therapeutic course and associated costs since the average cost per case of complicated appendicitis at $12,300 which is twice as expensive as uncomplicated appendicitis at $6,355 per case[1]. We hypothesize that the variability in the diagnosis of complicated appendicitis results in a discordance.

Method: An IRB-approved retrospective review of appendectomies (N=1311) from a 16-month period from 2010 and 2011, excluding interval or incidental appendectomies and including CT imaging, was analyzed for demographics, length of stay (LOS), post-operative antibiotics, and radiological (R), pathologic (P), and operative (O) reports. The classification of appendicitis as "perforated" was compared in a 3-way analysis between radiology (R), pathology (P), and operative reports (O) to identify the incidence of discordance. Classification was compared to LOS, to determine if the diagnosis was consistent with being "acute" (A) 0-48 hours admission or "perforated" (P) >48 hours.

Results: 1241 appendectomies met criteria to enter the three study sets: P+O, O+R, and P+R, (N= 1241, 550, and 550, respectively). In study subsets with radiology (P+R and O+R), 47% had a CT with a definite radiologic diagnosis in 44%. The discordance in diagnosis in P+O, P+R, O+R was 11%, 15.7% and 16.6%, respectively. Pathology and operative reports had the most consistent diagnoses with a concordance of 89%. The O+R group had 16.6% discordance, of which 35% of cases were intraoperatively determined to be perforated, but actually 38.9% of those cases had a LOS <48hrs, consistent with being acute nonperforated. The LOS in the >48 hours group was nontrivial with a median of 88 hours (range 50-272).

Conclusion: There is a substantial discrepancy between operative, radiologic, and pathologic reports with the greatest discordance occurring between radiologic and operative diagnoses. The variation in the LOS confirms this discordance. Although, the diagnostic classification of complicated and uncomplicated appendicitis are not standardized which contributes to the discordance, the consequences are substantial in terms of medical costs and patient length of stay. Standardizing the criteria for the classification of the type of appendicitis across specialties may improve diagnostic accuracy needed for meaningful clinical trials and to identify best practices for optimal use of hospital resources and health care costs that continue to be elusive.

Lumbar puncture opening pressure in spontaneous cerebrospinal fluid otorrhea

Deniz Gerecci

Mentors and Collaborators: KP Allen, B Isaacson, JW Kutz, CL Perez, and PS Roland

Objective: Determine the incidence of increased intracranial pressure, measured by lumbar puncture opening pressure, in patients with spontaneous cerebrospinal fluid (CSF) otorrhea.

Methods: This is a retrospective case review at a tertiary care referral center. Patients included have undergone repair of spontaneous CSF otorrhea between January 2007 and December 2011. These patients have subsequently undergone postoperative lumbar puncture with measurement of the opening pressure to determine the presence of increased intracranial pressure. The main outcome measure is the lumbar puncture opening pressure.

Results: 19 ears in 17 patients underwent surgical repair for spontaneous CSF otorrhea via a transmastoid or middle fossa craniotomy. The average age at the time of repair was 58.9 years, 82.4% of patients were female, and 94.1% of patients were obese (BMI >30). The left ear was more commonly involved in 68.4% of cases. An encephalocele was observed in 63.2% of ears. Elevated opening pressure (greater than 20 cm/H2O) was noted in 41.2% of patients, and the median opening pressure was 19 cm/H20. Of patients with elevated intracranial pressure, 55.6% were treated either medically or surgically to reduce ICP. Two patients underwent placement of ventriculoperitoneal shunts and three were treated with acetazolamide.

Conclusion: As has been reported in the literature regarding spontaneous CSF rhinorrhea, elevated intracranial pressure is common in patients with spontaneous CSF otorrhea with 41.2% of patients affected in this series. These patients frequently require intervention in the postoperative setting to reduce ICP.

Aging, Adherence, and Antiretroviral Therapy: A Systematic Review of Adherence in Older HIV-Infected Individuals

Luwam Ghidei

Mentors: Mark Simone M.D. and James Rudolph M.D., SM

Introduction: Older patients with HIV may be at greater risk of medication non-adherence due to factors such as medication complexity. side effects. cost and cognitive decline. However. Some studies suggest that older patients with HIV are better adherers than younger HIV-.infected individuals. Suboptimal adherence to antiretroviral therapy (ART) can lead to increased viral load. immunosuppression. drug resistant viral strains. co-morbidities and opportunistic infections. Understanding trends of adherence to ART in older adults is critical. especially as the population of people living with HIV grows older.

Objectives: The purpose of this systematic review and meta-analysis is to determine if older people with HIV are more likely to adhere to antiretroviral therapy than younger people with HIV.

Design: A systematic search in PubMed. Embase, and PsyclNFO was conducted in July 2012 to identify peer-reviewed articles evaluating adherence to ARV in older adults. Major keyword and subject terms describing HIV. older age. and adherence were crossed with one another using a Boolean search. Independent reviewers screened abstracts. applied inclusion criteria. and appraised studies for quality of evidence. Primary and secondary meta-analyses with heterogeneity assessments were conducted and reported adherence levels as the relative risk of non-adherence in the older patients compared to '.- younger patients. To identify publication bias. funnel plots were visually examined for asymmetry and quantified using the method of Peter. Data was abstracted from studies by two independent authors.

Results: The systematic search yielded 2308 articles using no restrictions. Our preliminary analysis has identified eleven studies for full inclusion criteria after abstract and full text review. The meta analysis conducted on all studies with short term (less than one month) assessments found that older age reduced risk fOf non-adherence (RR 0.74 (0.63, 0.88). Among the studies using a shorter follow up time frame. those using an electronic measurement of adherence also showed older adults are more likely to adhere to antiretroviral medications (RR 0.56.0.42- 0.74 95% CI).

Conclusions: In this systematic review and meta-analysis. we found that older adults with HIV have a reduced risk for non-adherence to ART than their younger counterparts. Future studies should seek to elucidate contributing factors of good adherence in older individuals with HIV.

Bacteria detected in trigonitis biopsies of peri-menopausal women with recurrent UTI's

Matthew Glover

Mentor: Philippe Zimmern M.D., Ph.D.

Introduction: In the murine model, the presence of intrabacterial communities (IBC) causing recurrent UTI (rUTI) has been demonstrated. We studied bladder biopsies of women with rUTI and trigonitis to establish a human correlate to this plausible mechanism for rUTI.

Methods: Following IRB approval, peri-menopausal women with a longstanding history of rUTI diagnosed with extensive trigonitis [as defined by office cystoscopic findings of inflammation of the trigone including pustules, bullous lesions and/or submucosal calcifications (Figure)] were scheduled for bladder biopsies and fulguration of trigonitis under anesthesia as outpatient. Deep cold-cup trigonitis biopsies as well as control biopsies from non-infected sites, and urine cultures were systematically obtained. Bladder biopsies were immediately placed in LB medium at pH 7.4, and plated on LB and McConkey agar. Bacterial characterization was obtained with the api® 20 E kit (Biomerieux). The ability of identified bacteria to produce biofilm was confirmed by an established biofilm assay using crystal violet and spectrophotometry.

Results: Over the past year, 8 Caucasian patients (mean age 67 years, range 49-81) met inclusion criteria. Four grew bacteria (including *E. coli* and *Pseudomonas*) from the trigonitis biopsy site but none from the control sites (Table). Urine cultures obtained just before biopsies were positive in only 3 patients with no correlation with trigonitis biopsy cultures. Identified gram negative bacteria were capable of biofilm formation.

Conclusion: To our knowledge, this study indicates for the first time bacterial growth from women with rUTIs and trigonitis, suggesting a link with the mouse model.

Measurement of the Aortic Pulse Wave Velocity in MRI: an Automated Noninvasive Technique for Computing Transit Time

Akshay Goel

Mentors and Collaborators. Ronald Peshock M.D., R. McColl PH.D., K King M.D., A Whittemore M.D.

Purpose: Aortic Pulse wave Velocity (APV) has been shown to be associated with end organ damage independent of age, sex, and hypertension duration. The purpose of this study is to evaluate an automated approach for computing transit time (Δt) for the measurement of APV as a tool for future investigations and clinical application.

Methods and Materials: Phase contrast cardiac gated MRI of the aorta in the transverse plane at the level of the pulmonary artery was utilized from the Dallas Heart Study-2 (DHS2), a multiethnic, population-based study of cardiovascular health. A three-step algorithm was used to analyze all 1884 phase contrast MRI studies from the DHS2 central database. The algorithm functions in three key steps: 1) Isolating contours for the ascending aorta and descending aorta using a computer vision technique known as the Hough Transform. 2) Using isolated contours and phase contrast MRI to generate flow curves for the ascending and descending aorta. 3) Computing Δt defined as the time shift between the flow curves in the ascending aorta (AA) and descending aorta (DA), calculated using the half maximum of AA and DA. Fifty of these studies uniformly distributed across all Δt were then randomly selected and manually analyzed with the standard approach utilizing QFlow (v. 4.1.6, Medis) and the corresponding manually derived flow curves were used to compute Δt. The results from the manual analysis using QFlow were compared to results from the automated algorithm using linear regression Bland-Altman difference analysis.

Results: The mean Δt in the 1884 studies analyzed with our automated tool was 19.8+/-6.5 ms. In the validation set of 50 studies, linear regression analysis showed an excellent correlation between the automated (A) and manual (M) methods (r=0.97, A = 1.01M-0.885 ms). Bland-Altman difference analysis showed strong agreement with no significant bias (mean difference (A-M) = -0.386 ± 0.768 ms).

Conclusion: Our automated approach for computing transit time (Δt) for the measurement of APV demonstrates excellent agreement with the standard manual method. These findings suggest this approach could serve as a useful tool for future investigations and clinical application.

Lost Kids: Discovering the Barriers and Bridging the Gap behind a Missing Demographic

Vatsala Goyal

Mentors: Jessica Nguyen DO; Zaiba Jetpuri DO; Nora Gimpel M.D.; Patti Pagels MPAS, PA-C

Context: Family Medicine (FM) aims to provide comprehensive care for all ages, and primary care physicians have been found in many studies to be the major providers of well childcare. Current ACGME guidelines for FM residents require 4 months of structured pediatric training, but there is no provision for number of pediatric encounters that must occur before graduation. The Parkland/UT Southwestern Family Medicine Residency Clinic (FMRC) reported that only 13.5% of patients are pediatric.

Objective: To identify caregiver's perceptions towards the pediatric clinical services offered at FMRC in order to attract and retain the pediatric population at the clinic. Also, to assess FM residents' perception towards the adequacy of the pediatric curriculum at FMRC.

Methods: Combined prospective cohort study and cross sectional study. **Setting:** Family Medicine Residency Clinic at Parkland Health and Hospital System, Dallas, TX. **Participants**: English or Spanish speaking caregivers, 18 or older, who came with pediatric patients (0-17 years) to the FMRC in a 5 week time frame. **Instrument:** Series of phone interviews after initial visit to assess caregiver satisfaction. Self-administered survey to assess residents' satisfaction.

Outcome Measures: Primary measured outcomes are patient satisfaction with quality of care, clinic environment, health education, and identifying patient barriers to care. A secondary outcome is adequacy of the FM residents' pediatric curriculum.

Results: Thirteen of 97 participating caregivers have completed their first phone interview. Eighty two percent of caregivers were Hispanic and 91.8% were female. Physician rating did not correlate with likelihood of returning to clinic (p=0.072). Thirty three percent of residents were dissatisfied with their pediatric training. The majority (94.4%) reported inadequate number of pediatric patients seen in clinic, and most desired additional training in the 13 months-17 years age group.

Conclusions: Caregiver satisfaction rate with pediatric services and resident satisfaction with pediatric training at FMRC will be used to define an intervention to increase and retain the number of pediatric patients seen in the clinic.

Rounding on Ward Patients in the Age of the Electronic Medical Record

Peggy Guo

Mentor: James Wagner, M.D.

Introduction: Integration of electronic health records (EHR) in public teaching hospitals is a new and exciting advancement in the medical field. However, there are very few studies that consider its effect on daily rounding behavior of attending physicians and their teams. In order to get a better representation of rounding behavior in the electronic age, rounding and teaching behaviors of a convenience sampling of ten health care teams were observed and recorded on a standardized checklist for two months. This study captures a portrait of rounding behavior in the electronic age, and this portrait can serve as an important baseline as the electronic health records are being introduced in hospitals around the nation.

Methods: Ten internal medicine teams were followed on days when they were not on call. Behaviors were recorded on a checklist which included sections assessing patient care, EHR use, teaching, and distractions for each patient encounter.

Results: Of the total 305 complete encounters observed with the team, 81 occurred in the rounding room, while the other 224 occurred in the wards. Data analysis is summarized in the following table:

Variable	Room	Ward	p value
Distractions/encounter	2.3	7.1	<0.0001
Access of EHR	41%	13%	0.0001
Percent of patients visited	41%	88%	---
Examination of patient by the attending	30%	70%	<0.0001
Time spent with each visited patient	245s	217s	0.04
Discussion of plan with patients	31%	69%	<0.0001
Exchange of information with the patient	33%	82%	<0.0001
Interactions with other healthcare personnel	85%	80%	0.34
Teaching during rounds	38%	47%	0.16

Discussion: Rounding behavior differs significantly depending on location of patient presentation. When presentation occurred in the wards, there are significantly more distractions and fewer opportunities for EHR access, yet, interaction with patients are higher for all patient care categories except for time spent with patient. This can be explained by the higher volume of patients seen by the team when they round in the wards. Although the difference in teaching is not Significant, more teaching is seen in the wards than in the rounding room. These are important observations, especially in a large teaching hospital where this study was conducted. This study can provide insight on the rounding behaviors in the new electronic age as well as provide a baseline in which rounding can be improved upon in the future on the rounding behaviors in the new electronic age as well as

Reading Speed and Preference with Two Common Commercially Available Handheld Devices in Patients with Age Related Macular Degeneration

Ankur Gupta

Mentors: Adam Miller M.D. and Yu-Guang He M.D.

Introduction: Age related macular degeneration (AM.D.) is a leading cause of blindness among the elderly in developed nations and is associated with reading difficulty in affected patients. Reading has been cited as the primary rehabilitation goal of AM.D. patients as this ability is considered critical to maintaining a good quality of life. Given the surge in commercially available handheld reading devices, patients with underlying vision defects often seek counsel regarding devices that are best suited to their condition. This study aimed to add to the currently available reading rehabilitation literature by comparing patient responses to the iPad 2 (LED backlit glossy display), the Amazon Kindle (a less-glossy, 16-level gray scale E-Ink display), and a standard print periodical.

Methods: This was a prospective nonrandomized trial that compared reading speed and preference between three types of reading modalities in AM.D. patients vs. age-matched, non-AM.D. controls. Patients were recruited from the clinic of one of the authors (YGH) if they met the following criteria: a diagnosis of AM.D. (either wet or dry), ability to read English at a 7th grade reading level, and best-corrected visual acuity better than 20/50 (Snellen score) at distance or J2 (Jaeger score) at near. Age-matched control group participants met the same visual acuity requirements. Three unique passages were chosen from a 7th grade reading level book with roughly the same length. Using the same font and size on all three modalities, participants were asked to read aloud different passages (randomized) from each. The subject was not assigned the same passage twice to prevent memorization of the text. Reading time per passage was obtained with a stopwatch. After the completion of three reading tasks, the patient was asked to complete a brief written survey regarding his or her experience with the three reading media.

Results: We enrolled 20 patients with AM.D. and 15 non-AM.D. control patients. All experimental patients in the study had the dry form of AM.D.. Among AM.D. group patients, the average time to read a passage in a periodical was 113.3 s; on an iPad 2, 117.5 s; on a Kindle, 118.4 s. Among non-AM.D. control patients, the average time to read a passage in a periodical was 91.9 s; the on an iPad 2, 97.5 s; on a Kindle, 97.3 s. A 2x3 ANOVA showed a nearly significant effect of group, $F(1,32) = 3.88$, $p = 0.058$ and a significant effect of device, $F(2,64) = 2.73$, $p = 0.073$.

Discussion: The study will require an increased sample size in the future as it is currently not possible to provide definitive results on which device AM.D. patients read faster with or felt most comfortable using. Although both groups demonstrated that reading a periodical was faster than reading with a handheld device, there was not a demonstrable difference in reading speed when comparing the two devices in either group.

Minimally Invasive Endoscopic Surgery for Sinonasal and Skull Base Tumors: Functional and SinonaSAL Outcomes

Brian Harrow

Mentor: Pete Batra M.D.

Background: Endoscopic surgery has emerged as a minimally invasive technique for treating sinonasal and skull base tumors, but much remains unknown regarding factors that impact sinonasal and quality of life outcomes of patients after such surgery.

Objectives: To evaluate intermediate-term functional outcomes of patients who have undergone endoscopic surgery for sinonasal and anterior skull base tumors, and factors that impact such outcomes.**Design, setting, and participants:** This single-institution observational cohort study included 94 patients with benign or malignant sinonasal and/or skull base tumors. **Measurements:** Demographic, perioperative, and Sinonasal Outcome Test-20 (SNOT-20) scores.

Results: Endoscopic surgery improved mean SNOT-20 scores following surgery. At 6 months post-surgery, the mean improvement was 0.36 points ($p<0.01$) on a normalized 1-5 scale. Statistically-significant improvements in SNOT-20 scores ($p<0.05$) were seen for patients in one or more of the following groups: (i) patients with benign tumors; (ii) women; (iii) patients age> 60; (iv) patients with no prior smoking history; (v) patients without prior chemotherapy or radiation treatment; (vi) patients with no prior surgical treatment; (vii) patients receiving endoscopic surgery without accompanying open surgery; and (viii) patients not receiving adjuvant chemotherapy or radiation. Patients who had received prior chemotherapy and/or radiation treatment showed a slight, statistically-insignificant increase in mean SNOT-20 scores (0.013 points; $p=0.9$). All other identified groups of patients showed improved SNOT-20 scores that did not rise to the level of statistical significance. At 6 months post-surgery, single variable Ordinary Least Squares (OLS) linear regression showed prior chemotherapy/radiation treatment to be the single most powerful variable ($p<0.01$; $R^2 = 0.15$) for explaining changes in SNOT-20 scores. Similarly, multiple variable OLS found the two strongest predictors of SNOT-20 changes to be (i) a prior history of smoking ($p<0.05$); and (ii) prior chemotherapy/radiation treatment ($p<0.01$) ($R^2 = 0.24$).

Conclusions: Endoscopic Surgery improves average SNOT-20 scores for patients with sinonasal and/or anterior skull base tumors, particularly in patients who have no prior history of smoking or treatment by chemotherapy and/or radiation.

Renal Function Outcomes Following Laparoendoscopic Single-Site (LESS) Pyeloplasty

Brian Harrow

Mentor: Jeffrey A Cadeddu M.D.
Contributors: A. Bagrodia, E. Olweny, S. Faddegon

Background: Laparoendoscopic single-site (LESS) pyeloplasty has emerged as the next step in the evolution of minimally invasive pyeloplasty repair, but the literature on this topic lacks renal function outcomes and involves small cohorts with short-term outcomes.

Objectives: To evaluate the intermediate-term outcomes of LESS pyeloplasty using diuretic renal scans, estimated glomerular filtration rate (eGFR), and CKD stage progression in over 50 patients. **Design, setting, and participants:** This single-institution observational cohort study is comprised of 53 consecutive patients with symptomatic ureteropelvic junction obstruction who underwent single-incision robotic LESS (R-LESS) or conventional LESS (C-LESS) pyeloplasty by a single treating surgeon. **Measurements:** Demographic, clinical, perioperative, and intermediate term postoperative outcomes.

Results: Fifty-three patients underwent LESS pyeloplasty by a single surgeon from October 2007 to July 2012. Mean operative time and mean blood loss were 202 minutes and 35 ml, respectively. Conversion to other procedures occurred in 4 LESS surgeries (7.8%). Median hospital stay was 2.0 days. No intraoperative complications occurred. Mean follow-up was 12.1 months. Postoperative complications occurred with 11 patients (21%). Of these, 9 were $\geq$ Clavien Grade 3, 7 of which occurred in the C-LESS group. Symptomatic resolution was achieved in 49/51 cases (96.1%). Postoperative split renal function and serum creatinine improved in 89% and 79% of cases respectively, but were not statistically different from preoperative values. Diuretic renal scans performed at an average of 10.3 months following stent removal indicated radiographic resolution of obstruction ($T_{1/2} \leq 20$ min) in 41/44 cases (93.2%) for the cohort. Paired differences in preoperative and posteroperative $T_{1/2}$ were statistically significant at p<0.01 for the overall cohort. The difference in the pre-op and post-op proportion of patients with $T_{1/2} \leq 20$ min and $T_{1/2} \leq 10$ min was significant at the p= 0.001 level.

Conclusions: LESS pyeloplasty, when performed robotically or laparoscopically, is safe and efficacious. Both approaches provide excellent intermediate-term outcomes in terms of symptomatic relief and radiographic resolution of obstruction.

The Medallion Model: A Review of Safety of Body Contouring Procedures in an Outpatient Facility

Rachel Hein

Mentors and Collaborators: Jeffrey Kenkel M.D., Kathryn Davis Ph.D., Roberto Cortez, Ryan Constantine, and Kendall Anigan.

Introduction: The number of body contouring procedures performed in an outpatient and office based setting has increased dramatically in the past decade. With these changes in operational theater, patient safety demands top priority. Patients who undergo outpatient surgery are responsible for effectively treating the pain, ambulation, and even thromboembolism prophylaxis.

The Medallion Model is unique in its nature and allows multiple same day procedures or longer operations to be performed in an outpatient setting while maintaining them in a hotel environment supervised by nursing care. This model offers peace of mind to both the patient and the physician while giving safe, effective care immediately post-surgery.

Methods: A retrospective review of 275 major body contouring patients was conducted. The purpose of this study was to look at the current model used at UT Southwestern Outpatient Surgery Center for major body contouring surgeries to determine safety, efficacy, and complication rates of patients cared for in this environment.

Major complications included a return to the operating room within 48 hours, wound infection requiring hospitalization, unplanned hospitalization, hematoma or seroma requiring surgical intervention, deep vein thrombosis, and pulmonary embolism. Minor complications included anything else requiring unplanned physician intervention within the first 30 days.

Results: Complication rate including major and minor complications was 21.09% (58 patients.) Thirteen patients had wound infections for a total of 4.73% The most common wound complication was seroma. There were no deaths, deep vein thrombosis, or pulmonary embolism. One patient was hospitalized due to wound dehiscence.

Discussion: Comparing results for major body contouring patients is difficult. Inclusion parameters vary as do author definitions of favorable results. In respect to previous published studies with similar parameters, our complication rates compare very favorably. The use of the "Medallion Model" for patient care after body contouring procedures shows considerable merit and could potentially reflect a template of care that could be adopted by both private and academic surgeons. Medallion allows the physician to perform multiple outpatient excisional procedures and improves patient safety following surgery.

Retrospective Study of Anti-Vascular Endothelial Growth Factor Therapy in the Treatment of Branch Retinal Vein Occlusion and Predictive Factors for Visual Outcome

Mehwish Ismaily

Mentor and Collaborators: Peng Lei M.D., Brian Harrow, Deborah Chong M.D., Rafael Ufret-Vincenty M.D.

Introduction: The number of patients in the United States affected by branch retinal vein occlusion (BRVO) is approximately 180,000. As a result of this condition, visual acuity can be severely affected by macular ischemia, macular edema, or complications of neovascularization. A positive correlation has been found between the severity of BRVO-associated macular edema and the level of vascular endothelial growth factor (VEGF) in the vitreous humor. Anti-VEGF intravitreal injections are the current standard of care, two of which include ranibizumab and bevacizumab with the former being much costlier ($1593/dose vs. $42/dose, respectively). This study compares the efficacy of both drugs in the treatment of BRVO using the following determinants: 1) integrity of the inner segment-outer segment (IS-OS) junction line and 2) integrity of the foveal capillary ring.

Methods: In a retrospective study of 8 patients diagnosed with BRVO, 5 patients received bevacizumab and 3 patients received ranibizumab. Primary outcomes included differences between initial best corrected visual acuity (BCVA) and best BCVA during follow up, integrity of IS-OS junction, and integrity of foveal capillary ring. Secondary outcomes included time from initial BCVA to best BCVA during follow up, number of injections prior to best BCVA, difference between initial central macular thickness (CMT) on optic coherence tomography (OCT) and best CMT during follow up, time from initial CMT to best CMT during follow up, number of injections prior to best CMT, and mean number of months between injections.

Results: In the bevacizumab group, average improvement in BCVA was 3.6 +/- 1.8 Snellen lines. Best BCVA was achieved on average after 2.2 +/- 1.6 months and 1.4 +/- 1.1 injections. In the ranibizumab group, average improvement in BCVA was 1.7 +/- 2.1 Snellen lines. Best BCVA was achieved on average after 2.4 +/- 2.2 months and 2.0 +/- 1.7 injections. In the bevacizumab group, average improvement in CMT was 404 +/- 41 um with best CMT occurring on average after 1.1 +/- 0.1 months and 1.0 +/- 0.0 injections. In the ranibizumab group, average improvement in CMT was 286 +/- 47 um with best CMT occurring on average after 2.7 +/- 1.1 months and 2.5 +/- 0.7 injections.

Discussion: Bevacizumab may be superior to ranibizumab with greater improvement in BCVA, fewer injections to achieve best BCVA, fewer injections needed during follow up course, greater improvement in CMT, shorter time interval to best CMT, and fewer injections needed to achieve best CMT. The integrity of the IS-OS junction correlated well with visual acuity response to anti-VEGF treatment. The integrity of the foveal capillary ring was equivocal. Although statistical significance was limited by the small sample size, we have provided tentative support for further study of the comparison of these two drugs.

Anticoagulant Use is Associated With Improved Biochemical Control of High-Risk Prostate Cancer Patients Treated With Radiation Therapy

Corbin Jacobs
Mentor: D. Nathan Kim M.D., Ph.D.
Collaborators: Kevin Choe M.D., Ph.D., Jingsheng Yan Ph.D., Xian-Jin Xie Ph.D., Raquibul Hannan M.D., Ph.D., David Pistenmaa M.D., Ph.D., Yair Lotan M.D., Claus Roehrborn M.D.

Introduction: The coagulation system modulates multiple cancer pathways, including tumor proliferation, angiogenesis, host immunologic defense, and metastasis. Prior studies have reported improved survival and freedom from biochemical failure (FFBF) in prostate cancer (PCa) patients taking aspirin and other anticoagulants (ACs). We reviewed the outcomes of patients with high-risk PCa who received ACs and definitive radiation therapy (RT).

Methods: Patients with nonmetastatic high-risk adenocarinoma of the prostate (stage ≥ T3a, or Gleason score (GS) ≥ 8, or prostate-specific antigen (PSA) ≥ 20) treated with definitive RT between 2005-2008 at UTSW were identified. The AC group consisted of patients who had warfarin, clopidogrel, or aspirin recorded on the medication list at any clinical visit. FFBF of patients was determined using the Phoenix definition. Log-rank test was used to correlate FFBF with the ACs. Univariate and multivariate analysis (MVA) of FFBF to pretreatment PSA, GS, stage, hormone use, total RT dose, and ACs was performed.

Results: Among the 76 patients identified, 45 (59.2%) comprised the AC group. Within the AC group, 43 were taking aspirin, 8 were taking warfarin, 8 were taking clopidogrel, and 13 were taking multiple ACs. Median follow up was 61.2 months (range 3.1-89.4) for the AC group and 55.1 months (range 6.5-88.9) for the non-AC group. Patients receiving ACs exhibited significantly improved FFBF compared to the control group (p=0.0018; log-rank test). The estimated 4-year FFBF was 83.7% and 63.2% for the AC and non-AC groups, respectively. Among the patients taking a single AC, only aspirin showed significantly improved FFBF (p=0.0037). The hazard ratio for T-stage was 1.18 (95% CI 0.75, 1.85; p=0.4672) in the AC group and 1.67 (95% CI 1.09, 2.58; p=0.0196) in the non-AC group, implying a benefit from taking the AC. Aspirin use, T-stage, and N-stage remained significantly correlated to FFBF (p=0.0002, p=0.0056, and p=0.0040, respectively). The early and late grade 2 toxicity rates for rectal bleeding were 7.7% in patients on multiple ACs and 0% for patients on a single AC or no AC. No patients experienced grade 3 rectal toxicity.

Conclusion: Use of ACs in high-risk PCa patients improved the FFBF after definitive RT without increasing rates of rectal bleeding. This suggests that daily use of a single anticoagulant, especially aspirin, in high-risk PCa patients treated with definitive RT decreases biochemical failure and may improve outcome. Large prospective data are needed to validate the findings of this study.

Reduction of DAB2IP Correlates With Increased Biochemical Failure in High-Risk Prostate Cancer Patients Treated With Radiation Therapy

Corbin Jacobs

Mentor: D. Nathan Kim M.D., Ph.D.
Collaborators: Vasu Tumati, David Hong, Payal Kapur M.D., David Pistenmaa, M.D., Ph.D., Xian-Jin Xie Ph.D., Jer-Tsong Hsieh Ph.D., Debabrata Saha Ph.D.

Introduction: DAB2IP reduction has been associated with aggressive prostate cancer (PCa) behavior. Preclinical data suggests that loss of DAB2IP leads to resistance of PCa cells to cytotoxic effects of radiation partly due to enhanced double strand break repair and by increasing resistance to apoptosis. Therefore, we performed a pilot study to determine whether DAB2IP status could serve as a novel prognostic biomarker following radiation therapy (RT) in high-risk PCa patients.

Methods: Patients with high-risk disease (stage ≥ T3a, or Gleason score (GS) ≥ 8, or prostate-specific antigen (PSA) ≥ 20) treated with definitive RT between 2005-2012 at UT Southwestern were identified. Immunohistochemistry analysis for DAB2IP protein was performed on the biopsy specimens. DAB2IP tumor status was scored by an expert genitourinary pathologist. Freedom from biochemical failure (FFBF) of patient cohorts with and without DAB2IP reduction was determined using the Phoenix definition. Log-rank test was used to correlate FFBF with DAB2IP status. Univariate and multivariate analysis (MVA) of FFBF to pretreatment PSA, GS, stage, hormone use, total RT dose, and DAP2IP status was performed.

Results: 42 patients with high-risk PCa treated with RT were evaluated. DAB2IP reduction was seen in 11 patients (26.2%) whereas 31 patients (73.8%) retained DAB2IP. Median follow up for all patients was 23 months (range 1.4-76.1). Patients retaining DAB2IP exhibited markedly improved FFBF compared to patients with reduction of DAB2IP (p=0.035; log-rank test). The estimated 2-year FFBF was 91.6% and 65.5% for the DAB2IP retained and reduced groups, respectively, while the 4-year FFBF was 84% and 32.7%, respectively. Univariate analysis demonstrated DAP2IP status, GS, and N-stage as variables with statistically significant association to FFBF at this point of follow up. On MVA, including DAB2IP status, hormone use, hormone duration, and GS groups, DAB2IP status remained significant at p=0.0309.

Conclusion: DAB2IP deficiency in high-risk PCa patients portended a significantly worse FFBF after definitive RT. This suggests that DAB2IP deficiency may be a prognostic biomarker in that population. Limitations of this study include small sample size and short follow up. Additional studies are ongoing to evaluate these same patient specimens for expression of proteins in the DAB2IP pathway including androgen receptor, BCL-2, and EZH2. Implications for developing therapeutic intervention strategies to enhance radiation response for patients found to have DAB2IP reduced PCa are being investigated.

Extending immunization of children and adolescents in low-income areas of Dallas County

Stephanie Kim

Mentors: Nora Gimpel M.D., Patti Pagels, MPAS, PA-C; Nancy Volk

Context: Despite the extensive CDC recommendations for pediatric vaccination, vaccine-preventable diseases continue to be a problem. North Dallas Shared Ministries free clinic (NDSM) provides immunizations to uninsured and underinsured patients free of charge, but there is both underutilization of resources by the patients at times and lack of resources by the provider at other times, thus resulting in low immunizations rates. This study will provide suggestions that can be generally applied to primary care clinics that provide immunization services.

Objective: To increase the number of immunizations of children between the ages of 0-18 administered by NDSM through training volunteers and using outreach to improve access. **Human Subjects Review**: Waived by UT Southwestern IRB. **Design**: Cross-sectional survey. **Setting**: Dallas community, Texas; NDSM; UT Southwestern Medical School (UTSW). **Patients or Other Participants**: Incoming or current medical students at UTSW were recruited to complete all training and volunteer at NDSM. Caregivers of uninsured or underinsured pediatric patients (ages 0-18) receiving one or more immunization at NDSM were selected to survey their demographics and recruitment strategies.

Outcome Measures: Immunizations rate, perceptions of the service and learning experience by the UTSW medical students.

Anticipated Results: Thirty UTSW medical students were selected and 22 participated in training and volunteering (73%). The students' perception of the experience was generally very positive, with the overall quality receiving a score of 1.74 on a scale of 1~5, 1 being excellent and 5 being very poor. The number of pediatric patients receiving immunizations during June~July 2012 was increased by 9.3% from 2011.Outreach through schools and churches were effective, resulting in 19/38 (50%) being new patients.

Conclusions: Factors that effectively increase the immunization rate, both through increasing providers and increasing patients, were identified. This study will provide suggestions that can be generally applied to primary care clinics that offer immunization services.

Comparing Rural and Urban Burn Injury Admissions to Parkland Memorial Hospital Regional Burn Center

Michael Lee

Mentors: Steven Wolf M.D.
Contributors: K. Manchanda, J. Triantafyllou, A. Burris, V. Jones

Introduction: Risk of burn injuries varies widely across populations and locations. Effective burn prevention programs should identify and target the most vulnerable populations. This retrospective study compared the prevalence and characteristics of urban and rural burn injury admissions at Parkland Memorial Hospital Regional Burn Center.

Methods: Random samples from an inpatient database containing information from 1982 to 2010 were analyzed. Examination of medical records revealed the locations of the burn incidents. Utilizing the appropriate Rural Urban Commuting Area Code, burn locations were categorized as rural or urban.

Results: Although many more burns occurred in urban areas, the proportion of urban burns was not significantly different from the proportion of the state's urban population. No significant differences were found between urban and rural burns for patient age and gender, burn size, frequency of inhalation injury, length of hospitalization, physical location of injury (indoors/outdoors), units of blood and plasma given, days spent on a ventilator, days spent intubated, and days spent in the ICU. However, relatively more African Americans were burned in urban areas, while relatively more European Americans were burned in rural areas ($p < 0.05$). Although the proportions of other burn causes were not dissimilar, the proportion of burns caused by flames was higher in rural areas ($p < 0.05$).

Conclusions: The differences in patient demographics and burn causes warrant further investigation. Future research should examine how these factors have changed over time.

Applicability of Research to Practice: Research on burn demographics is invaluable for designing effective burn prevention programs that target at-risk populations and specific types of burn injuries. These findings suggest that rural fire safety is a potential target for burn prevention.

Drug Abuse Patterns in Pain Subjects on Opioid Therapy

Cheng-ting Lee

Mentor: Jianren Mao

Background: Abuse of prescription opioid and/or illicit drug is a significant challenge in chronic pain management. Social stigma, opioid-induced hyperalgesia, and individual perception of pain often further complicate treatment approach and duration. However, it is unclear whether drug abuse patterns would differ between clinical pain patients and subjects participating in pain research studies.

Methods: We reviewed the results of Random Urine Tests (RUT) conducted between 1/1/2003 and 12/31/2011 in 1) clinical patients treated at the Massachusetts General Hospital (MGH) Pain Clinic (Clinical Group) and 2) study subjects intended to participate in IRB-approved pain studies at the MGH Center for Translational Pain Research (Study Group). Drugs of abuse (DOA) were defined as unprescribed controlled substances and recorded, along with demographic and socioeconomic data, medical history, opioid dose regimen, types and duration of pain.

Results: In the Study Group (n=515), 515 RUT were conducted and 56 (10.9%) showed DOA. Of them, 69.6% were detected in subjects on opioid therapy. Cannabinoids (32.1%), cocaine (32.1%), and benzodiazepam (23.2%) were most commonly abused. While 6 out of the 7 healthy volunteers with drug abuse were male (86%), the rest of the Study Group drug abusers were rather equally divided between females (47%) and males (53%). In the Clinical Group (n=1,227), 1,067 RUT were conducted and 335 (31%) showed DOA. Of them, 85% were detected in subjects on opioid therapy. Cannabinoids (54%), cocaine (26%), and benzodiazepam (21%) were also the most commonly abused. While both study groups have a larger percentage of females, more males than females showed DOA in RUT.

Conclusion: Both clinical pain patients and study subjects share similar drug abuse patterns. Those with positive DOA in both groups also share similar socioeconomic backgrounds. Although the Study Group subjects were informed ahead of time that a RUT was part of the protocol's preliminary screening test, a large number of them were still tested positive with DOA. For the Clinical Group, those patients with positive DOA demonstrate a noticeably higher percentage for clinical comorbidities such as substances abuse and psychological disorders. Details regarding the impact of opioid therapy on drug abuse are currently under investigation.

Regional Brain Atrophy Clusters are Associated with CRP, IL-18, and BNP

Richard Lucarelli

Mentors and Collaborators: Amit Khera M.D., Ronald Peshock M.D., R. McColl, C. Ayers, M. Weiner, K.S. King

Purpose: Multiple biomarkers have been associated with total brain atrophy. However, little is known about their relationship to segmental atrophy in a large, multi-ethnic, population-based sample.

Materials and Methods: 3D-MPRAGE brain images obtained at 3T from 2082 participants of the Dallas Heart Study (DHS) 2 were analyzed with Freesurfer and outlier analysis was performed. Divisive eigenvalue clustering of 89 brain segments yielded 24 groups with linked atrophy patterns. Plasma C-reactive protein (CRP), IL-18, homocsysteine and B-type natriuretic peptide (BNP) obtained 7 years prior during DHS 1 were available for 1343, 840, 1333 and 1331 participants, respectively. Multivariate linear regression analysis with adjustments for age, ethnicity, and gender were used to demonstrate associations between biomarkers and atrophy clusters.

Results: Nine atrophy clusters were associated with CRP (P=0.0001-0.0380: Insula and Medial Orbito-Frontal Cortex, Parahippocampii, Fusiform Gyrus and Inferior Temporal Lobe, Inferior Frontal and Superior Temporal Cortex, Frontal Cortex, Middle and Superior Temporal and Inferior Parietal Cortex, Somatosensory Cortex, Thalamus/Palladium/Putamen, and Pars orbitalis and Lateral Orbital-Frontal Cortex).
Three atrophy clusters were associated with IL-18 (P=0.003-0.0134: Frontal Cortex, Pars orbitalis and Lateral Orbital-Frontal Cortex, and Inferior Frontal and Superior Temporal Cortex).
Six atrophy clusters were associated with BNP (P=0.0053-0.0383: Right Cingulate Cortex, Insula and Medial Orbito-Frontal Cortex, Lateral Occipital Cortex, CSF, Nucleus Accumbens Area, and Amygdala and Hippocampus). Homocysteine did not have any significant correlations.

Conclusions: The markers studied had associations with distinct patterns of segmental atrophy indicating they may have unique interactions in different brain regions. This suggests that distinct inflammatory and other pathways may be at work in specific regions of the brain and that their localized effects may be obscured by approaches evaluating solely total brain volumes.

Variations in Hemoglobin Levels for Burn Patients

Kshitij Manchanda

Mentor: Steven Wolf, M.D.
Collaborators: Michael Lee, Jonathan Triantafyllou

Burn patients are initially managed by stabilizing the Airway, Breathing, and Circulation (ABC's). Because of severe blood loss from the injury, transfusions with packed RBCs have been used to prevent anemia. However, there is no "strict" protocol as to when transfusions should be administered and very little research has been done to analyze the variations in hemoglobin over time.

Fifty random samples were collected from an inpatient database in 2011 for this retrospective study. The patients studied were at least 18 years of age and had at least a 20% TBSA burns. Hemoglobin measurements are recorded on routine CBCs and this data is recorded across hospitalization along with the time of blood withdrawal.

The data was plotted to demonstrate variability in hemoglobin with time for the first 50 days of hospitalization. The hemoglobin concentration was initially very high (>15 gms/dl) most likely reflecting the loss of both fluid and RBCs and then decreases markedly to between 7 and 8 gms/dl within 3 to 4 days. After this, the hemoglobin value stays relatively constant with little variability among subjects despite blood withdrawals and transfusions throughout the patient's stay. The data follow a first order curve which fits closely to a logarithmic regression with an r^2 value of 0.8.

Maintaining fluid and cellular volume are key to stabilizing burn patients when admitted. We showed that hemoglobin concentration decreases logarithmically in the first few days of hospitalization that then stabilizes into a narrow range. This is perhaps related to monitoring and intermittent transfusion to compensate for ongoing losses and inadequate synthetic response. These findings will help define a more useful approach/protocol to blood transfusions in burn victims.

Selective Laser Trabeculoplasty (SLT): Predictors of failure

Nathan L. Markel

Mentor and Collaborators: Karanjit S. Kooner M.D. and Eric J. Chang

Purpose. SLT is widely used to control intraocular pressure (IOP) in glaucoma. We wished to determine predictive factors for long term success of SLT performed by full time faculty at a University Eye Clinic in Dallas.

Methods. Charts of patients with primary open angle glaucoma who underwent SLT between 2001 and 2011 were reviewed retrospectively. Those with follow up < 3 months, prior ALT/SLT, filtering procedure or inadequate data were excluded. The dependent variable was time to failure after SLT. Failure was defined as any additional medication, ALT/SLT, or glaucoma filtering surgery. All patients were treated with 360° SLT. Logistic regression and receiver operating characteristic (ROC) analysis was performed to assess correlation between time to failure after SLT and age, pre-op IOP, C/D ratio, visual field defect (VFD), family history of glaucoma, refractive error, hypertension, diabetes, number of medications, laser energy used, central corneal thickness.

Results. Evaluable data was obtained on 189 patients; mean age 64, 44% male, 56% female, 49% white, 32% black, 12% Hispanic and 7 % others. 29.6% (56/189) were classified as SLT failures. Failure and non-failure patients had equal follow-up duration of median 2 yr. Age and laser energy were not significant predictors of SLT. In multivariable logistic regression models, statistically significant risk factors associated with SLT failure were family history of glaucoma (odds ratio (OR) = 1.7, 95% CI: 1.1-2.7, p=0.02), higher pre-op IOP (OR =1.1, 95%CI: 1.0-1.15, p=0.03), and moderate to severe VFD (OR =2.6, 95% CI: 1.3-5.2, p=0.006); ROC AUC = 0.71 (95% CI : 0.62-0.80).

Conclusions. SLT results were better in patients without family history of glaucoma and who had lower pre-op IOP and mild to moderate visual field defects.

Glutamatergic Signaling in the Anterior Cingulate Cortex in Schizophrenia

Caitlin Meyer

Mentors and Collaborators: Carol A. Tamminga M.D., Wei Li,
Subroto Ghose M.D., Ph.D.

Imaging studies in schizophrenia indicate that both the hippocampus and anterior cingulate cortex (ACC) show reduced gray matter volume and reduced activity during task related activation in schizophrenics compared with normal controls. Post-mortem molecular findings suggest declarative memory impairments may be linked to alterations in glutamatergic transmission in both the hippocampus and ACC. In the hippocampus, a reduction in dentate gyrus (DG) glutamatergic output could simultaneously generate a change in homeostatic plasticity processes in cornu ammonis 3 (CA3) that result increased activity in reaction to reduced afferent stimulation from the DG onto CA3 neurons (a process that could increase the pattern completion functions of CA3) *and* a decrease in glutamatergic signaling functions specific to the DG associated with pattern separation. In the anterior cingulate, decreased excitatory and/or increased inhibitory glutamatergic transmission could decrease error detection functionality. Cumulatively, the increase in pattern completion functionality caused by increased activity in the CA3 coupled with decreases in pattern separation functionality in the DG of the hippocampus along with decreased error detection signaling in the anterior cingulate could result in false associations that generate psychotic content while laying down new memories. To investigate this model we have collected hippocampal and anterior cingulate post-mortem tissue from a cohort (n=40) of 20 schizophrenics (10 off-drug, and 10 on-drug) and 20 matched normal controls. The hippocampus was dissected into 5 subunits (enterhinal cortex, subiculum, CA3, cornu ammonis 1, and DG) while the ACC was dissected into glutamatergic cortical layers I-III, and GABAergic layers Va-VI. We are currently measuring the protein levels of glutamate receptor subunits and postsynaptic scaffolding and signaling proteins using Western Blot analysis in the 5 subunits of the hippocampus and layers I-III, and Va-VI of the ACC. Our preliminary data demonstrates increased excitatory glutamatergic signaling activity in the CA3, as well as decreased excitatory glutamatergic signaling activity in the DG of schizophrenic hippocampi thus supporting our model. PSD95 is also increased in anterior cingulate cortex in layers 1-3 of schizophrenia tissue suggesting an increase in synaptic strength within this area, possibly due to increased afferent stimulation from the hippocampus. Results from this model could present novel pharmacological treatment targets for schizophrenia as well as guide

Utilizing Caprini Score and ASA Score as Predictors of Morbidity in Plastic Surgery Procedures

Travis J. Miller

Mentor: Jeffrey M. Kenkel M.D.

Goals: The Caprini Risk Assessment Model (RAM) has been validated as an effective tool in defining risk and prophylactic guidelines for venous thromboembolism in postoperative patients, but its efficacy in risk assessment for other complications has not been analyzed. The American Society of Anesthesiologists (ASA) score is another system that evaluates systemic health of patients preoperatively. Previous work has shown that ASA score has predictive value for perioperative complications, but this scale has not been applied purely for plastic surgery procedures. Our investigation analyzes the efficacy for these scales to predict complications in plastic surgery procedures and directly compares these scales for this purpose.

Methods: The study population included all eligible plastic surgery patients from January 2008 to January 2012 including reconstructive, body contouring, and cosmetic procedures. Caprini Score was calculated using the 2005 Caprini RAM using data from patient records. ASA score was calculated by the attending anesthesiologist present for the encounter. Patients were followed for 30 days after each encounter and complications were noted if present. Complication was defined as one or more of the following: infection, dehiscence, erythema, necrosis, seroma, hematoma, delayed wound healing, partial flap failure, flap thrombosis, full flap failure, or deep vein thrombosis (DVT).

Results: 1599 unique patient encounters were identified for our study. The overall complication rate as defined above was 29.71% and DVT incidence was 1.50%. Patients with a Caprini score of >8 were more likely to experience complications compared to patients with a Caprini score of 0-2 (odds ratio [OR] 3.16, $p < .001$) or 3-4 ([OR] 2.34, $p < .001$). Patients with an ASA score of 3 were significantly more likely to experience wound complications compared to patients with an ASA score of 1 ([OR] 3.14, $p < .001$) or 2([OR] 1.31, $p = .042$). In directly comparing Caprini and ASA scores, patients with a Caprini score of >8 were more likely to experience wound complications than patients with an ASA score of 1 ([OR] 3.71, $p < .001$) or 2 ([OR] 3.63, $p = .032$), but there was no significant difference in complication rates found between a Caprini score of >8 and an ASA score ≥3 ([OR] 1.16, $p = .513$).

Conclusions: The Caprini RAM and ASA score both show increases in risk as each score increases. A 1 point increase in ASA score is comparable to a relatively large increase in Caprini score. At high Caprini (>8) and high ASA (≥3) scores, there is no evidence to suggest a difference in prognostic value between the two systems

Low Dialysate Sodium Reduces Systolic Blood Pressure in Patients with Intradialytic Hypertension

Christopher Molina, BS;

Mentor and collaborators: Jula Inrig M.D., MHS, Kristin D'Silva; Peter van Buren M.D.; Catherine Kim M.D.

Background: Intradialytic hypertension (HTN), defined as an increase in systolic blood pressure (SBP) >10 mmHg from pre to post-hemodialysis (HD), occurs frequently in approximately 15% of HD patients. Patients with intradialytic HTN exhibit significantly higher SBP and have increased risk for non-access related hospitalization and mortality. Both chronic impairments in endothelial cell (EC) function and acute intradialytic increases in plasma endothelin-1 have been observed in patients with intradialytic HTN. In vivo studies identified acute increases in sodium (Na) to be associated with EC dysfunction suggesting dialysate [Na] gradients may regulate intradialytic SBP. Thus, we hypothesized low vs high dialysate-to-serum [Na] would decrease SBP during HD and limit the occurrence of intradialytic HTN.

Methods: 16 adult ESRD patients with intradialytic HTN were randomized into a 3-week, 2-period crossover study comparing the acute effects of low vs high dialysate-to-serum [Na] on intradialytic SBP. High dialysate [Na] was set as patient's serum Na +5mEq/L and low dialysate [Na] was set as patient's serum Na -5mEq/L with a lower limit of 134 mEq/L. Repeated measures and mixed linear regression (adjusted for randomization arm, subject, time, and session) were used to compare differences in the absolute and intradialytic change in SBP between low vs high dialysate [Na].

Results: Baseline predialysis serum [Na] (137.5 mEq/L) decreased (-0.5 mEq/L) with low dialysate [Na] and increased (+2.4 mEq/L) with high dialysate [Na]. Compared to high dialysate [Na], both SBP (parameter estimate -9.9 mmHg, p<0.0001) and the change in SBP (-6.1 mmHg, p=0.0005) were significantly lower with low dialysate [Na] (Figure 1 and Table 1). Furthermore, both SBP and the change in SBP during HD (parameter estimates -8.3 mmHg and -9.9 mmHg respectively, p<0.0001) were much lower among participants randomized to low followed by high dialysate [Na] compared to participants randomized to high followed by low dialysate [Na].

Conclusions:
Treatment with low dialysate-to-serum [Na] significantly lowers intradialytic SBP and may act to reduce the risk of non-access related hospitalizations and mortality in HD patients with intradialytic HTN. This intervention could be further explored in other hypertensive HD patients.

The Wait for the Weight:
Pediatricians' Communication about Weight
to Overweight and Obese Latino Children and their Parents

Sergio Montaño

Mentor and Collaborators: Christy Turer M.D., Glenn Flores M.D., and Kim Hoang

Background: Latinos are among the most overweight (OW) racial/ethnic groups of US children. It is unknown, however, whether language barriers impact the communication of childhood OW.

Objective: To determine whether and how language incongruence is associated with communication about OW for Latino children.

Design/Methods: Cross-sectional analysis of video- or audio-recorded primary-care visits with pediatricians and OW (body mass index ≥85th%) 6-12 year-old Latino children recruited from academic and community clinics. Language proficiency was assessed using US Census Bureau questions, with language incongruence (LI) defined as pediatrician limited Spanish proficiency combined with parent limited English proficiency (LEP). Recorded visits were analyzed and transcribed. Direct communication of OW, who broached the topic first, use of growth charts, and communication of a weight-management plan were determined by reviewing recordings and transcripts.

Results: The 26 visits (18 video and eight audio) included 26 participants and 15 pediatricians (including 10 resident/attending pairs). The mean child age was nine years old; 100% were OW and 84% were obese. 89% of parents were OW and 60% were LEP. 43% of pediatricians were Spanish-proficient. Pediatrician-parent language was incongruent in 24% of visits. Direct communication of OW occurred in 90% of language-congruent (LC) vs. 50% of LI visits (P=.03). Parents were the first to broach the topic of OW in 10% of LC vs. 50% of LI visits (P=.03). Pediatricians used growth charts in 80% of LC vs. 0% of LI visits (P<.001). Weight-management plans were conveyed in 55% of LC vs. 33% of LI visits (P=.4). One pediatrician stated, "You are not growing any taller, so you have to do the hard adult thing and [lose weight]." At least one culturally relevant dietary recommendation was made in 19% of visits. One pediatrician noted, "Less fat, less *manteca*, less *avena*, less sugar," and another, "No tacos. You need to buy fruit."

Conclusions: Pediatrician-parent LI is associated with a lower likelihood of direct communication of child OW/obesity and use of growth charts, but a higher likelihood of parents, instead of doctors, being the first to broach the topic of OW. Regardless of LI, many OW Latino children do not receive weight-management plans or culturally relevant dietary recommendations.

Intravascular Ultrasonography Analysis of the Everolimus-Eluting Stent in Coronary Chronic Total Occlusions

Rachita Navara

Mentors: Emmanouil S. Brilakis M.D., Ph.D. and Bavana Rangan BDS

Purpose: Coronary artery disease (CAD) is consistently the number one cause of death for both men and women worldwide. Of the millions of patients diagnosed with CAD, approximately 1 in 5 is found to have a coronary artery that has been 100% blocked for three months or longer, representing the most formidable subset of atherosclerosis: chronic total occlusion (CTO). While drug-eluting stents have demonstrated success in patients with less severe coronary atherosclerosis, little is known about their efficacy in CTOs, which are currently managed by bare metal stents associated with high rates of restenosis. The present study aims to evaluate the effectiveness of the novel Everolimus-Eluting Stent (EES) in CTOs, using intravascular ultrasonography (IVUS) to assess restenosis.

Methods: One hundred consecutive CTO patients who were successfully treated using EES at the Dallas VAMC between 2009-2012 were enrolled in the AngiographiC Evaluation of the Everolimus-Eluting Stent in Chronic Total Occlusions (ACE-CTO trial: NCT01012869). Patients underwent follow-up angiography and IVUS imaging at 8 months and clinical follow-up for up to 12 months. The primary endpoint of this study, binary angiographic restenosis, was defined as >50% minimum lumen diameter stenosis, as assessed by 8-month follow-up quantitative coronary angiography in the treated coronary segment. The primary endpoint of the IVUS analysis was 8-month in-stent neointimal hyperplasia (NIH) volume, defined as the difference between stent and lumen volume.

Results: Of the 226 patients who underwent CTO percutaneous coronary intervention (PCI) during the enrollment period, 129 were eligible and 100 agreed to participate. Mean age was 64±7 years, and 99% of the patients were men. Patients had high prevalence of hypertension (91%), hyperlipidemia (90%), diabetes (47%), prior myocardial infarction (51%), and prior PCI (21%). The CTO target vessel was the right coronary artery (70%), left anterior descending artery (16%), circumflex (13%), or left main (1%). The mean number of implanted stents was 3.3±1.3, mean stent diameter was 2.8±1.1 mm, mean stent length was 85±34 mm, and 94 patients had overlapping stents. Binary angiographic restenosis was 45%. Follow-up IVUS analysis of 55 patients revealed low median minimum lumen area (3.3 mm^2) and high NIH volume (103.6 mm^3).

Conclusions: Everolimus-eluting stent implantation in CTOs is associated with high rates of angiographic restenosis and high NIH volume, suggesting the need for novel therapeutic strategies to improve outcomes in this complex and challenging lesion subgroup.

Postpartum Thromboembolism in the Obstetric Patient

Fiona Nicholson

Mentors and Collaborators: Karen Wilson M.D., Heather Lytle M.D., MPH, Jeanne Sheffield M.D.

Introduction: To evaluate the incidence and risk factors of postpartum thromboembolism (TE) over 20 years.

Methods: From December 1, 1992 through December 2009, all women who had a postpartum thromboembolic event, up to 6 weeks after delivery, were identified by ICD-9 code; charts were verified for accurate diagnosis. The incidence of TE by mode of delivery was identified. Maternal demographics and antenatal characteristics were evaluated. Women identified at risk for TE were given SCDs and/or medical anticoagulation for prophylaxis otherwise an early ambulation protocol was utilized.

Results: 48 women were identified to have a postpartum TE. The incidence of postpartum TE has ranged from 0/1,000 to 0.49/1,000, highest in the last 2 years. It is more common in the cesarean delivery (CD) group when compared to the vaginal delivery (SVD) group (5/10,000 vs 8/100,000). No TEs were identified in women who underwent cesarean hysterectomy (n=417). Furthermore, women who had a TE postpartum were more likely to be older (29.5 ± 6.8 yrs vs 25.2 ± 5.9 yrs, p <0.001), have increased BMIs (33.9 ± 8.0 vs 31.1 ± 5.7, p= 0.002), underwent CD (p <0.001), have HTN (p= 0.002), deliver preterm (37.7 ± 3.7wks vs 39.3 ± 2.2wks, p <0.001), have prolonged rupture of membranes >24 hrs (p= 0.007), and have multiple gestation (p <0.001).

Conclusions: Our overall incidence of postpartum TE is significantly lower in comparison to nationally published rates despite an increasing number of CDs. Additionally, traditional risk factors for TE remain valid.

Prevalence of obesity in an ethnically diverse pediatric HIV population

Jennifer Nwankwo

Mentors and Collabortators: Roy Kim M.D., MPH, Janeen Graper, Alejandro de La Torre, Ximena Lopez, Theresa Barton M.D.

HIV infection disproportionately affects children and adolescents in minority groups. Minority children are also more likely to be obese and suffer from obesity related comorbidities. In spite of these factors, there remains a paucity of data with respect to the burden of obesity in the pediatric HIV population. We hypothesized that HIV infected children from minority groups would have a greater prevalence of obesity compared to non-minority HIV infected children, and similar to published national norms. Furthermore we hypothesized that HIV infected children from minority groups would have lower height and weight measurements compared to non-minority HIV infected children. We conducted a chart review of a racially diverse cohort of HIV infected children seen at an urban medical center and examined the prevalence of obesity and dyslipidemia. Age, height, weight, gender, markers of virologic control, and medications were recorded. Statistical analysis consisted of univariate and bivariate descriptive statistics stratifying by race and ethnic group. Obesity was defined as a body mass index (BMI) z-score >=2.

The records of 180 patients (mean age 16, range 3-20y) were reviewed. The overall obesity prevalence was 7% compared to 18% from published population based norms. Within our cohort, obesity prevalence was 9.5% among non-Hispanic black individuals and 3% among Hispanic individuals however the differences were not statistically significant (Fisher exact =0.3). As continuous variables, height z-score, weight z-score, and BMI z-score did not differ significantly between race/ethnic categories. Underweight, defined as a weight z-score < -2 was associated with Hispanic ethnicity (p=0.03). This relationship was maintained after controlling for markers of virologic control. For the entire group, height z-score correlated directly with CD4 nadir (Pearson correlation 0.17; p=0.03) as did the weight z-score (correlation 0.17, p=0.04). However, BMI z-score was not related to the CD4 nadir. Secular changes in the treatment of HIV over time may play a role in the association between virologic control and growth since age at the time of the data collection was associated with a lower CD4 nadir (p<0.01), higher viral load (p=0.02), and lower height z-score (p=0.04). In summary, obesity was less common among HIV infected pediatric cohort compared to non-infected population norms. BMI z-score or obesity status was not associated with race or ethnicity.

Fractionated Cyberknife Radiotherapy for Intracranial Neoplasms

Aaron Plitt

Mentor: Samuel Barnett M.D.

Introduction: The Cyberknife is a frameless robotic radiosurgery system used to deliver radiation in a single fraction or sometimes using a hypofractionated approach. Fractionation has the advantage of allowing normal cells a time to recover between treatment sessions. Using the Cyberknife with a more conventional fractionation strategy (~25 fractions) may have all of the benefits of the Cyberknife's accuracy, as well as the fractionation benefit of conventional external beam therapy.

Methods: 37 patients were identified with intracranial neoplasms that were treated with fractionated Cyberknife radiotherapy. All patients underwent treatment at The University of Texas Southwestern Medical Center between March 2008 and January 2012. Fractionated Cyberknife treatment plans were compared to simulated conventional plans in each case.

Results: Tumor control was achieved in 34 patients (92%) with a mean follow-up of 20 months. Mean total dose was 47.9 (34 – 50.4 Gy) delivered in 25-28 fractions. One patient showed an interval increase in tumor size without enhancement. Two patients developed increased enhancement and slight enlargement of the cystic component of the tumor. Another patient developed increased T2/FLAIR signal change adjacent to the treatment volume consistent with radiation toxicity. No patients developed progressive visual loss. The fractionated Cyberknife plans were more conformal and had sharper dose distributions than the simulated conventional plans in each case.

Discussion: Intracranial lesions that are refractory to medical and surgical treatment are challenging lesions. Fractionated Cyberknife radiotherapy may be useful in managing these patients. Visual outcomes and tumor control rates are satisfactory. Long term radiographic follow-up is necessary.

Efficacy of the Camp CHAMPS youth obesity intervention.

Archana Reddy

Mentors and Collaborators: Nora Gimpel M.D., Brad Walsh, Donna Persaud M.D., Sobha Fuller, Jeffrey Howard, Sue Pickens

Context: Pediatric obesity rates in the US tripled during 1980-2002. Children with a high BMI percentile rank are at risk for being obese as adults. Camp CHAMPS is a 4-day free summer camp teaching nutrition, fitness and self-esteem to overweight and obese children in Dallas County. **Objectives**: To determine the effect of Camp CHAMPS on participants' (1) knowledge and behavior regarding nutrition, fitness, and the risks of overweight and obesity, and (2) BMI before and after camp.

Methods Observational study pre- and post-intervention using a prospective cohort. Setting: General community. **Participants**: Children age 10-16 who attended camp and completed pre- and post-camp survey (n=83) are study subjects for objective 1; all children who attended camp and participated in health screening (n=249, 41% Hispanic, 36% African American) are study subjects for objective 2. **Instrument**: Validated 20-question multiple choice self-administered written survey assessing knowledge and behavior regarding nutrition, fitness, and risks of overweight and obesity.

Outcome Measures: (1) % participants who improved their knowledge & behavior score on survey questions; (2) change in BMI z-score.

Results: Analysis performed on 8 of 20 survey questions measuring knowledge showed significant improvement ($p<0.05$) in some areas at the end of camp, while in other areas no significant improvement was seen. The 12 questions measuring behavior will be analyzed at 3 and 9 months post-camp. Anticipated Results: Follow-up measurements at 3 and 9 months will show significant improvement in knowledge and behavior, as well as a decrease in BMI.

Conclusions: Preliminary results indicate significant knowledge improvement in some areas regarding nutrition, fitness, and risks of overweight and obesity. Further data is needed to determine long-term knowledge gain and change in behavior and BMI.

Music Therapy Improved Patient Satisfaction but Had No Effect on Endothelial Function Among Patients Undergoing Cardiac Catheterization: Results from the Functional Change in Endothelium after Cardiac Catheterization With and Without Music Therapy (FEAT) trial

Lindsay Ripley

Mentor: Emmanouil Brilakis M.D.

Background: Music therapy may reduce stress during invasive procedures. We examined the effect of music therapy on patient satisfaction and endothelial function in patients undergoing cardiac catheterization.

Methods: Seventy patients undergoing cardiac catheterization were randomized to music therapy (MusiCure, by Niels Eje; relaxing music designed for therapeutic use, n=36) or no music therapy (n=34). Reactive hyperemia peripheral arterial tonometry was performed before and after catheterization using the EndoPAT 2000 (Itamar Medical Inc., Caesarea, Israel) to measure the reactive hyperemia index (RHI). All patients completed an anxiety questionnaire after catheterization.

Results: Mean age was 62 ± 8 years and 99% of the patients were men. Patients in the two study groups had similar baseline characteristics and underwent similar procedures (Table). Overall, the RHI increased from 1.76 ± 0.59 before to 1.98 ± 0.56 after catheterization (p=0.01). There was no significant difference in RHI change and in State-Trait Anxiety Inventory score between the two study groups, but patients receiving music therapy reported higher satisfaction from the procedure.

Conclusion: Among patients undergoing cardiac catheterization, music therapy improved patient satisfaction but had no effect on RHI, which increased in both groups.

Obesity and Outcomes Following Burns in the Pediatric Population

Evan Ross

Mentors: Agnes Burris RN, Joseph Murphy M.D.

Purpose: While obesity is associated with increased mortality and decreased functional outcomes in adult burn patients, the ramifications of larger than average body size in the pediatric burn population are less well understood. Building on the finding that obese pediatric burn patients have a significantly longer length of hospital stay than their lean counterparts, the present study sought to determine whether obesity was associated with poor outcomes following burn injuries.

Methods: Data on patients ≤ 18 years of age who were admitted to a large regional burn unit between the years of 2000 and 2010 and for whom height and weight data was available (n=540) was collected from the hospital's burn database. Using the definition of obesity as ≥ 95thpercentile of weight for height according to the World Health Organization growth charts (< 2 years of age) or BMI for age according to the Centers for Disease Control growth charts (2 to 18 years of age), outcomes were compared between thermally-injured children classified as obese (n=155) and those classified as non-obese (n=385). Outcome parameters examined were total body surface area injury (TBSA), % full thickness injury, days in the ICU, non-ICU hospital days, days requiring mechanical ventilation, incidence of sepsis, pneumonia, number of operations, and overall mortality. All data was collected in accordance with IRB (#STU 032012-032) regulations.

Results: Obese and non-obese thermally injured children did not differ significantly with respect to TBSA, percentage of full thickness burn, or overall mortality. However, these groups were significantly different with respect to age (obese=7.26±0.46 years, non-obese=9.36±0.32 years, p=0.00015) and days requiring mechanical ventilation (obese=4.86±1.28 days, non-obese=2.72±0.49 days, p=0.029). When considering only those thermally injured children admitted to the BICU without inhalation injury (n=177), the obese (n=46) and non-obese (n=131) groups did not differ significantly with respect to TBSA, percentage of full thickness burn, or overall mortality. However, significant differences between these groups were noted for number of days spent in the ICU (obese=18.59±5.12 days, non-obese=9.38±1.79 days, p=0.017) and number of days requiring mechanical ventilation (obese=11.65±3.87 days, non-obese=3.87±0.83 days, p=0.002).

Conclusion: These data show thermally injured obese pediatric patients required longer and more intensive medical support in the form of BICU care and respiratory intervention. Counter to findings in adult populations, differences in mortality were not observed. Collectively, these findings suggest obesity as a risk factor for increased morbidity in the pediatric burn population.

Decreasing Medication and Medical Supply Shortage and Waste in North Texas

Jennifer Rossen

Mentors and Collaborators: Nora Gimpel M.D.; Patti Pagels MPAS, PA-C
Kristin D'Silva; Georgia Saniuk; Ian Walker

Context: With rising poverty, more uninsured patients, and growing prevalence of chronic diseases, there has been an increasing need for charitable clinics across the United States. While there are limited resources for those in need, medical waste is also a national problem. Objective: To evaluate the need for and efficacy of a program to improve medical supply and reduce medical waste in North Texas Association of Charitable Clinics (NTACC). Human Subjects review: Expedited approval from the UT Southwestern Institutional Review Board. Design: Cross-sectional survey. Setting: Charitable clinics in North Texas and a local medical supply warehouse. Participants: Thirty-nine charitable clinics associated with NTACC. Instrument: Forty-seven-item web based survey.

Outcome Measures: Main: specific needs of the clinics and warehouse. Secondary: interest in a program targeted to decrease shortage and waste. Preliminary Results: Sixteen clinics completed the survey (response rate: 41%). Clinics reported heart disease (94%), endocrine disorders (76%), and chronic respiratory disorders (47%) as the most frequently treated conditions. Clinics also reported anti-hypertensive (76%) and diabetes medications (76%) as the most frequently prescribed and in-shortage medications. More clinics ran out of and disposed of medications (71% and 71%, respectively) than medical supplies (29% and 6%, respectively). Clinics expressed interest in a program to decrease shortage and waste. The warehouse was interested in volunteer efforts and opportunities to decrease shortage and waste.

Conclusion: The most frequently treated conditions were chronic illnesses; this was also reflected in the medications most commonly prescribed and most frequently in shortage. Charitable clinics can focus individual and collaboration efforts on medications and supplies for treating chronic illnesses in addition to enhancing education and prevention programs aimed at decreasing the prevalence of these diseases. Programs are being developed to decrease shortage and waste in the clinics and warehouse.

A new appraisal of TIPS created with expanded-polytetrafluoroethylene covered stents

Krishna C. Sajja

Mentors: Bart L. Dolmatch M.D and Don C. Rockey M.D.

Background: Transjugular intrahepatic portosystemic shunts (TIPS) created with expanded poly-tetrafluoroethylene (ePTFE)-covered stents have largely replaced bare metal stents. Short-term shunt patency is typically assessed with protocol Doppler ultrasound (US), while little information exists with regard to long-term patency.

Aims: We investigated the accuracy of Doppler US in assessing TIPS patency as well as long-term clinical outcomes.

Methods: A retrospective analysis of 59 patients with covered stents used for TIPS between January 2001 and December 2011 was performed.

Results: Fifty-four patients had early (median 9 days) Doppler US follow-up. Seven of 8 patients with an abnormal baseline US required stent revisions. None of the 46 patients with normal baseline Doppler US required revisions within the first 6 months; 6 of these patients subsequently had an angiogram because of symptoms, but all TIPS were patent. Fifty-two patients survived for long-term (>6 months) follow-up, averaging 654 days and 3 Doppler US exams. Five of 6 patients with abnormal follow-up Doppler US required revisions, whereas none of the 46 patients with normal follow-up US had revisions. The recurrence of symptoms of portal hypertension and/or hepatic encephalopathy (HE) was low (4/52 patients). No significant predictors of long-term stenosis were identified. Post-TIPS HE was independent of pre-TIPS HE or Child-Pugh score.

Conclusions: Short-term patency and that at approximately 2 years after TIPS placement was 87% and 77%, respectively. We conclude that Doppler US at least 1 week after TIPS is warranted, but repeated Doppler US follow-up is probably not necessary in the absence of clinical symptoms.

Evaluation of Early Transcutaneous Bilirubinometry (ETcB) to Predict Subsequent Hyperbilirubinemia

Meghan E. Saumur

Mentors: Gregory L. Jackson M.D., William D. Engle M.D.

Background: TcB is well-established for non-invasive bedside monitoring of trends in neonatal bilirubin values. It is not known whether an ETcB value will assist in (a) predicting subsequent TcB values, or (b) the need for evaluation of, or treatment for, hyperbilirubinemia.

Purpose: To determine whether an ETcB value alone – or used to calculate a rate of rise (ROR) in TcB – will identify those neonates who are at higher risk for subsequent jaundice and/or a higher likelihood of needing phototherapy (PHT).

Methods: ETcB values were obtained within 6h of delivery from a convenience sample of neonates admitted to the Parkland Newborn Nursery. ROR was calculated as the average hourly increase between ETcB and subsequent TcB obtained at 18-36h of age. The predictive values relating (a) ETcB alone and/or ROR to subsequent TcB values, and (b) need for PHT, were determined.

Results: 516 study neonates had a mean birth weight of 3401±468 grams and gestational age of 39±1.4 weeks; 83% were Hispanic, and 53% were male. Correlations between ETcB and TcB values at 24h, 36h, and 48h were r=0.31, 0.40, and 0.32 respectively (all p values <0.001). Predictive indices are shown:

| | TcB >95 %ile at 42-66 hours* | | | | |
	Sens	*Spec*	*PPV*	*NPV*	p^{ψ}
ETcB[¥]					
0.80	0.87	0.50	0.16	0.97	0.0007
0.90	0.78	0.57	0.16	0.96	0.002
ROR[§]					
0.11	1.00	0.13	0.11	1.00	0.09
0.18	0.83	0.48	0.15	0.96	0.007
0.25	0.52	0.88	0.31	0.95	0.00003

As shown above for the 95th %ile, and using ETcB or ROR as the predictor cutoff for subsequent TcB, the NPV was always ≥0.95. For neonates with ROR ≥0.25, 79% had TcB >75th %ile at 42-66h (vs 32% with ROR <0.25; p<0.001). Median ETcB was 2-fold higher in those neonates who were subsequently treated with PHT (p=0.002), and ROR was ≥0.30 mg/dL in 63% of these neonates.

Discussion: These results suggest that ETcB may provide a useful baseline and have clinical utility primarily in identifying those neonates at low risk of subsequent hyperbilirubinemia.

Analysis of Free Flap Breast Reconstruction Failures: Are specific patient characteristics associated with free flap failure?

Natalie M. Sciano

Mentors and Collaborators: Jordan Farkas M.D., Roberto Cortez, Travis Miller, Kathryn Davis Ph.D.., Jeffrey M. Kenkel M.D.,

Purpose: This study was performed to gain insight on the patients who have undergone free flap breast reconstructive surgery. Recognizing certain patient variables, as risk factors for developing free flap failure, is invaluable. This knowledge can provide surgeons the benefit of foresight when assessing patients pre and postoperatively. The goal was to identify specific characteristics that predisposed patients to developing flap failure.

Methods: A retrospective chart review was completed on patients who had received free flap breast reconstructive surgery during January 2008 to January 2012. A cohort of 124 patients receiving free flap reconstruction was identified using the Current Procedural Technology (CPT) code 19364. A number of patient variables which include general characteristics, comorbidities, and surgical characteristics were analyzed to determine their contribution toward a patient's development of free flap failure. Patients were categorized into two groups- those without and those with flap failure. A comparison of the means and proportions was performed to determine statistical significance between the two groups. The level of statistical significance for this univariate analysis was set at a $P < 0.05$.

Results: All of the 124 patients identified were female. The overall flap success rate was 91.94 percent, with only ten patients experiencing flap failure. Of the factors analyzed in this study, there was not an identified patient characteristic that predisposed a patient to developing free flap failure.

Conclusions: Flap failure is an unfortunate risk of reconstructive surgery that needs to be minimized at all costs. No specific patient variables were identified as predisposing risk factors that could contribute to free flap failure. Institutions should strive to educate all breast reconstruction candidates on their options and risks which can help increase the volume of patients acquiring reconstruction. In the future, other investigations with a larger sample size should be done to yield more beneficial information for the physician and patient.

Speech and Language Performance of 3 Year Old Children Born Preterm: A Preliminary Report

Laurie Seidel

Mentor and other collaborators: Debra Weinberger, M.D., Anna Cobbs, M.S., Catherine Regetz, M.S., CCC-SLP, Roy Heyne, M.D., Emily Tobey, Ph.D., and Thomas Campbell, Ph.D.

Introduction: The association between preterm birth and an increased risk for cognitive impairment and academic struggles later in life is well established. In particular, the tendency for preterm infants to show delayed language acquisition even without evidence of brain damage has been the subject of much recent research. We hypothesized there would be a positive association between birth weight/gestational age of preterm infants and their speech and language performance at 3 years of age.

Methods: We recruited 43 children from the Low Birth Weight Clinic at Children's Medical Center Dallas and the Pediatrix Tots Clinic at Baylor University Medical Center with a mean age of 37.8 months (range 36-45 months). Their mean gestational age was 28.6 weeks (range 23-35 weeks) and mean birth weight was 1219.8 grams (range 550-2525 grams). Children had no history of hearing loss, structural abnormalities such as cleft lip or palate, or prolonged mechanical ventilation after NICU discharge. Each child underwent a hearing screening, the Battelle Developmental Inventory Screening Test, and 40 of the 43 children underwent the Goldman-Fristoe 2 Test of Articulation (GFTA). Each child's spontaneous speech was recorded during a 30-minute interactive play session with their primary caregiver. Their speech was then transcribed and analyzed using the Systematic Analysis of Language Transcripts (SALT) program, matching each participant to a group of control children based on age and gender. SALT measures included percent intelligibility, total number of words, number of different words, and words per minute. Finally, the primary caregiver completed the MacArthur-Bates Communicative Development Inventory-III for each child.

Results: Performance on the MacArthur-Bates and SALT measures did not correlate with birth weight or gestational age. SALT analysis showed that our participants produced significantly shorter utterances, did not use as many different words, and were significantly less intelligible than controls. The mean age equivalent on the Battelle was 36.3 months (range 14-51 months).

Discussion: Preliminary analysis does not support a correlation between birth weight/gestational age of preterm infants and speech and language performance at age 3 years. Therefore, a higher birth weight or later gestational age does not imply a lesser risk for preterm infants. Thus, it is critically important that parents and pediatricians alike remain vigilant when assessing the speech and language of all children who were born preterm, regardless of birth weight or gestational age.

HOLMIUM:YAG LASER BRONCHOSCOPY:
Use of the Holmium:YAG Laser for Relief of Symptoms from Tracheobronchial Obstruction

John J. Squiers

Mentor: J. Michael DiMaio M.D.

Background: Patients suffering severe tracheobronchial obstruction caused by intrinsic and extrinsic factors are vulnerable to dyspnea, respiratory failure, obstructive pneumonia, and death. Palliative laser bronchoscopy procedures have been developed to annihilate the tracheobronchial obstruction under anesthesia. Several different lasers have been implemented previously, with mixed results. The new holmium:YAG laser may provide improved functional status. This laser is designed to combine the precise cutting of CO_2 lasers with the strong coagulating ability of the Neodymium:YAG laser while minimizing the disadvantages of these lasers. This is the largest case series describing the application of the holmium:YAG laser for benign and malignant obstructive disease in the tracheobronchial tree.

Methods: The data was collected from 98 patients, with either benign or malignant tracheobronchial obstruction, who underwent interventional bronchoscopy in the operating room with laser ablation between January 2004 and November 2011.

Results: The holmium:YAG laser was used in 171 procedures performed on 98 patients with either benign or malignant disease. Symptomatic improvement was demonstrated in 92% of all benign etiology cases and 72% of all malignant etiology cases. As expected, long-term (measured at 2 years) survival was much higher in the benign group as compared to the malignant group.

Conclusions: Patients with tracheobronchial obstruction suffer significant discomfort, poor functional status, and an increased risk of death. Laser bronchoscopy should be considered primarily as a palliative, rather than curative, procedure. The holmium:YAG laser was designed to combine several advantages of older lasers while minimizing disadvantages. In this study, we demonstrate the safe addition of the holmium:YAG laser to previously established lasers in a large series of patients. Our series demonstrates that the holmium:YAG laser adds to the arsenal available to thoracic surgeons in the treatment of complex airway disease.

In-vivo Biomechanical Human Anterior Vaginal Wall Prolapse Properties Determined by Cutometer-Like Device

Caitlin Stevens

Mentor: Philippe Zimmern M.D.
Contributors: Mio Yanagisawa, Rachel Towns, Adam Romman, Elizabeth Mosier, Charles Chuong, Jingsheng Yan, Xian−Jin Xie, Robert Eberhart

Introduction: In an ongoing investigation to improve management of pelvic organ prolapse (POP), a cutometer-like device (BTC−2000 from SRLI) has been adapted to induce deformation of human vaginal wall (HVW) *in vivo*. Stress-strain curves have been generated to derive visco-elastic properties of the tissue. Here, extrinsic risk factors associated with POP development were assessed to determine their impact, if any, on the biomechanical properties obtained by this device.
Method: Following IRB approval, women with symptomatic stage > 2 anterior vaginal compartment POP requiring surgical repair were tested intra−operatively under general anesthesia at the start of surgery to evaluate their HVW properties with the BTC−2000. A prior study on intra and inter−rater reliability of measurements established satisfactory reproducibility (1). The same systematic methodology was used in this study, including measurement at the bladder neck level and at a reference point (suprapubic region). Relationships between measurements of laxity, elastic deformation, elasticity and several recognized risk factors for POP – age, BMI, parity – were examined. Patients with narrow vagina precluding probe insertion were excluded.
Results: From 2008 to 2012, 69 women were studied, the majority Caucasian, with mean age 61 (29−90), BMI 27 (19−43), and parity 2 (0−6). No statistically significant difference for univariate analysis was noted for either HVW or the suprapubic region when comparing the older group (>65) to their younger counterparts, the overweight patients (BMI>25) to their normal weight counterparts, or parity among subjects. Furthermore, no statistical correlation by Pearson or Spearman coefficients was found between the measurements and these clinical variables.
Conclusion: A cutometer−like device (BTC−2000) can elicit valuable intrinsic HVW biomechanical tissue properties that appear to reflect inherent properties of the vaginal wall in women with symptomatic anterior vaginal wall compartment prolapse.

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Parameters that Predict for High Grade Rectal Toxicity in Prostate Cancer (Pca) Patients Undergoing Stereotactic Body Radiation Therapy (SBRT) – Analysis of Phase I/II Study at UT Southwestern (UTSW).

Chris Straka

Mentors: Robert Timmerman M.D., D. Nathan Kim M.D., PH.D.

Introduction: Conventional radiation therapy (CRT) is a well-accepted option for PCa treatment with high disease control rate, and low (< 3-5%) risk of rectal toxicity. SBRT, unlike CRT, delivers higher doses of radiation in 1-5 fractions, reducing treatment time significantly (from 8-9 weeks to ~ 2 weeks). Benefits of SBRT include improved patient convenience, significant healthcare cost reduction, and it has strong biologic rationale. A dose escalation phase I study (Boike et. al, JCO 2011) established 45-50 Gy in 5 treatments as effective and safe. Phase II study at 50 Gy was recently completed. Interim analysis unexpectedly revealed a significant number of grade 3+ delayed rectal events. We performed a rigorous analysis to determine potential etiology and methods to avoid occurrence of such rectal events.

Methods: Clinical parameters evaluated include tumor stage, Gleason grade, prostate volume, comorbid conditions (diabetes, smoking history, immunosuppression), race, age, and baseline bowel function score. Treatment planning parameters collected and evaluated included rectal wall volume receiving high doses of radiation, target volume size, rectal wall size, and degree of circumferential radiation to the rectal wall. Uni/multivariate analysis and correlative studies were conducted.

Results: 59 low/intermediate risk Pca patients were enrolled in this phase I/II study at UTSW. Median follow-up for all patients is 25.5 months. Tumor control rate is 99% to date. No patients experienced high grade rectal toxicity at 45 and 47.5 Gy, but at 50 Gy 10.8% experienced ≥ grade 3 rectal toxicity. Significant parameters were rectal volume receiving 50 Gy, HR of 2.67 (1.25, 5.71), p=.0113; rectal circumference irradiated by 24 Gy, 39 Gy and 50 Gy, HR of 1.1 (1.01,1.2) (p=.03), 1.2 (1.01, 1.38) (p=.04), and 1.22 (1.01, 1.47) (p=.04) respectively; and possibly diabetes HR 6.86 (0.83, 56.8) (p=.074). All 4 patients with grade 3+ rectal toxicity had > 3.5 cm^3 rectal wall irradiated by 50 Gy. All patients without rectal toxicity had < 3.5 cm^3 rectal wall irradiated by 50 Gy.

Discussion: We have determined the absolute threshold dose volume constraint to avoid rectal toxicity for SBRT of Pca. These findings contribute significantly to the radiobiology of bowel tolerance. If anatomy does not permit safe rectal dose constraints, dose reduced SBRT or alternatively CRT should be considered. When rectal constraints are met, or when 45-47.5 Gy prescription dose is used, SBRT seems to be a potent, safe, convenient and cost effective treatment for patients with low/intermediate risk PCa.

**Road map to consensus treatment plans for adults with morphea:
Establishing current practice trends**

Amanda Strickland

Mentor: Heidi Jacobe M.D.
Contributors: Nicole Fett, Christopher Hansen, Kari Connolly,

Background: Therapeutic clinical trials are challenging in rare disorders like morphea, but needed given recent reports documenting wide variation treatment among providers. One solution is to determine comparative efficacy of common treatments by comparing patients treated with a consensus treatment plan (CTP) with a universally accepted outcome measure. The first step in creating a CTP is gathering data on current practice. This study characterizes treatment regimens offered to adult patients with morphea by members of the Medical Dermatology Society (M.D.S) as the first step in developing a CTP for adults with morphea.

Objective: To determine current approach to treatment among dermatologists with experience in the treatment of morphea(M.D.S members).

Design: Cross-sectional survey of M.D.S members.

Setting: Web-based survey (Survey Monkey)

Main Outcome Measures: Frequency count analysis of responses for severity, activity, and treatment of 6 subtypes of morphea: plaque, linear, generalized, mixed, deep, and lichen sclerosus

Results: M.D.S respondents vary treatment according to morphea subtype. More severe forms of morphea were treated with systemic agents, while less severe forms were treated with topicals. The choice of systemic agents, duration, dose, and combination treatments varied widely. Phototherapy was used relatively infrequently. M.D.S members used systemic immunosuppressives in generalized and linear morphea less frequently and for shorter time periods compared with prior reports in rheumatology.

Conclusions: Dermatologists have more variation in their approach to treatment of morphea patients than rheumatologists. Accounting for this variation will be crucial in the development of CTP for morphea if they are to be adapted by dermatologists.

Attitudes and Trends in the Treatment of Morphea: A National Study

Nicole Strickland

Mentors: Heidi Jacobe M.D., Gopal Patel

Introduction: Morphea, or localized scleroderma, is an inflammatory disorder of both adults and children that can lead to severe cosmetic and functional impairment due to excess collagen deposition in the dermis and subcutaneous tissues. The attitudes of the main specialists caring for these patients, dermatologists and rheumatologists, have not been directly evaluated in regards to evaluation and treatment. Given the multidisciplinary management of this disease and the lack of a national perspective on physicians' current treatment regimens, there is no uniform standard of care for morphea, and the indications for aggressive treatment are not widely accepted among providers. We report here the results of a national cross-sectional survey of both dermatologists and rheumatologists, showing current practice patterns of evaluation and treatment of morphea in the United States.

Methods: A web-based cross-sectional survey was administered to physicians who were randomly selected from the current American Academy of Dermatology, Society of Pediatric Dermatology, and the American College of Rheumatology Membership Directories.

Results: Physician approach to evaluation and treatment of morphea is driven by the specialty training of the physician rather than the disease characteristics. For evaluation of morphea, all specialties de-emphasized subtyping morphea, instead strongly relying on the history and physical exam, a modality based on physician training. Over all morphea subtypes, dermatologists tended to utilize external treatments (topical steroids, phototherapy), while rheumatologists preferred systemic treatments (methotrexate, antimalarials/antibiotics, systemic steroids). Both specialties are willing to refer patients to their colleagues in other specialties when evaluation or treatments extend beyond their own training. For some morphea subtypes, each specialty did not have a clear consensus on first and second-line treatment.

Discussion: This is the first study to concurrently assess the evaluation and treatment practices of main stakeholders in morphea care. With the lack of standardized guidelines, dermatologists and rheumatologists rely heavily on specialty training for assessing and treating morphea patients. Even within a specialty, there are no clear agreements on treatment choices for individual morphea subtypes. This study 1) provides support for the necessity to develop evidence-based practice guidelines; 2) emphasizes the need for interdisciplinary collaboration that is already in place among these stakeholders; and 3) shows a national perspective on morphea care that can be used as a platform to launch consensus statements on morphea treatment.

Quantifying subjective pain scores in hospitalized burn patients

Jonathan Triantafyllou

Mentors and Collaborators: Steven Wolf M.D., M. J. Lee BA, K. Manchanda BME, BA, A. Burris RN, V. Jones RN

Pain management is an important component of patient care in the hospital setting, and burn patients represent a particularly challenging population. Despite the fact that subjective pain scores are a routine part of the medical record, relatively little research has been done to quantify this data and its clinical utility.

A retrospective study to examine pain scores from an inpatient burn unit in 2011 was performed. The patients studied had at least 10% TBSA burns and a hospitalization of at least 48 hours. Routine pain assessment occurs approximately every four hours and includes data from both verbal and nonverbal scales as well as an acceptable level of pain.

The data reflect the challenges of pain management in burn patients. Reported pain is significantly higher during the daytime hours and wanes at night ($p < 0.05$), likely reflecting the awake state and discomfort of dressing changes and physical therapy. While there is considerable variability in pain from day to day, on average pain scores actually increase throughout the course of the hospitalization ($p < 0.05$ for a linear regression). Consistent with previous studies, there is a poor correlation between the extent of burn injury (TBSA), patient characteristics, and average pain scores.

The pain experienced while recovering from a burn injury has important physiological and psychological ramifications and should not be taken lightly. Further research on this patient population can quantify subjective pain scores in relation to analgesic regimens and painful interventions during hospitalization.

Effectiveness of Drug Therapy in an Enthesitis-Related Arthritis Cohort

Carla Upperman

Mentor: Tracey Wright M.D.
Collaborators: Jose Rossello-Urgell M.D., Ph.D.- Baylor Institute for Immunology Research

Introduction: Enthesitis- related arthritis (ERA) is a subset of juvenile idiopathic arthritis characterized by inflammation of the joints and/or entheses. Children may experience significant morbidity including poor growth, joint damage, and functional disability without treatment. While several therapies including nonsteroidal anti-inflammatory drugs (NSAIDs), disease-modifying anti-rheumatic drugs (DMARDs), and biologics are available, it remains to be determined which therapy or combination of therapies is most effective. Our objectives were to 1) characterize a cohort of ERA and 2) compare the effectiveness of therapies in controlling disease activity in ERA.

Methods: We performed a retrospective chart review of subjects with ERA from the Texas Scottish Rite Hospital for Children. Demographics, clinical features, and drug exposure were recorded.   We compared the active joint count (AJC) and erythrocyte sedimentation rate (ESR) at baseline and at the end of the study period for the entire cohort. We grouped subjects by prescribed treatment after the baseline visit and performed a propensity score analysis to determine the impact of treatment choice on the AJC and ESR.

Results: Of the 119 reviewed subjects suspected to have ERA, 53% were eligible for study inclusion. The majority of the cohort was male (89%) and Caucasian (89%). Presence of the HLA-B27 antigen (87%) and onset of arthritis in a male over 6 years of age (87%) were the most common inclusion criteria met. Few subjects had acute uveitis (2%). At the baseline visit, NSAIDs were the most common medications prescribed (39%) while few were prescribed DMARDs (6%) or biologics (8%). The median AJC and ESR significantly decreased from baseline to 1 year after diagnosis (AJC: 2 vs 1; $p<0.0001$; ESR: 22 vs 9; $p=0.0003$). NSAID use significantly increased the AJC ($\beta =1.4$, 95% CI: 0.4, 2.3; $p=0.004$) and ESR ($\beta =12.6$, 95% CI: 3.3, 21.8; $p=0.008$). Biologic use significantly decreased the ESR ($\beta = -12.8$, 95% CI: -21.3, -4.3; $p=0.003$) but did not have a significant effect on the AJC.

Conclusion: While NSAIDs were commonly prescribed after diagnosis, they had a negative impact on the outcome by increasing the AJC and ESR. In contrast, biologics significantly decreased the ESR. Lack of effect by DMARDs and biologics may be secondary to the small number of subjects in each treatment category or the timing of their use later in the first year after diagnosis. Future studies will evaluate a larger ERA cohort to allow further comparisons by treatment group.

Why Are There So Few Latino Doctors? Latino Parents' Perspectives on Barriers and Potential Solutions

David Valadez

Mentors and Collaborators: Glenn Flores M.D., Roger Romero, Jacob Garcia, Anwar Jackson, Blanca Villaseñor BA, Rashmi Shetgiri M.D., MS

Background: Latinos constitute 16% of the US population, but < 3% of US physicians. Little is known about the reasons for this disparity, particularly from the perspective of Latino parents. The study aim was to examine parental perspectives on barriers to Latino adolescents' pursuit of a career in medicine, and potential solutions for increasing the number of Latino doctors.

Methods: Focus groups and interviews were conducted of parents of Latino teens, stratified by children's immigration status and enrichment-program participation. 14 questions were asked about barriers to a medical career, diversity in medicine, enrichment programs, and solutions for increasing the number of Latino doctors. Sessions were audiotaped, transcribed, and analyzed using margin coding and grounded theory. Themes were independently identified by 3 coders; disagreements were resolved by consensus.

Results: The 15 participants had a mean age of 42 years. Participants stated that medicine is a demanding profession with a lengthy career path. Barriers to pursuing a medical career include lack of information about higher education and medical careers. One participant said, "They don't know of all the opportunities that could help them, they have to really look for them. It's not advertised." Financial barriers, immigration status, cultural stereotypes, racism, and lack of support from families and schools also were noted. Participants stated that the growing Latino population requires more Latino doctors, and that shared language and culture lead to improved care. Suggested solutions include better access to educational information, parental and school support, government-assisted financial aid, and more enrichment programs. Enrichment programs were noted to be beneficial by providing information, enhancing motivation, and increasing exposure to medicine.

Conclusions: Parents identified many barriers to medical careers for Latino youth, and the need for more Latino doctors. Parental and school support and financial aid were noted to be especially important for Latinos to pursue a medical career. Providing information for parents and teens on careers in medicine and financial assistance may be potential solutions. Incorporating this information into enrichment programs and increasing access to such programs may increase the number of Latino doctors.

A Descriptive Analysis of Patient Encounter Data from the UT Southwestern Ede Jodi Humanitarian Relief Trip to Haiti

David Vermette

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Background: Every day, millions of Haitians struggle against hunger, poverty, and illness. This situation has been exacerbated in recent years by a series of hurricanes, famines, the 2010 earthquake, and the cholera outbreak, which began in the Artibonite region. Physicians and students at UT Southwestern operate a charitable clinic in Pont Sonde in Artibonite, Haiti, to alleviate the burden of preventable, communicable, and chronic disease.

Objective: To determine the range and burden of disease in the patient population of a rural primary care clinic in a developing tropical country.

Methods: Data from all patient encounters during a weeklong relief trip in March 2012 were analyzed for Haitians who received medical treatment at a primary care clinic in the Artibonite region of Haiti. Demographic data, diagnoses, and prescribed medications were recorded and tabulated.

Results: There were 843 medical visits recorded during the humanitarian relief trip. Children under 18 years accounted for 48% of clinic visits. Of the 406 pediatric patients seen, 52.7% were female. Child ages ranged from seven days to 17 years (mean 4.5, S.D 4.4 years). The most common diagnoses for pediatric patients were dermatologic infections such as tinea and scabies (29%), gastrointestinal diseases (22%), and respiratory infections (22%). Five percent of pediatric patients were anemic. Every child was given Mebendezole to empirically treat intestinal worms, and children younger than five years were given Vitamin A to reduce morbidity and mortality of infectious diseases. Of the 437 adult patients seen, 72.1% were female. Patient ages ranged from 18 to 95 (mean 47.8, S.D. 19.0). In adult patients, the ten most prevalent diagnoses were muscle/joint pain, hypertension, GERD, eye irritation, headaches, UTI, cataracts, vaginitis, abdominal pain, and allergic conjunctivitis, accounting for 61% of the total diagnoses. Nearly 30% of adult patients had muscle/joint pain, 21% had hypertension, and 20% had GERD.

Conclusions: Haitians residing in the Artibonite region in Haiti require targeted healthcare interventions, health education programs, and sustainable management and prevention strategies for chronic diseases. This research can be used immediately for future missions to similar developing tropical countries to better supply their trips and prepare for the conditions on the ground, allowing for more efficient diagnosis and treatment.

Neural activity during the Stop Signal Task, a measure of inhibitory control, predicts relapse in cocaine-dependent patients

Lan Chi Vo

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Relapse is a prevalent phenomenon in addiction. Impaired inhibitory control is associated with relapse and is a significant predictor of cocaine use and treatment retention. Functional magnetic resonance imaging (fMRI) was, therefore, used to examine the association between BOLD response during the Stop Signal Task (SST, a measure of inhibitory control), and time to relapse in cocaine-dependent patients. Forty-nine 2-4 weeks abstinent cocaine-dependent participants were assessed and then followed weekly for up to 26 weeks as outpatients. Relapse was defined as any use of cocaine during the follow up period. The patients were categorized into 27 relapsers (relapsed within 30 days) and 22 abstinent (did not relapse at 30 days). BOLD response during successful inhibition ("stop success") during SST was compared between groups (z>2.3, p=0.05). The left lateral occipital cortex had greater activation in relapser compared to abstinent. Regions of interest (ROIs) were also identified using mean percent BOLD signal change in the combined patient group. Percent BOLD change values were calculated within the significantly activated voxels during SS (voxel-based analysis, P = 0.15). Identified clusters, in additional to the left lateral occipital cortex, were used in discriminant analysis through the Statistical Product and Service Solutions software to predict group membership. The left lateral occipital cortex and the left lateral orbitofrontal cortex/anterior insular clusters resulted in 79.6% N-fold cross-validated prediction of group membership. These regions can be used to identify those at risk of relapse and offer insights into mechanisms of relapse.

Predictors of Ketogenic Diet Efficacy in Children Based on the Electroencephalogram

Ian Walker

Mentor: Rana Said M.D.

Introduction: The ketogenic diet (KD) has proven to be an effective therapy for children with medically-refractory epilepsy. Numerous studies have consistently shown a significant reduction in seizures in patients regardless of seizure type or etiology. However, there is little data as to whether electrographic features are predictive of diet efficacy and how evolution of electroencephalogram (EEG) findings over time correlate with clinical improvement. We sought to determine the correlation between seizure reduction on KD and improvement in EEG.
Methods: We collected data from the KD database, Neurophysiology database, and medical records of children on the KD at Children's Medical Center from July 2005 to July 2012. We aimed to identify possible predictors for clinical seizure reduction (efficacy) on KD as it correlates with baseline and serial follow-up EEGs. In particular, we examined characteristic electrographic patterns (spikes, spike density, organization of background, slowing, electrographic seizures, state variation) serially for the duration of treatment with the diet.
Results: We reviewed 89 patients on the KD. 8 patients were excluded (2 did not have epilepsy, 4 on the KD for <1 week, 1 with no EEGs, and 1 had incomplete data). Of 81 patients, 45 had 2 or more EEGs; the others only had 1 EEG. We assessed overall positive response rate: 28% (23/81) had >95% reduction in seizures: 34.5% (28/81) had >75% reduction, 17.2% (14/81) had >50% reduction. 19.7% (16/81) were non-responders (<50% reduction), with 6% (5/81) showing worsening of seizures on KD. We developed scoring criteria to analyze EEG characteristics. This included the degree of encephalopathy, frequency of interictal spikes, and the presence of seizures. Each parameter was given a numerical value. The degree of change was determined between serial EEGs for each response rate category. The positive effect on serial EEGs was most notably found in children who had a >95% reduction in seizures. There was an improvement in electrographic determination of encephalopathy (as assessed by slowing of the posterior dominant rhythm, the presence of an anterior-posterior voltage-frequency gradient, the presence of background slowing, and the presence of state variation). There was a fourfold decrease in interictal spike frequency in this group also. In children who had a >75% reduction, the most frequent etiology was genetic (47.6%).
Conclusions: Our results confirm past data indicating the efficacy of the KD in the most refractory group of patients with epilepsy. Our responder rate, however, was higher than the national average, with 79.7% of children demonstrating at least a 50% reduction in seizures. Electrographically, the measures that correlated greatest with KD efficacy were improvement in encephalopathy and reduction in interictal spikes. Serial EEGs are helpful in predicting positive outcomes on KD.

Metabolic Syndrom, Cardiovascular Risk and Insulin-resistance in Pediatric survivors of brain tumors treated and radiation

Susan Wu

Mentor and Collaborators: Daniel C. Bowers M.D., Raven Cooksey M.D.,Lynn Gargan Ph.D., Amit Gode M.P.H., Laura Klesse M.D., Ph.D., Jon Oden M.D., Gloria Vega Ph.D.

Introduction: Brain tumors are the most common solid tumor of childhood, with survival rates exceeding 70%. Late effects of treatment include neurocognitive deficits, endocrine deficiencies, and elevated risk for adverse cardiovascular events. No study to date has examined metabolic syndrome (MS) in the pediatric brain tumor survivor population. Our primary aim is to identify the prevalence of MS in radiated and non-radiated survivors, as measured by truncal obesity, hypertension, hyperlipidemia, and insulin resistance. This will also be the first study to examine bone mineral density, as well as the relationship between leptin and adiponectin and cardiovascular risk factors, in this population.

Methods: Eligible patients between the ages of 10 and 20 at the time of the study who were more than one year off therapy were identified in the neuro-oncology follow-up database. Patients with neurofibromatosis and craniopharyngiomas were excluded. We intend to enroll 100 patients (50 radiated, 50 non-radiated). In addition to vitals taken at the time of their clinic visit, participants were asked to provide a fasting blood sample for a lipid panel and insulin, glucose, leptin, and adiponectin assays. Patients also underwent a Dual-energy X-ray Absorptiometry (DXA) scan to evaluate percent body fat and bone mineral density.

Results: We have enrolled 82 patients (50 radiated, 32 non-radiated); enrollment is expected to continue through the spring of 2013. Preliminary data analysis indicates that the prevalence of metabolic syndrome in the pediatric brain tumor survivor population seen at Children's is twice as high among those who received cranial radiation, compared to patients who did not (20% vs. 9%). Radiated patients were more likely to have elevated triglycerides (p=.016), elevated HOMA-IR values (p=.023), and lower total bone mineral density (p=.011). There were no significant differences in percent body fat, waist circumference, total cholesterol, LDL, or HDL between the two groups. Leptin and adiponectin assays are being run at this time.

Conclusions: This is the first study evaluating metabolic syndrome in pediatric brain tumor survivors in the United States. Our findings suggest that exposure to cranial radiation may have significant consequences that remain clinically latent for years following therapy. Future research will help elucidate the mechanism underlying such late effects and identify possible interventions in order to maintain quality of life for our patients.

Prediabetes Range Fasting Glucose and Hemoglobin A1C Levels and Their Associations with Subclinical Atherosclerosis: Observations from the Dallas Heart Study

Frank Xing

Mentors and Collaborators: M. Odette Gore, Ian J. Neeland, Colby R. Ayers MS, Andre Paixao, Aslan T. Turer M.D., Darren K. McGuire M.D.

Background: Present thresholds defining prediabetes by impaired fasting glucose (IFG) and hemoglobin A1c (A1C) categorize ~1/3 of the US adult population at-risk for diabetes, and on this basis have been criticized for being too liberal. However, their associations with subclinical atherosclerosis remain poorly defined.

Methods and Results: Prediabetes status was determined (FPG 100-125mg/dL and/or A1C 5.7-6.4%) and coronary artery calcium (CAC) was measured in 2,373 adults age 30-70 free from medically-treated diabetes or cardiovascular disease participating in the Dallas Heart Study 2, a population-based cohort with mean age 49 years, mean BMI 30.5 kg/m2, including 60% women and 64% non-white. Subjects with vs. without prediabetes were older (52 vs. 48 yrs; $p<0.001$), and more likely to be men (63% vs. 53%; $p<0.001$) non-white (71 vs. 61%; $p<0.001$), and obese (58% vs. 40%; $p<0.001$). The prevalence of CAC (Agatston score >10) was higher in those with vs. without prediabetes (31% vs. 21%; $p<0.001$), with no statistical difference in CAC prevalence between prediabetes sub-groups with IFG-only, A1C-only, or both ($p<0.877$). Analyzing FPG and A1C each continuously as univariable predictors of CAC, the optimized threshold for FPG was 96 mg/dl and for A1C was 5.5%. Similarly, the optimized FPG threshold to predict the composite outcome of mortality, MI, stroke or coronary revascularization over a median 8.4 yrs of follow-up (169 total events) among 2,880 DHS-1 participants enrolled 2001-2002 was 106 mg/dl; A1C was not measured in DHS-1.

Conclusions: Our results suggest that the present glycemic thresholds to identify prediabetes are associated with increased atherosclerosis, and perhaps even lower thresholds might be considered to capture the spectrum of increased clinical risk associated with dysglycemia below the diabetes range

Photoprotective habits of cutaneous lupus erythematosus patients

Shirley Y. Yang

Mentors and Collaborators: Ira Bernstein Ph.D., Danielle Q. Lin, and Benjamin F. Chong M.D.

Background/Purpose: Ultraviolet radiation is a well-documented trigger of skin lesions in patients with cutaneous lupus erythematosus (CLE). Though CLE patients are advised to practice photoprotection to prevent disease flares, their degrees of adherence to a regular photoprotective regimen can be variable. We sought to determine the relationship between photoprotective habits and various clinical and demographic characteristics of CLE subjects at the University of Texas Southwestern (UTSW) Medical Center.

Methods: A cross-sectional survey on photoprotective habits was administered to 105 CLE subjects at UTSW Medical Center. For each photoprotective method (e.g., applying sunscreen, wearing long-sleeved shirts, hats, and sunglasses, seeking shade), subjects were asked to choose their frequency of use from a 4-point Likert scale (1=rarely, 2=sometimes, 3=often, and 4=always). Overall sun protection habits (SPH) scores were calculated by taking the numerical average. Additional data including demographics, Fitzpatrick skin type, CLE subtype, smoking history, and history of photosensitivity were also collected. Statistical comparisons were performed using Fisher's exact tests for r x c contingency tables, Kruskal-Wallis tests, and Mann-Whitney U tests. $p < 0.05$ was considered statistically significant.

Results/Conclusions: Overall SPH scores were significantly lower in the medium-skinned (skin types III-IV; 2.7±0.7, p=0.01) and dark-skinned (skin types V-VI; 2.5±0.7; p<0.001) CLE patients than the light-skinned CLE patients (skin types I-II; 3.2±0.6) (p=0.001). This disparity may be due to misconceptions that dark-skinned CLE patients have regarding their decreased need for photoprotection. There were also significant differences between groups categorized by age at visit (p=0.04), with the SPH scores of the 61 and older age group (3.1±0.6) significantly higher than those of the 31-40 (2.5±0.7; p=0.01) and the 41-50 (2.5±0.8; p=0.02) age groups. The 31-50 year old age group overlaps with the most common age range for onset of lupus erythematosus, which is between 20 to 40 years of age. This highlights the need for photoprotection education to be targeted towards this specific age group of CLE patients who are likely to be newly diagnosed.

A Study Of Trauma Memory in Survivors of the 9/11 Attacks Using the Deese-Roediger-McDermott Memory Paradigm

Dinara Yangirova

Mentor: Carol North M.D.

Background. PTSD has been found to be associated with abnormalities in memory function. This relationship has not previously been studied with the Deese-Roediger-McDermott (DRM) paradigm in disaster-exposed populations. The DRM paradigm uses semantically related and unrelated intrusions in an immediate test of recited word lists. It was hypothesized that PTSD would be associated with false alarms to critical lures in the DRM paradigm.

Methods. Approximately three years after the 9/11 attacks, a volunteer sample (N=379) was recruited from members of eight participating agencies (three agencies in the WTC towers and one nearby agency, three agencies that provided 9/11 disaster recovery services, and an airline that lost personnel and property in the attacks). This sample was assessed for individual disaster experience and related psychiatric status using a fully structured diagnostic interview to assess full *DSM-IV-TR* criteria. At the end of the interview, the DRM paradigm was administered to test participants' recognition of words.

Results. No associations were found between PTSD or other psychopathology and DRM memory variables. The only predictor of false alarms to critical lures was direct exposure to 9/11 trauma, which was not associated with correct identification of recited words or with false alarms to unrelated lures.

Discussion. The study's hypothesis that PTSD would be associated with false alarms to critical lures was not supported. The finding that direct 9/11 endangerment was associated with critical lures was unexpected. The results suggest that neural processing of trauma exposure may involve associative processes of overgeneralization in cognitive processing coupled with insufficient inhibition of responses to associated but harmless stimuli. The findings of this study also support the importance of differentiating psychopathology such as PTSD from normal physiologic fight-or-flight responses to trauma in studies of memory and neurobiological investigations of trauma and its effects in future research.

From free clinic to medical home: Accessing community-oriented primary care

Andrew Yu

Mentor and Collaborators: Jessica Ballou, Shaam Mahaseneh, Rosemary Peterson, Mary Westerman,

Background: A large proportion of Dallas County adults seen at free clinics are eligible for primary care services through the Parkland Community-Oriented Primary Care (COPC) system. As patients with an established medical home have superior health outcomes compared to those who only seek care sporadically, we were interested in what factors affect successful referral to Parkland Health Plus (PH+), the payor of the COPC system.

Design: Longitudinal cohort study

Participants: Free clinic patients who are Dallas County residents age 18 or older and have never applied for or received PH+ in the past

Methods: Participants were educated based on standardized scripts. Demographic and health attitudes were collected via survey. Follow-up calls were made to check enrollment status. At the study's end, records were cross-checked with Parkland EMR to verify last known status.

Results: 137 persons were educated and referred to Parkland. Of these, 84 participants enrolled in our study and were followed to at least 4 weeks. 54 patients (64%) did not make any appointment for PH+ coverage. 30 patients (36%) made an appointment for PH+. 17 were approved, 11 were no-shows, 1 qualified for other coverage, and only 1 was ineligible. Of the 17 approved, 14 had COPC appointments at last check. The only demographic factor that predicted if a patient made a PH+ appointment was chronic disease diagnosis ($p = 0.041$). Age, gender, race, language, education status, and place of birth were not significant. Certain health beliefs encompassing perceived necessity of care, language barriers, and documentation hurdles were also significantly associated with making a PH+ coverage appointment.

Conclusions: Although the majority of participants did not seek PH+ coverage, those who went to their appointment were largely successful in establishing a medical home, suggesting that the Parkland system is accessible to motivated individuals. Given the preventative benefits of primary care, it is important to develop interventions that influence individuals to proactively seek primary care while still healthy.

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