2014 UCSF Multidisciplinary Resident Research Symposium

Wednesday, May 21
4:30pm-7:30pm
Millberry Union All-Quads and Game Room

Sponsored by the UCSF Clinical and Translational Science Institute’s Resident Research Training Program (RRTP) and the UCSF School of Medicine’s Pathway to Discovery’s Molecular Medicine (MM) Pathway
UCSF Resident Research Symposium
Sponsored by CTSI and the Molecular Medicine Pathway

We are pleased to offer for the first time a combined Clinical/Translational and Molecular Medicine Research Symposium dedicated to the research accomplishments of our residents. The mission of CTST, the training component of CTSI, is to create a pipeline and training system that enhances the number, quality, and cross-disciplinary skills of clinical and translational researchers at UCSF. The Molecular Medicine Pathway aims to enrich the residency experience with opportunities to engage with clinician-scientists and peers, to engage with current scientific literature, and to develop mentoring relationships in order to support career development.

The primary goal of the CTSI Resident Research Training Program (RRTP) is to create opportunities for all residents to gain fundamental knowledge in clinical and translational research methods and evidence-based medicine skills. Additionally, we aim to inspire residents to pursue future opportunities in investigation. CTST sponsors a one month course (Designing Clinical Research) which provides residents with the opportunity to gain fundamental skills and to develop their own research proposal in small group sessions with close guidance from the faculty. CTST also offers two funding opportunities; the Resident Research Funding (RRF) award, which provides up to $2000 per academic year to UCSF residents for qualified clinical and translational research expenses not covered by their mentor or other sources; and the Resident Research Travel (RRT) award, which provides $600 matching funds to support travel to present research findings at a scientific meeting.

The main goal of the graduate medical education component of the Molecular Medicine Pathway (MMP) is to create a community of and for basic science oriented residents across all specialties in the UCSF School of Medicine and other professional schools. We are here to help these physician-scientists achieve their career goals in academia. Activities throughout the year include social gatherings, a mentoring/career-development workshop, and the annual resident research symposium co-sponsored with the CTSI.

We thank you for joining us today to celebrate the accomplishments of this year’s participants.

Douglas Bauer, MD  
Associate Director, RRTP

Emily von Scheven, MD, MAS  
Co-Director, RRTP

Miriam Kuppermann, PhD, MPH  
Co-Director, RRTP

Anna Bakardjieva, MD  
Co-Director, MMP

Ben Cheyette, MD, PhD  
Co-Director, MMP
Schedule of Events

4:30 pm  Welcome & Resident Research Program Overview
*Emily von Scheven, Co-Director, CTSI Resident Research Training Program*
*Ben Cheyette and Anna Bakardjiev, Co-Directors, Molecular Medicine Pathway*

4:45 pm  Comments by the Dean
*Sam Hawgood, Dean, School of Medicine*

5:00 pm  Resident Oral Papers
*Moderated by Emily von Scheven*

Speaker Name: Henry Krigbaum, MD
Title: Morbidity and Mortality in U.S. Veterans Following Short versus Long Cephalomedullary Nailing of Intertrochanteric Hip Fractures
Residency Program: Orthopaedic Surgery
Research Mentor: Alfred Kuo, MD

Speaker Name: Allison J. Kwong, MD
Title: Hepatic Toxicity from Rifampin Prophylaxis for Latent Tuberculosis in Liver Transplant Candidates: A Case-Control Study
Residency Program: Internal Medicine
Research Mentor: Francis Y.K. Yao, MD

Speaker Name: Chaz Langelier, MD, PhD
Title: Pathogen Identification in Tanzanian Children Hospitalized for Cerebral Malaria and Culture-Negative Febrile CNS Disease
Residency Program: Internal Medicine
Research Mentor: Joe DeRisi, PhD

Speaker Name: Patrick Peebles, MD
Title: MyPICS: Photo Identification Cards of a Medical Team on an Inpatient Pediatric Ward
Residency Program: Pediatrics
Research Mentor: Glenn Rosenbluth, MD

Speaker Name: Catherine L. Chen, MD, MPH
Title: Prevalence and Cost to Medicare of Unnecessary Preoperative Medical Testing Prior to Cataract Surgery
Residency Program: Anesthesia and Perioperative Care
Research Mentor: R. Adams Dudley, MD, MBA

6:15 pm  Mentors of the Year Awards
Clinical/Translational Recipient: Lindsey A. Criswell, MD, MPH, Chief, Division of Rheumatology
Molecular Medicine Recipient: Tippi MacKenzie, MD, Associate Professor of Surgery

6:30 pm  Poster Viewing and Reception
Golden Gate Room
Mentors of the Year Award

It is well recognized that mentoring is a critical factor in academic success. The success of residents embarking on a research project is highly influenced by the quality of their mentorship. Thus, we would like to recognize the contributions of the many faculty who have assisted with the research endeavors presented today.

Today we are recognizing two faculty mentors for outstanding excellence in mentoring. This year’s awardees were selected from many outstanding nominations.

Clinical/Translational Mentor

Lindsey A. Criswell, MD, MPH

Nominating Residents’ Comments:

“She has been wonderfully accessible and has allowed me to maintain my enthusiasm for research even while doing residency. She is a world-renowned scientist but still manages to find time to mentor trainees like me. She has also mobilized resources for me by connecting me with other people in the lab that have helped me conduct the research that I’m presenting here (which is still a work in progress).”

“Lindsey Criswell is an incredible research mentor: accessible, engaged, and enthusiastic despite her many other roles and responsibilities. She has invested significant time in my project, meeting frequently, suggesting tangible goals and providing constructive feedback that inevitably helps me progress. Lindsey is a very involved mentor but also fosters the ideal amount of autonomy and independent thought. Being a leader in her field of genetics, she always has the broader objectives in mind and offers thoughtful suggestions that guide the project to meet those objectives. Not all great researchers make great mentors, but Lindsey certainly excels at both.”

Molecular Medicine Mentor

Tippi MacKenzie, MD

Nominating Resident’s Comments:

“Dr. MacKenzie is an excellent mentor who has a passion for in utero transplantation and therapy. She has guided me through rigorous coursework over the past 2 years and has challenged me to consider possibilities outside of the box. Dr. MacKenzie has provided constructive feedback that has structured me to become a better clinician scientist.”
Abstracts:
Oral Presentations

UCSF Resident Research Symposium

Wednesday, May 21st, 2014

Millberry Union Conference Rooms
Abstract title: Morbidity and Mortality in U.S. Veterans Following Short versus Long Cephalomedullary Nailing of Intertrochanteric Hip Fractures

Resident’s name: Henry Krigbaum, MD

Name of program: Orthopaedic Surgery

Purpose: Both long and short cephalomedullary nails (CMNs) are used to treat intertrochanteric hip fractures. In fractures without subtrochanteric extension, the indications for the use of short versus long nails are unclear. Previous studies have shown increased blood loss and operative times with long nails. We hypothesized that short nails (less than 250 mm) would be associated with lower rates of perioperative morbidity and mortality due to shorter operative times and less instrumentation of the femoral canal.

Methods: Databases of the Department of Veterans Affairs (VA) were used to identify implant type (short versus long), patient characteristics, comorbidities, short-term complications, readmissions, and mortality in patients who underwent cephalomedullary nailing for intertrochanteric femur fractures from 1999 to 2010. Patients under the age of 60 were excluded, as were patients with femoral neck fractures, pathologic fractures, and revision surgeries. Univariate and multivariate analyses were performed to evaluate for differences in patient characteristics, intraoperative factors, and outcomes.

Results: Implant information was obtained for 2,565 patients who were treated with CMNs. Of these, 705 cases had the specific post-operative diagnosis of intertrochanteric hip fracture. There were 364 cases treated with short CMNs and 341 cases treated with long CMNs. Univariate analysis showed no significant differences in patient characteristics, length of pre-operative hospital stay, individual post-operative complications, post-operative length of stay, or death within 30 days or 1 year. Significantly more patients treated with short nails developed at least one complication (26% vs 20%; p = 0.042). The use of short nails was associated with significantly lower operative times as well as lower incidences of postoperative anemia. There was a strong trend toward a higher rate of revision surgery within one year for short nails (1.1% versus 0%), which nearly reached statistical significance (p = 0.052). In order to control for confounding, multivariate analyses were performed, which showed no significant differences in the rates of development of at least one complication, readmission, or death. Long nails were more expensive than the corresponding short implants.

Conclusions: Despite longer operative times, there were no significant differences in short-term morbidity and mortality between patients with intertrochanteric hip fractures treated with either long or short nails. The effects of specific fracture types on outcomes and the economic consequences of the higher costs of long nails should be further investigated.
Abstract title: Hepatic Toxicity from Rifampin Prophylaxis for Latent Tuberculosis in Liver Transplant Candidates: A Case-Control Study

Resident’s name: Allison J. Kwong, MD

Name of Program: Internal Medicine

Purpose: Background: Prophylaxis for latent tuberculosis infection (LTBI) is recommended for liver transplant (LT) candidates to prevent re-activation of TB after LT, but the prevalence of LTBI and the risk of hepatotoxicity from chemoprophylaxis have not been well characterized.

Methods: The study cohort included consecutive patients ≥18 years of age who were listed for primary LT between March 2009 and March 2013. Exclusion criteria were acute liver failure as the indication for LT or a history of active TB. Cases were those with LTBI defined as a positive PPD or quantiferon test without active TB. Controls were patients without LTBI, matched by age, gender, diagnosis of hepatocellular carcinoma, and baseline MELD score. Our protocol for chemoprophylaxis in patients with LTBI was rifampin 300 mg twice daily for 4 months while on the LT waiting list. The primary outcome of this study was hepatotoxicity defined as an increase in total bilirubin by ≥2 mg/dL or an increase in MELD score by ≥5 points within 6 months after initiating rifampin. The risk of hepatotoxicity was compared between cases and controls with chi-square p values accounting for matched data, and predictors of hepatotoxicity were assessed in LTBI cases by logistic regression.

Results: Of 989 patients listed for LT during the study period who met inclusion criteria, 607 (61%) completed PPD or quantiferon testing. Among them, 101 patients (17%) were diagnosed with LTBI: 74% were male; 35% were Asian, 25% were white, 23% were Hispanic, 8% were Arab or Middle Eastern, 6% were black, and 4% were of other races. Thirty-two of 101 patients received rifampin for LTBI chemoprophylaxis. Compared to 162 matched controls, 38% of cases versus 18% of controls had an increase in total bilirubin by ≥2 points (p=0.006). An increase in MELD score of ≥5 points was observed in 41% of cases and 18% of controls (p=0.004). The risk of hepatotoxicity, based on an increase in both total bilirubin by ≥2 points and MELD by ≥5 points, was 38% in the rifampin group versus 11% in the controls (p<0.001). Rifampin was discontinued prematurely in 47% patients, mainly due to hepatotoxicity. In an exploratory analysis, only age (odds ratio 0.88 per year, 95%-CI 0.79-0.99, p=0.03) predicted hepatotoxicity from rifampin, whereas gender, baseline MELD score, and etiology of liver disease did not.

Conclusions: Conclusion: We observed a 17% prevalence of LTBI among LT candidates. Compared to matched controls, rifampin use is associated with a significantly greater risk of hepatotoxicity. Re-appraisal of the most appropriate regimen and timing of chemoprophylaxis for LTBI based on its risks and potential benefits is needed.
Abstract title: Pathogen Identification in Tanzanian Children Hospitalized for Cerebral Malaria and Culture-Negative Febrile CNS Disease

Resident’s name: Chaz R. Langelier, MD, PhD

Name of program: Internal Medicine

Purpose: Febrile CNS disease is responsible for significant morbidity and mortality in developing regions of the world and can result in irreversible cognitive disability in the absence of effective treatment. Despite this, the etiologies of such illnesses remain poorly understood, due in part to the limited availability of clinical diagnostic tools. Cerebral malaria (CM), defined clinically as coma in the setting of parasitemia, is a severe disease variant that predominantly affects children and historically has been thought to account for a large percentage of febrile central nervous system (CNS) disease. A growing body of research now suggests that plasmodial infections may be responsible for a much smaller proportion of febrile coma than previously appreciated. Consistent with this are several recent studies suggesting that retinopathy-negative CM may be due to non-malarial pathogens. Given that the responsible agent for most cases of febrile non malarial CNS (NMC) remain unknown, current clinical practices are nonspecifically directed and thus may fail to cover clinically important pathogens leading to poor treatment outcomes and significant morbidity and mortality. Metagenomic platforms that incorporate ultra deep sequencing of microbial genomes now offer an advanced approach to understanding previously un-diagnosable clinical syndromes. Here, we utilized deep sequencing to characterize the spectrum of microbial pathogens present in the CSF of Tanzanian children presenting to district hospitals for treatment of coma and a fever, and meeting criteria for either CM according to World Health Organization (WHO) criteria or a non-malarial febrile CNS condition. Overall, these efforts aim to determine the etiology of febrile CNS disease in an East African population and examine the prevalence of co-infection in patients diagnosed with cerebral malaria.

Methods: Next generation sequencing was utilized to characterize the spectrum of microbial pathogens present in CSF from Tanzanian children admitted to district hospitals for treatment of coma and a fever and meeting criteria for either CM or NMC according to World Health Organization criteria. Study patients received IV antimalarial and antibiotic treatment per WHO standards upon admission, as well as diagnostic studies including blood smear and cultures of both blood and CSF. Total RNA was purified from the CSF of 20 patients with NMC who were blood and CSF culture-negative and 25 patients diagnosed with CM according to WHO criteria. DNA libraries were prepared and subjected to paired-end ultra-deep sequencing on an Illumina HiSeq instrument. To screen for pathogens, low quality, low complexity sequences and human derived sequences were removed using the Bowtie2 algorithm, and the remaining reads were analyzed using the BLASTn and BLASTx bioinformatic algorithms.

Results: Sequences aligning with bacterial pathogens were detected in 50% of culture-negative CSF samples from the NMC cohort and more than 40% of samples in the CM cohort. Bacterial pathogens identified included Streptococcus pneumoniae, Pseudomonas Aeruginosa, Acinetobacter baumannii, Hemophilus influenzae, Neisseria menigitidis, Escherichia coli and Salmonella enteritica. The fungal pathogen Cryptococcus neoformans was also identified.

Conclusions: These data suggest that a significant percentage of children diagnosed with CM may be co-infected with virulent bacterial or fungal pathogens. Our results also indicate that a sizeable fraction of culture-negative febrile CNS disease in Tanzanian children may be due to treatable bacterial and fungal pathogens. It is possible that co-infection may be a significant determinant of disease severity and in part responsible for the high mortality and morbidity of cerebral malarial infections. If true, these findings could impact the clinical management of CM and NMC in East African nations burdened with these syndromes. To overcome limitations of small sample size, analysis of an expanded cohort of NMC and CM patients is currently underway. In addition, quantitative PCR directed at a panel of meningeal bacterial and fungal pathogens is being performed to verify these results.
Abstract title: MyPICS: Photo Identification Cards of a Medical Team on an Inpatient Pediatric Ward

Resident’s name: Patrick Peebles, MD

Name of program: Pediatrics

Purpose: In training hospitals, families often find it difficult to identify and understand the roles of their many inpatient care providers. A previous study at a children’s hospital found that distributing a photo sheet with providers’ names and roles led to increased provider identification and improved satisfaction of care. We modified the intervention to photo identification cards distributed by providers.

Methods: We conducted a controlled trial of distributing photo cards, also known as MyPICS (“Physicians Involved in Care and Support”) cards, by inpatient physicians at UCSF Benioff Children’s Hospital from April 2012 - January 2014. Cards were created for each physician on a general pediatrics ward. Card information included the provider’s name, photo, level of training, prior education, 2-3 fun facts, and a description of the provider’s role (resident or attending). During times of data collection, providers distributed their cards to families in one hall (intervention) and not to families in another hall (control). We asked families in the intervention and control groups to identify their providers in a photo quiz. Both groups were surveyed on satisfaction of care using the American Board of Internal Medicine Patient Satisfaction Questionnaire (ABIM-PSQ). Lastly, parental attitudes toward trainee involvement were assessed using a survey. Means were compared by two-sided t-tests.

Results: 100 families participated in the study: 44 in the intervention group and 56 in the control group. The baseline demographics of both groups were similar. On average, families in the intervention group were better able to identify their providers with 50% correct identification vs. 18% by the control group (p < 0.001). On the ABIM-PSQ (1 = poor and 5 = excellent), families in the intervention group scored an average of 4.63 vs. 4.32 in the control group (p = 0.02). The mean of parents' attitudes toward trainee involvement (1 = lowest, 5 = highest) was 4.27 in the intervention group vs. 4.06 in the control group (p = 0.12).

Conclusions: On an inpatient pediatric ward, physician distribution of baseball-style photo cards led to increased identification by families of their inpatient physicians and increased satisfaction with care.
Abstract title: Prevalence and Cost to Medicare of Unnecessary Preoperative Medical Testing Prior to Cataract Surgery

Resident’s name: Catherine L. Chen, MD, MPH

Name of program: Anesthesia and Perioperative Care

Purpose: Current guidelines state that routine testing is not indicated for preoperative evaluation in any patient undergoing cataract surgery, since it neither decreases adverse events nor improves surgical outcomes. We sought to determine adherence to the preoperative testing guidelines and the putative costs resulting from lack of compliance.

Methods: Using Medicare claims data, we analyzed the prevalence and cost of preoperative testing in a 50% random sample of beneficiaries undergoing cataract surgery in the year 2011. We created a hierarchical model to assess for independent provider and patient characteristics associated with preoperative testing.

Results: Of the 448,531 Medicare beneficiaries who underwent cataract surgery, 237,125 (52.9%) had at least one preoperative test ordered. The rate of preoperative testing varied widely among care teams; 36.1% of care teams ordered preoperative tests in more than 75% of their patients. The amount paid by Medicare for preoperative evaluation in our sample was $45.3 million, including $16.5 million for testing alone. In adjusted models, patient characteristics associated with undergoing testing included increased age (AOR 1.1 per 10 year increase in age) and higher Charlson Comorbidity Index (AOR 1.56, 1.87 and 2.87 for score of 2, 3 and 4+, respectively). Provider characteristics significantly associated with undergoing testing include being in the Northeast region (AOR 1.81), having a higher concentration of ophthalmologists per capita (AOR 1.21), and being in the highest quartile of Medicare expenditures per beneficiary by HRR (AOR 1.24).

Conclusions: Preoperative testing prior to cataract surgery still occurs frequently despite clear guidelines recommending against it. Interventions to decrease inappropriate utilization of preoperative tests could result in substantial yearly cost savings for Medicare.
<table>
<thead>
<tr>
<th>Name</th>
<th>Program</th>
<th>Mentor</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Asa Clemenzi-Allen</td>
<td>Internal Medicine</td>
<td>Sarah Doernberg</td>
</tr>
<tr>
<td>Noelle Ebel</td>
<td>Pediatrics</td>
<td>Melvin Heyman</td>
</tr>
<tr>
<td>Joseph Ebinger</td>
<td>Internal Medicine</td>
<td>Christopher Barnett</td>
</tr>
<tr>
<td>Nneka Edwards-Jackson</td>
<td>Pediatrics</td>
<td>Valerie Flaherman</td>
</tr>
<tr>
<td>Sara Handley</td>
<td>Pediatrics</td>
<td>Henry Lee</td>
</tr>
<tr>
<td>Sean Kivlehan</td>
<td>Emergency Medicine</td>
<td>Prasanthi Ramanujam</td>
</tr>
<tr>
<td>Chaz Langelier</td>
<td>Internal Medicine</td>
<td>Joe DeRisi</td>
</tr>
<tr>
<td>Renuka Nayak</td>
<td>Internal Medicine</td>
<td>Lindsey Criswell</td>
</tr>
<tr>
<td>Adam Numis</td>
<td>Neurology</td>
<td>Heather Fullerton</td>
</tr>
<tr>
<td>Juno Obedin-Maliver</td>
<td>Obstetrics, Gynecology and RS</td>
<td>Rebecca Jackson</td>
</tr>
<tr>
<td>Kristoff Olson</td>
<td>Internal Medicine</td>
<td>Peter Ganz</td>
</tr>
<tr>
<td>Heidi Schmidt</td>
<td>Internal Medicine</td>
<td>Alka Kanaya</td>
</tr>
<tr>
<td>Lindsey Sheffler</td>
<td>Orthopaedic Surgery</td>
<td>Michelle James</td>
</tr>
<tr>
<td>Christopher Stauffer</td>
<td>Psychiatry</td>
<td>Joshua Woolley</td>
</tr>
<tr>
<td>Julian Villar</td>
<td>Emergency Medicine</td>
<td>Christopher Fee</td>
</tr>
</tbody>
</table>
Abstracts:
Poster Presentations

UCSF Resident Research Symposium

Wednesday, May 21\textsuperscript{st}, 2014
<table>
<thead>
<tr>
<th>Name</th>
<th>Residency Program</th>
<th>Mentor</th>
<th>Abstract Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jonathan Budzik</td>
<td>Internal Medicine</td>
<td>Payam Nahid</td>
<td>Pyrazinamide Resistance, Mycobacterium tuberculosis Lineage and Treatment Outcomes in San Francisco, California</td>
</tr>
<tr>
<td>A. Asa Clemenzi-Allen</td>
<td>Internal Medicine</td>
<td>Sarah Doernberg</td>
<td>The Impact of Socioeconomic Status on Clinical Outcomes in Patients with Staphylococcus Aureus Bacteremia</td>
</tr>
<tr>
<td>Chris Derderian</td>
<td>Anatomic Pathology</td>
<td>Tippi MacKenzie</td>
<td>Depletion of Mouse Fetal Host Hematopoietic Stem Cells Improves Engraftment Following In Utero Cell Transplantation</td>
</tr>
<tr>
<td>Noelle Ebel</td>
<td>Pediatrics</td>
<td>Melvin Heyman</td>
<td>Growth Differences in Early- Compared to Later-Onset Pediatric Inflammatory Bowel Disease</td>
</tr>
<tr>
<td>Joseph Ebinger</td>
<td>Internal Medicine</td>
<td>Christopher Barnett</td>
<td>Systolic Heart Failure Due to Stimulant Drug Use Is Common and Associated with Heavy Health Care Utilization in a County Hospital Population</td>
</tr>
<tr>
<td>Lindsay Hampson</td>
<td>Urology</td>
<td>Maxwell Meng</td>
<td>Tobacco Use and Smoking Cessation in Urology Patients</td>
</tr>
<tr>
<td>Sara Handley</td>
<td>Pediatrics</td>
<td>Henry Lee</td>
<td>Outcomes of Extremely Preterm Infants after Delivery Room Cardiopulmonary Resuscitation in a Population-Based Cohort</td>
</tr>
<tr>
<td>Cerine Jeanty</td>
<td>Surgery, Plastic Surgery &amp; East Bay Surgery</td>
<td>Tippi MacKenzie</td>
<td>Patients and Mice with Gastrochisis Have Increased Innate Lymphoid Cells and Eosinophils in Herniated Organs: A Potential Mechanism for T Cell-Mediated Bowel Inflammation</td>
</tr>
<tr>
<td>Philip Kurien</td>
<td>Anesthesia and Perioperative Care</td>
<td>Louis Ptacek</td>
<td>Period 2 Protein Modulation of Immune Function after Chronic Jet Lag</td>
</tr>
<tr>
<td>Brian Lau</td>
<td>Orthopaedic Surgery</td>
<td>Richard Souz</td>
<td>Inter- and Intra-rater Reliability of Patello-Femoral Kinematic Quantification by Fast Spin Echo MRI</td>
</tr>
<tr>
<td>Emily Levy</td>
<td>Pediatrics</td>
<td>Chris Dvorak</td>
<td>Safe and Effective Prophylaxis with Intravenous Pentamidine in the Pediatric Hematopoietic Stem Cell Transplant Population</td>
</tr>
<tr>
<td>Renuka Nayak</td>
<td>Internal Medicine</td>
<td>Lindsey Criswell</td>
<td>DNA Methylation Patterns Associated with Lupus Nephritis</td>
</tr>
<tr>
<td>Juno Obedin-Maliver</td>
<td>Obstetrics, Gynecology and RS</td>
<td>Rebecca Jackson</td>
<td>Vaginal Hysterectomy as a Viable Option for Female-to-Male (FTM) Transgender Men</td>
</tr>
<tr>
<td>Anobel Odisho</td>
<td>Urology</td>
<td>Peter Carroll</td>
<td>Variation in the Cost of Robot Assisted Radical Prostatectomy</td>
</tr>
<tr>
<td>Name</td>
<td>Residency Program</td>
<td>Mentor</td>
<td>Abstract Title</td>
</tr>
<tr>
<td>---------------------</td>
<td>------------------------------------</td>
<td>-----------------------</td>
<td>-------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Lisa Patel</td>
<td>Anatomic Pathology</td>
<td>Phuoc Le</td>
<td>Developing Pediatric Acute Care Evidence-Based Algorithms for Rural Clinics in Chiapas, Mexico</td>
</tr>
<tr>
<td>Suha Patel</td>
<td>Obstetrics, Gynecology and RS</td>
<td>Jennifer Smith</td>
<td>HIV Seropositivity and Multiple Concurrent HPV Infections as Risk Factors for Abnormal Cervical Cytology among Female Sex Workers in Nairobi</td>
</tr>
<tr>
<td>Merisa Piper</td>
<td>Surgery, Plastic Surgery &amp; East Bay Surgery</td>
<td>Laura Esserman</td>
<td>Mammographic Changes After Oncoplastic Reduction Mammaplasty</td>
</tr>
<tr>
<td>Jubin Ryu</td>
<td>Dermatology</td>
<td>Tejal Desai</td>
<td>Creating Microstructured Films for the Treatment of Cutaneous Fibrotic Disorders</td>
</tr>
<tr>
<td>Lindsey Sheffler</td>
<td>Orthopaedic Surgery</td>
<td>Lisa Lattanza</td>
<td>Radiation Exposure to Breast Tissue in Female Orthopaedic Surgeons</td>
</tr>
<tr>
<td>Lawrence Shiow</td>
<td>Pediatrics</td>
<td>David Rowitch</td>
<td>PGE2 Mediated Oligodendrocyte Precursor Arrest</td>
</tr>
<tr>
<td>Christopher Stauffer</td>
<td>Psychiatry</td>
<td>Joshua Woolley</td>
<td>The Effects of Intranasal Oxytocin and Attachment Avoidance on Response to Social and Drug-Related Stimuli in Patients with Opioid Use Disorder Receiving Opioid Replacement Therapy</td>
</tr>
<tr>
<td>Alanna Stone</td>
<td>Internal Medicine</td>
<td>Anh Innes</td>
<td>Tuberculosis Screening for Diabetic Patients in Community Clinics in Kunming, China</td>
</tr>
<tr>
<td>Belinda Waltman</td>
<td>Internal Medicine</td>
<td>Lindsey Criswell</td>
<td>Lupus Risk Alleles with High Ethnic Variability Worldwide</td>
</tr>
<tr>
<td>Melisa Wong</td>
<td>Internal Medicine</td>
<td>Sunny Wang</td>
<td>Impact of Comorbidity and Age on Survival among Older Veterans with Early Stage Non-Small Cell Lung Cancer (NSCLC)</td>
</tr>
<tr>
<td>Lara Zimmermann</td>
<td>Neurology</td>
<td>Claude Hemphill</td>
<td>Decompressive Hemicraniectomy and Contusion Expansion in Traumatic Brain Injury</td>
</tr>
<tr>
<td>Matt Zinter</td>
<td>Pediatrics</td>
<td>Anil Sapru</td>
<td>Infections, Interventions, and Mortality of Pediatric Bone Marrow Transplant Patients in the Intensive Care Unit</td>
</tr>
</tbody>
</table>
Abstract title: Pyrazinamide Resistance, Mycobacterium tuberculosis Lineage and Treatment Outcomes in San Francisco, California

Resident’s name: Jonathan Budzik, MD, PhD

Name of program: Internal Medicine

Purpose: Pyrazinamide (PZA) is a first line agent for the treatment of active tuberculosis. PZA is also considered a potent companion drug for newer regimens under development. There are limited data on the demographic, clinical, and pathogen characteristics of PZA resistant tuberculosis.

Methods: Using a retrospective cohort study design, we evaluated all PZA resistant M. tuberculosis (MTB) and M. bovis cases reported in San Francisco from 1991 to 2011. Demographic, clinical, and molecular data were analyzed. MTB lineage was determined for all PZA resistant strains and compared to PZA susceptible strains.

Results: PZA resistance was identified in 1.8% (50 of 2,842) of mycobacterial isolates tested, corresponding to a case rate of 0.3 per 100,000 in the population. Monoresistant PZA infection was associated with the Hispanic population ([OR], 6.3; 95% [CI], 1.97-20.16) and 48% of cases were due to M. bovis. Infection with monoresistant PZA was also associated with extrapulmonary disease ([OR], 6.0; 95% [CI], 2.70-13.26). There was no statistically significant difference between treatment failure and mortality rates in patients infected with PZA monoresistance compared to pansusceptible controls (4% vs. 8%, p = 0.51), or those with PZA and MDR resistance (PZA-MDR) compared to MDR controls (18% vs. 29%, p = 0.40). PZA resistance was not associated with MTB lineage.

Conclusions: Across two decades of comprehensive epidemiologic data on tuberculosis in San Francisco County, PZA resistance was uncommon. PZA resistance caused predominantly extrapulmonary disease and was more common in Hispanics compared to other ethnicities, with nearly half the cases attributed to M. bovis. No association was found between PZA monoresistance and MTB lineage. Treatment outcomes were not adversely influenced by the presence of PZA resistance.
**Abstract title:** Evaluating the Impact of Socioeconomic Status on Clinical Outcomes in Patients with *Staphylococcus aureus* Bacteremia

**Resident’s name:** A. Asa Clemenzi-Allen, MD

**Name of program:** Internal Medicine

**Purpose:** *Staphylococcus aureus* bacteremia (SAB) is a leading cause of bloodstream infections, carrying high rates of morbidity and mortality. Limited research exists on the impact of socioeconomic status (SES) on complications and severity of illness in patients with SAB.

**Methods:** This was a prospective cohort study of all adult patients with a first episode of SAB presenting to San Francisco General Hospital, the San Francisco County hospital, from 2008-2012. Subjects were identified by a comprehensive infection surveillance system. Primary predictors were percent of individuals under the federal poverty limit (POV) or median household income (MHI) within each patient’s given zip code, and homelessness. Primary outcomes were intensive care unit (ICU) admission, meeting systemic inflammatory response syndrome (SIRS) criteria on admission, and diagnosis of vertebral osteomyelitis or endocarditis. Multivariate logistic regression controlling for HIV status, age, race, gender, injection drug use and the Charlson comorbidity index was used to assess the impact of SES on primary outcomes.

**Results:** There were 437 unique individuals with first presentations of SAB, of which 406 had homelessness data and 398 had zip code, median income and poverty data. 94/406 (23.2%) of individuals were homeless. In separate logistic regression models MHI and POV were not associated with ICU admission, but homelessness was protective against admission to the ICU (OR 0.39, 95% CI 0.19, 0.80). No variables were predictive of meeting SIRS criteria on admission. MHI, POV and homelessness were not associated with diagnoses of vertebral osteomyelitis/discitis or endocarditis. Post-hoc Cox proportional hazard modeling revealed no association between homelessness and mortality, readmission or SAB recurrence at 90 days.

**Conclusions:** In an ethnically and economically diverse safety-net population, lower neighborhood socioeconomic status was not associated with complications at presentation including endocarditis, vertebral osteomyelitis/discitis, ICU admission and meeting SIRS criteria in patients with SAB. Homelessness was protective against ICU admission, suggesting SES may impact triage decision-making.
Abstract title: Depletion of Mouse Fetal Host Hematopoietic Stem Cells Improves Engraftment Following In Utero Cell Transplantation

Resident’s name: Chris Derderian, MD

Name of program: Anatomic Pathology

Purpose: In utero hematopoietic cell transplantation (IUHCTx) is a promising strategy to treat congenital disorders as the fetal host can potentially be tolerized to transplanted cells early in gestation. However, levels of engraftment have been low and fetal host conditioning strategies to increase space in hematopoietic niches have not been widely explored. We hypothesized that depletion of fetal host hematopoietic stem cells (HSC) using an antibody against the c-kit receptor (ACK2), a strategy which selectively depletes HSC by disrupting stem cell factor (SCF) signaling, would improve engraftment after HSC transplantation.

Methods: Fetal C57B6.CD45.2 (B6) mice were injected with increasing doses of ACK2 (2.5-50 µg/fetus) or isotype control antibody on E14.5 and surviving pups were transplanted with congenic B6.CD45.1 fetal liver mononuclear cells (2.5×10^6 cells/pup) on day of life 1 (P1, 7 days after in utero injection), allowing post-transplantation host monitoring. Host HSC depletion and residual serum ACK2 concentration were examined on P1. Peripheral blood chimerism, defined as donor/(donor+host) CD45 cells, as well as the lineage distribution of chimeric cells, were determined beginning 4 weeks after transplantation.

Results: Survival to birth among fetuses injected with 2.5, 5, or 10 µg of ACK2 was similar to controls (control: 74%; 2.5 µg: 80%; 5 µg: 71%; 10 µg: 60%, p=0.2 by chi-square test, n?45/group) but was significantly lower at higher concentrations (20 µg: 37%; 50 µg: 31%, p<0.001 vs. control, n?70/group). Transient anemia and leukopenia were observed on P1 with doses ≥ 5 µg which resolved by P7 (n=17). Four of 19 pups treated with ACK2 (2.5-10 µg) and observed long-term had patchy coat discoloration, possibly a manifestation of disruption of C-kit+ melanocyte migration. > In utero ACK2 treatment resulted in significant and dose-dependent depletion of host HSCs (defined as Lin-Sca-1+C-kit+, KLS) in the bone marrow of treated animals by P1. Seven days after ACK2 treatment (5 µg/fetus) total number of KLS cells within the bone marrow was 2.4±0.7×10^5 compared to 2.3±0.2×10^6 in control mice (p<0.01, n ? 14 for each group), a 10-fold reduction in the number of KLS cells. Additionally, antibody cleared from the serum There was no depletion of KLS cells in the liver. Residual ACK2 antibody was undetectable in the serum by P1, validating our strategy of in utero depletion and neonatal transplantation. > In animals receiving neonatal transplantation, ACK2 depletion resulted in a significant increase in levels of engraftment 4 weeks after transplantation compared to controls (control: 3.3±0.3%; 2.5 µg: 13±1.4%; 5 µg: 10±2.4%; 10 µg: 11±2.0%, p<0.05 for each dose vs control by ANOVA). Accordingly, we detected an increased number total bone marrow KLS cells 7 days after transplantation in ACK2 treated animals compared to controls (412±45.9 vs. 933±112 cells, p=0.01, n?3/group). Moreover, levels of chimerism increased over time in treated animals (12 weeks: 2.5 µg: 190%; 5 µg: 170%; 10 µg: 160%) while they remained unchanged in controls. Overall, levels of chimerism achieved with ACK2 treatment were significantly higher than that observed in animals that received in utero transplantation without ACK2 depletion.

Conclusions: We have demonstrated that fetal HSC depletion using ACK2 can lead to clinically relevant levels of donor cell engraftment with minimal toxicity. In previous studies with this antibody, host HSC depletion required either immunodeficient animals or concurrent irradiation, whereas we achieved depletion in wild-type fetal hosts, suggesting differences in fetal vs. adult HSC sensitivity to SCF signaling. Future studies should explore this strategy to improve engraftment in large animals models of IUHCTx.
Abstract title: Growth Differences in Early- Compared to Later-Onset Pediatric Inflammatory Bowel Disease

Resident’s name: Noelle H. Ebel, MA, MD

Name of program: Pediatrics

Purpose: Linear growth impairment is a known complication of pediatric Inflammatory Bowel Disease (IBD) occurring more commonly in patients with Crohn’s disease (CD) than in those with Ulcerative Colitis (UC). However, while growth failure in older children and adolescents may be the first presenting sign of IBD, few studies have addressed if the same is true for infants and young children with an earlier onset of disease. Additionally, longitudinal growth in early onset patients has not been well described. The primary aim of our study was to compare longitudinal growth in patients with early compared to later onset IBD.

Methods: We retrospectively studied 200 pediatric patients diagnosed with IBD followed at UCSF between 1999 and 2013 of whom 32 had early onset IBD (defined as 0-6 years old) and 168 with later onset IBD (defined as 7 years of age and older). Growth parameters were recorded at the time of diagnosis and 3 subsequent time points: 12 months from diagnosis, at the last follow-up visit and 12 months prior to the last visit. Growth data was then converted to z-scores for further comparisons. The number of hospitalizations and IBD related surgeries were also examined as a proxy for disease severity along with medication usage with a specific focus on steroids.

Results: Patients with early onset IBD were more likely to have a change in diagnosis with a trend towards a final diagnosis of Ulcerative Colitis (UC) (p=0.084), while patients with later onset IBD were more likely to have a faster change in diagnosis with a mean of 33 days compared to 211 days for early onset patients (p = 0.006). Patients with early onset IBD had higher BMI z-scores at the time of diagnosis (0.582 for early compared to -0.154 for later onset patients, p=0.001). There was no difference in height or weight z-scores at the time of diagnosis or change in height z-score over the course of disease for early compared to later onset IBD patients. However, patients with early onset UC showed poorer longitudinal growth over the course of their disease with a change in height z-score of -0.238 compared to patients with later onset UC who had a change in height z-score of -0.051 (p=0.026). There was a trend towards higher steroid usage in patients that were 0-3 years old (p=0.053). However, there were no significant differences in change in height z-scores between early compared to later onset IBD patients based on cumulative steroid exposure over the first 3 years of disease following diagnosis.

Conclusions: We describe epidemiologic characteristics and their association with longitudinal growth in patients with early compared to later-onset IBD. When accounting for duration of symptom onset prior to diagnosis, patients with early-onset IBD had higher BMIs at the time of diagnosis. We also describe a novel finding, that patients with early-onset UC have poorer longitudinal growth when compared to patients with later-onset UC. Finally, we observed that there was no difference in change in height z-score between early compared to later onset patients even after adjusting for length of follow-up. To our knowledge, our study is the first to characterize longitudinal growth in early compared to later onset IBD based on Pediatric IBD consensus guidelines.
Abstract title: Systolic Heart Failure Due to Stimulant Drug Use Is Common and Associated with Heavy Health Care Utilization in a County Hospital Population

Resident’s name: Joseph Ebinger, MD

Name of program: Internal Medicine

Purpose: In 2010, over 350,000 individuals used methamphetamine regularly, with an estimated 8.63% lifetime use in the United States. That same year, methamphetamine use was associated with 102,961 ED visits, a 71% increase from 2009, many of which were for heart failure, which has anecdotally been linked with stimulant use.

Methods: We performed a retrospective chart review of all San Francisco General Hospital patients with an echocardiogram between July 2007 and September 2009 showing new moderate-severe or severe left ventricular systolic dysfunction. We then performed chart review to determine etiology of heart failure, demographic information and resource utilization.

Results: A total of 479 patients were included, 179 (37%) had a final diagnosis of stimulant induced cardiomyopathy, defined as recorded stimulant use and no evidence of ischemia or other causes of cardiomyopathy. Of stimulants (82.6%) were due to cocaine and (35.7%) were attributed to methamphetamine. Of these, 33 had used both substances. Compared with non-stimulant induced cardiomyopathy, those whose heart failure was attributed to stimulant use were younger (62.5 vs. 49.3 years old, p<0.01), were more likely to be female (26.2% vs 16.2%, p< 0.01), smokers (74.3% vs 36%, p<0.01) and were more likely to be African American (53.1% vs 22%, p<0.01). There was no difference in BMI or rates of diabetes. These patients were also more likely to revisit the ED (7.9 vs 3.1, p<0.01) and to be readmitted (3.52 vs 2.58, p<0.01).

Conclusions: Patients with stimulant induced cardiomyopathy, compared with non-stimulant users with heart failure, were younger, more likely to be female and African American. These patients also utilize healthcare resources at a higher level than non-stimulant heart failure patients, with a higher readmission rate that may disproportionally effect hospitals that serve this patient population.
Abstract title: MilkMoney: A Financial Incentive Intervention to Increase Breastfeeding Rates among Low-Income, Inner-City African American WIC Clients

Resident’s name: Nneka Edwards-Jackson, MD

Name of program: Pediatrics

Purpose: African American infants served by the Supplemental Nutrition Program for Women, Infants, and Children (WIC) come from low-income populations with higher health morbidities who could benefit from the health advantages associated with breastfeeding. Breastfeeding rates among African American mothers are lower as compared to other racial and ethnic groups. The availability of formula from WIC may negatively influence breastfeeding rates among young African American mothers. This study aims to develop a financial incentive program to encourage breastfeeding among low-income African American WIC clients.

Methods: This is a randomized controlled pilot study that will enroll ten newly postpartum African American mothers and infants delivered at San Francisco General Hospital (SFGH). Mothers will be contacted via phone at 1 week, and then 1, 2, 4, and 6 months. Mothers in the intervention group will receive financial incentives for breastfeeding at each time point: a breastfeeding support package worth $65 for initiation and a $50 Visa Debit card for breastfeeding at each subsequent time point. Quantitative data will be collected on process outcomes (recruitment, enrollment, and follow-up) and clinical outcomes (breastfeeding at each time point). Fisher’s exact tests will be used to assess the effect of the incentive intervention. Qualitative data will be obtained from post-intervention focus groups.

Results: Subject enrollment will begin May 2014.

Conclusions: MilkMoney is a unique intervention that aims to improve breastfeeding rates among African American mothers and infants, thus reducing racial health disparities. Results from this pilot will be used to guide larger randomized trials to evaluate this intervention’s effectiveness. In the future, the success of MilkMoney could be used to guide WIC policies in terms of the incentives provided to encourage new mothers to breastfeed.
Purpose: Smoking is the leading risk factor associated with death and disability-adjusted life-years and is particularly relevant to the urologic community given that cigarette smoking has been linked to bladder cancer, renal cell carcinoma, upper tract urothelial carcinoma, and erectile dysfunction. Furthermore, smoking also has a significant impact on surgical recovery and is associated with increased perioperative and wound healing complications, including longer hospital stays, higher rates of ICU admission, and higher costs of care. Evidence has shown that smoking cessation around the time of surgery may lead to higher smoking cessation rates as well as decreased perioperative risks. Despite this, smoking cessation is not routinely advised to patients undergoing urologic surgery.

We designed a resident-led initiative targeted at urologic patients undergoing surgery at UCSF Mt. Zion Cancer Center and UCSF Parnassus Hospital starting August 2013. Our set goal was to elicit the smoking status of at least 80% of our perioperative patients who stayed at least one night in the hospital and to obtain an inpatient smoking cessation consult for those patients who were active smokers. A hospital-based financial incentive of $400 would be provided to each resident if our department was able to accomplish our 80% goal in 3 out of 4 quarters in 2013-2014.

Methods: Starting 8/1/2013, the residents and nurse practitioners on the urology service elicited the smoking status of urology patients undergoing surgery who would be staying at least one night in the hospital. Those patients who were smokers were asked for their permission and, if granted, a smoking cessation consult was obtained. The recommendations of the consult were followed both in-hospital and post-discharge according to the patients’ wishes. Patients who refused the smoking cessation consult were provided with educational material on smoking cessation. T-test for continuous outcomes and chi-squared analysis for categorical outcomes were used for two-sided tests of equal variance, with a p-value of < 0.05 considered significant.

Results: As of 4/1/2014, 659 patients had been assessed in total. 9.3% were current tobacco users, 35.1% were past users, and 55.7% were never users. Current smokers were more likely to be younger and female (both p = 0.02). Past users were more likely to have a cancer diagnosis or tobacco-related diagnosis (both p < 0.01). 79% of smokers underwent a tobacco cessation consult and there were no predictors in univariate analysis that predicted likelihood of refusing a consult. Patients who had a consult were significantly more likely to be prescribed nicotine-replacement therapy during their hospitalization (97.4% vs. 40.0%, p < 0.01). The vast majority (81%) of patients receiving consults were also discharged with nicotine-replacement therapy.

Prior to the initiative, 0% of our patients’ smoking status was assessed and no patients were ever referred by our service to the inpatient smoking cessation consult service. Our department showed significant improvement, achieving 59% assessment rate in quarter 1, 86% in quarter 2, and 100% by quarter 3.

Conclusions: As urologists, screening for tobacco use is important, as 1 in 11 patients undergoing inpatient surgery are current smokers. Furthermore, these individuals are more likely than never smokers to be younger and female, and we must avoid screening bias to identify these individuals. Our quality improvement initiative has demonstrated drastic improvement in both identifying patients’ smoking status and obtaining a perioperative smoking cessation intervention for current smokers, suggesting that this is a fast, feasible, and easily-implemented assessment to identify smokers and obtain smoking cessation counseling and treatment for patients at a time when they are perhaps most amenable to quitting. Further analysis of smoking cessation rates is being conducted in a randomized trial to determine the success of the perioperative smoking cessation intervention and predictors for successful cessation in this population.
Abstract title: Outcomes of Extremely Preterm Infants after Delivery Room Cardiopulmonary Resuscitation in a Population-Based Cohort

Resident’s name: Sara C. Handley, MD

Name of program: Pediatrics

Purpose: To evaluate the relationship between delivery room cardiopulmonary resuscitation (DR-CPR) and outcomes in a population based cohort of extremely preterm infants.

Methods: This was a cohort study of 22-27+6/7 weeks gestational age infants, born from 2005-2011 in California. DR-CPR was defined as chest compressions and/or epinephrine use. Multivariable logistic regression was used to examine associations between DR-CPR and outcomes, with stratification by gestational age. Odds ratios (OR) with 95% confidence intervals (CI) were estimated.

Results: There were 13,758 infants, with 856 (6.2%) receiving DR-CPR. Infants receiving DR-CPR had lower birth weight (767 ± 205g vs 819 ± 204g, p < 0.0001) and lower Apgar scores. For infants born at 22-23+6/7 weeks, outcomes were similar between the two groups. Infants born at 24-25+6/7 weeks receiving DR-CPR were more likely to have grade 3 or 4 intraventricular hemorrhage (OR 1.36, 95% CI 1.07, 1.72). Infants born at 26-27+6/7 weeks receiving DR-CPR were more likely to die in the first twelve hours (OR 2.35, 95% CI 1.14, 4.86) or prior to hospital discharge (OR 1.81, 95% CI 1.30, 2.51), have early onset sepsis (OR 2.84, 95% CI 1.68, 4.82), grade 3 or 4 intraventricular hemorrhage (OR 2.10, 95% CI 1.56, 2.82), and require postnatal steroids (OR 1.36, 95% CI 1.03, 1.79). Adjusted hospital DR-CPR rates varied, with median rate 5.7% (interquartile range 2.9%-8.9%).

Conclusions: Extremely premature infants receiving DR-CPR generally had worse outcomes than infants not receiving DR-CPR. The degree of mortality and morbidity varied by gestational age.
Abstract title: Patients and Mice with Gastroschisis Have Increased Innate Lymphoid Cells and Eosinophils in Herniated Organs: A Potential Mechanism for T Cell-Mediated Bowel Inflammation

Resident’s name: Cerine Jeanty, MD

Name of program: Surgery, Plastic Surgery & East Bay Surgery

Purpose: The pathophysiology of intestinal inflammation and diminished motility in gastroschisis is poorly understood. We recently reported that patients with gastroschisis have activated T cells in the blood, and intestinal infiltration of eosinophils and T cells, suggesting early activation of the adaptive immune system as seen in inflammatory bowel disease (IBD). We now analyze human and murine innate immune cells, such as innate lymphoid cells (ILC), eosinophils, natural killer (NK) cells, and granulocytes, which may drive precocious maturation of T cells in gastroschisis.

Methods: We collected intestinal specimens from patients with gastroschisis (n=4) and healthy controls (n=4) undergoing bowel resection. We also harvested intestine and liver of transgenic fetal mice that develop a spontaneous abdominal wall defect in utero. We isolated intestinal and hepatic lymphocytes, stained for markers of innate immune cells, and analyzed the samples using flow cytometry.

Results: Patients with gastroschisis have increased ILC in the intestine compared to controls (p=0.03). Similarly, mice with gastroschisis have elevated ILC and eosinophils, as well as NK cells and granulocytes in intestine and liver compared to controls (Table 1). Importantly, the changes in the mouse are observed predominantly in herniated organs exposed to amniotic fluid.

Conclusions: ILC and eosinophils, which are known to regulate T cell activation and induce tissue damage in IBD, are increased in the intestine of patients and mice with gastroschisis. These findings suggest a mechanism for the early maturation of T cells, and indicate that this mouse is a suitable tool to investigate therapeutic measures to decrease bowel damage in gastroschisis.
Abstract title: Period 2 Protein Modulation of Immune Function after Chronic Jet Lag

Resident's name: Philip A. Kurien, MD

Name of program: Anesthesia and Perioperative Care

Purpose: Circadian rhythm is maintained by molecular clocks at the cellular level and provides context for coordination of various tissue intrinsic and extrinsic processes. Immune cells express clock proteins and cytokines in a rhythmic pattern, outlining circadian rhythm specificity within particular immune subsets (i.e. T cell versus macrophage). Given the distinct function of immunologic subsets in response to an inflammatory stimulus, it is likely that circadian proteins play an important role in coordinating inflammation related to different kinds of antigens. Previous experiments have linked circadian rhythm to immune susceptibility in the setting of simulated chronic jet lag and, independently, daily peaks of circulating immune cells and expression of cytokines. Collectively, data from these experiments intimate causality through the modulation of core clock machinery, specifically the transcription factor BMAL.

Methods: To investigate the effect of altered BMAL levels on immune function we employ the model of Familial Advanced Sleep Phase (FASP). FASP transgenic mice harbor mutations in the Period 2 gene and confer reduction in PER2 protein phosphorylation resulting in an advanced phase phenotype and altered BMAL cycling. Transgenic mice and wild-type litter mates are subjected to chronic experimental jet-lag and subsequently injected with LPS to induce an inflammatory response. Tissues are harvested for cytokine analysis, gene expression, and cellularity.

Results: Here we show that FASP transgenic mice rapidly recover after simulated chronic jet lag as evidenced by actigraphic measurements. The pattern of phosphorylation of endogenous Per2 protein is significantly altered between groups. After recovery from simulated jet lag, FASP mice demonstrate persistent changes in monocytic cellular composition in circulation and the spleen, and have altered cytokine generation after inflammatory stimulation compared to wild-type controls ex vivo.

Conclusions: FASP transgenic mice recover from simulated jet lag and have altered immune responses when challenged with LPS compared to wild-type litter mates. The precise mechanism of by which the molecular clock governs this process remains to be elucidated.
Abstract title: Inter- and Intra-rater Reliability of Patello-Femoral Kinematic Quantification by Fast Spin Echo MRI

Resident’s name: Brian C. Lau, MD

Name of program: Orthopaedic Surgery

Purpose: Patellofemoral pain (PFP) is one of the most common conditions and affects nearly 25% of the population. The most accepted cause of PFP is patellofemoral maltracking or malalignment, leading to abnormal stresses on the subchondral bone which may increase incidence and severity of patellofemoral osteoarthritis. Current clinical and radiographic assessments demonstrate only marginal ability to diagnose and follow PFP. In vivo MR-based patello-femoral kinematic evaluation presents a potentially non-invasive and reproducible method to directly assess patella movement while also providing valuable information concerning the status of patellar cartilage. The purpose of this study is to determine the intra- and inter-rater reliability of a novel semi-automated program for MR-based patellofemoral kinematics.

Methods: Sixteen subjects (10 with PFP and 6 without PFP served as controls) participated in the study (age: 30.8 years (range 24-41), 8 female). MR imaging was performed using a 3T scanner (General Electric, WI) and an in-house built loading apparatus mounted on the scanner table. Two sets of T2-weighted MR images, fat-saturated fast spin-echo (FSE) images of one knee (controls: dominant knee; PFP patients: knee with patellofemoral pain) were acquired. The first set of images were acquired in full extension (0 degrees) with 25% of the subject’s weight load applied at the bottom of subjects’ foot by a footplate through a pulley system, and the next set was acquired in 30 degrees of knee flexion with the same amount of load. Following image acquisition, regions of interest are segmented on the images with novel in-house spline-based semi-automated software designed for this project. To date all subjects have been segmented once by 2 separate raters for inter-user reliability and 5 patients have been segmented for intra-user reliability.

Results: Intraclass Correlations Coefficients (ICC) of calculated kinematic parameters reached good to excellent levels of reliability for intrauser-rater and interuser-rater reliability (0.8-1.0) for Patella Flexion, Patella Tilt, Patella Rotation, Patella Translation (Anterior-Posterior, Medial-Lateral, and Superior to Inferior), Contact Area (Extended and Flexed), and Contact Area Translation (Anterior-Posterior, Medial-Lateral, and Superior to Inferior).

Conclusions: The preliminary results of this study demonstrate that patello-femoral kinematics using novel MRI based software can be quantified in a highly reliable fashion and has the potential to assist in diagnosing and tracking patients with patellofemoral knee pain. We will continue processing all subjects and compare patella kinematics between control and PFP patients. We will also correlate patella kinematics between groups with cartilage degeneration as defined by T1rho MRI imaging.
**Abstract title:** Safe and Effective Prophylaxis with Intravenous Pentamidine in the Pediatric Hematopoietic Stem Cell Transplant Population

**Resident’s name:** Emily R. Levy, MD

**Name of program:** Pediatrics

**Purpose:** Background: Without prophylaxis, Pneumocystis Jiroveci pneumonia (PCP) develops in 5-15% of pediatric hematopoietic stem cell transplant (HCT) patients with mortality rates above 50%. Trimethoprim-sulfamethoxazole is standard PCP prophylaxis, however, intravenous (IV) pentamidine is frequently used to avoid bone marrow suppression. Monthly IV pentamidine has variable efficacy in HCT pediatric patients with PCP infection rates of 0-10%, and higher breakthrough in those <2 years old. To increase efficacy, UCSF administers prophylactic IV pentamidine every 2 weeks, as pharmacokinetic studies demonstrate a 10-14 day elimination half-life.

Objective: To quantify the efficacy and toxicities of bi-monthly IV pentamidine PCP prophylaxis in the pediatric HCT population.

**Methods:** We retrospectively reviewed records of all pediatric patients 12/1/2006 – 1/1/2012 who received IV pentamidine. We identified HCT patients and collected data regarding demographics, clinical course, rationale for pentamidine, laboratory values, and adverse events.

**Results:** Over 5 years, 267 pediatric patients underwent HCT, of which 85 (with a total of 112 HCTs) received IV pentamidine as PCP prophylaxis (95 individual courses; 482 total doses; 241 patient-months). Twenty-three (27%) patients were ≤2.0 years old at pentamidine initiation. No patients were diagnosed with PCP at any time during or after IV pentamidine; 3 patients underwent bronchoalveolar lavage with negative silver stain.

The average course was 2.5 months (5 doses; st dev 6). The most common initiation reason was myelosuppression and the most common discontinuation reason was resolved myelosuppression.

Four patients (4.7%; 0.8% doses) experienced a major side effect, all involving infusion-related hypotension (1 anaphylaxis, 1 with altered mental status). Five patients (5.8%, 1.0% doses) experienced a minor side effect prompting discontinuation (2 infusion reactions, 1 nausea, 1 rash, 1 anemia). Pentamidine was discontinued for possible contribution in two patients (2.4%; 0.4% doses) who developed pancreatic dysfunction and one patient (1.2%; 0.2% doses) who developed cyclic elevated liver function tests with abdominal pain. No courses were discontinued based on only renal or liver laboratory values.

**Conclusions:** Bi-monthly IV pentamidine for PCP prophylaxis has comparable safety in the HCT pediatric population to previously described toxicities of monthly IV pentamidine. It should be considered as the 2nd line option to trimethoprim-sulfamethoxazole as it trended towards higher prophylactic efficacy than previous reports for monthly IV pentamidine, particularly in the very young.
Abstract title: DNA Methylation Patterns Associated with Lupus Nephritis

Resident's name: Renuka R. Nayak, MD, PhD

Name of program: Internal Medicine

Purpose: Genetic and epigenetic factors contribute to the development and progression of systemic lupus erythematosus (SLE). New technologies enable genome-wide examination of these factors and their influence on SLE manifestations. Research has already demonstrated that genetic polymorphisms are associated with lupus nephritis, but few studies have examined epigenetic modifications associated with lupus nephritis patients. While genetic polymorphisms are fixed, epigenetic modifications are inherited but also modifiable by environmental factors. Therefore epigenetic modifications can provide insight into the development and progression of SLE nephritis, which affects about half of patients with the disease. The focus of this study is to examine which, if any, DNA methylation patterns are associated with lupus nephritis.

Methods: We enrolled 326 consecutive Caucasian non-smokers with SLE, 80 of whom carried a diagnosis lupus nephritis. We used the Illumina Infinium HumanMethylation450 BeadChip to examine ~480,000 epigenetic marks (i.e. methylation marks) on the genomic DNA of each patient. This high-throughput array profiles CpG sites in ~23,000 genes and assesses methylation for sites in promoters, 5' and 3' regions, gene bodies, CpG islands, CpG island shores, and outside of CpG islands. As part of our preliminary analysis, we identified methylations marks that were associated with lupus nephritis using a Wilcoxon Rank Sum test.

Results: Preliminary analyses using Wilcoxon Rank Sum testing showed there were 8 methylation marks that were associated with lupus nephritis. We will refine these results by performing multivariate analyses in order to control for factors such as age, disease duration and processing of samples. Future studies also will examine candidate genes that are known to play roles in the development of lupus nephritis.

Conclusions: DNA methylation marks are associated with lupus nephritis. Further characterization of these marks will be useful in understanding the pathogenesis of lupus nephritis and stratifying patients to determine their risk of lupus nephritis.
Abstract title: Vaginal Hysterectomy as a Viable Option for Female-to-Male (FTM) Transgender Men

Resident’s name: Juno Obedin-Maliver, MD, MPH

Name of program: Obstetrics, Gynecology and RS

Purpose: According to the 2011 Institute of Medicine Report and emphasized by the American Congress of Obstetricians and Gynecologists (ACOG) committee opinion, transgender individuals encounter significant healthcare barriers. ACOG charges obstetrician gynecologists (OB/GYNs) to help eliminate these barriers to care by creating non-discriminatory practices and assisting with transitioning. This includes supporting social, medical, and surgical aspects of the gender-affirmation process. OB/GYNs are able, without additional training, to perform hysterectomies for transgender men, and total vaginal hysterectomies (TVH) are the least morbid and most cost-effective form of hysterectomy. However, prior studies have challenged the viability of TVH for FTM without documenting comparative evidence on hysterectomy route, complication rates, conversion rates, or differences relative to cis-gender women (cis-women).

The purpose of this study is to demonstrate that TVH are a safe and procedurally viable option for transgender men.

Methods: We present data from a retrospective cohort of all hysterectomies performed for benign indications at a single urban county hospital from 2000-2012. The two comparison groups are transgender men and cis-women.

Results: A total of 948 hysterectomies were performed for benign indications during the time period of interest. Of those, 34 were for FTM. Preliminary data demonstrates that, compared with cis-women, FTM were younger, had fewer pregnancies and deliveries, had smaller uteri, had lower BMI, were usually on testosterone prior to surgery, and were more likely to have concurrent oophorectomies. The primary indication for hysterectomy for FTM was pain (53%) versus bleeding (46%) for cis-women. TVHs were performed in 24% of FTM compared with 39% of cis-women. There was no difference in complication or conversation rates between the two groups.

Conclusions: From these data, we note that TVH is a viable option for FTM. Furthermore it is long considered a safe, viable, and cost-effective option that should therefore be considered for FTM undergoing hysterectomy and gender-affirmation surgery. We hope these data will encourage other OB/GYNs to consider TVH as a minimally-invasive option in serving FTM. Providing this service may be part of promoting equality of transgender individuals and augmenting access to care for this often marginalized population.
**Abstract title:** Variation in the Cost of Robot Assisted Radical Prostatectomy

**Resident’s name:** Anobel Y. Odisho, MD, MPH

**Name of program:** Urology

**Purpose:** Cost analysis efforts in surgery have focused on comparing treatment options. However, identifying surgical procedures in which significant supply cost variation exists can focus attention on opportunities for cost-effectiveness. We evaluate one high-volume procedure within our institution, robotic-assisted laparoscopic prostatectomy (RALP), to identify variation in surgical supply case costs.

**Methods:** All RALPs performed at our institution over a one-year period (9/2012 – 9/2013) were identified. Surgical supply costs were identified as the institution-negotiated rate for each item used during a case. Surgical supply costs were evaluated for each surgeon and analyzed with one-way analysis of variance and adjusted pairwise t-tests. Itemized average supply costs per case were also evaluated to determine drivers of increased cost. To assess the potential association of higher supply cost with decreased case length, sensitivity analyses were performed by monetizing case time ($69/minute) and evaluating combined supply and time costs.

**Results:** Over a one-year period, 282 RALPs with or without lymphadenectomy were performed by 4 urologic oncologists (volume range 15-205). Mean case supply cost varied significantly by surgeon (p < 0.001), with a mean supply cost of $1,429.82 per case for all providers and individual provider means ranging from $1284.85 to $2523.54. Sensitivity analyses confirmed variation in supply cost was not mitigated by differences in case duration, as there was no statistically significant variability in total cost when supply and time costs were combined (p = 0.268).

Analysis of aggregated itemized supply costs by surgeon revealed that individual surgeons’ supply costs were impacted by differential utilization of specific supplies. Overall, the main drivers of increased cost variation were hemostatic agents (Tisseel, Floseal), Endo-GIA stapler use, Hem-O-Lok clips, and LapraTy suture clips.

**Conclusions:** Analysis of OR supply utilization shows significant variation in supply case costs. These data show that differential use of certain expensive supplies results in a significant increase in cost. These data must now be reconciled with patient outcomes to identify how we can provide the highest value of care and maintain excellent patient outcomes while lowering costs.
Abstract title: Developing Pediatric Acute Care Evidence-Based Algorithms for Rural Clinics in Chiapas, Mexico

Resident's name: Lisa H. Patel, MS, MD

Name of program: Anatomic Pathology

Purpose: Partners in Health has prioritized standardizing and simplifying care based on evidence and adapted to the resources of health systems. This project focused on expanding their existing library of algorithms for acute care complaints.

Methods: This project chose three basic pediatric acute care complaints and used a combination of literature review, existing algorithms in American hospitals, and field experience to develop algorithms for Mexican physicians operating in remote parts of Chiapas with limited access to resource or information. In addition to the algorithms, an accompanying explanation with quiz questions were developed as part of PIH's growing library of algorithms they hope to ultimately upload to digital devices that physicians can use as a resource. The three algorithms developed included neonatal sepsis, acute head trauma, and anaphylaxis. Each of the algorithms underwent peer review by an attending physician in pediatrics.

Results: The three algorithms were integrated as part of PIH's growing library and will become a part of standard training for their yearly incoming class of new physicians.

Conclusions: The first phase of the project is developing and implementing algorithms, with future focus on how algorithms change practice, knowledge, and patient care.
Abstract title: HIV Seropositivity and Multiple Concurrent HPV Infections as Risk Factors for Abnormal Cervical Cytology among Female Sex Workers in Nairobi

Resident’s name: Suha J. Patel, MD

Name of program: Obstetrics, Gynecology and RS

Purpose: Most HPV infected women will not develop cervical cancer. The incidence of cervical cancer is highest, however, in Eastern Africa. Female sex workers (FSW) are at high risk for sexually transmitted infections (STIs), including HPV, since they have high numbers of sexual partners. Examining who develops abnormal cytology among this highly exposed group of women may be helpful in continuing to identify clinically relevant risk factors in a region of the world with the highest incidence of invasive cervical cancer. We examined the distribution of HPV types and risk factors for abnormal cervical cytology among 296 female sex workers from Nairobi, Kenya.

Methods: An ancillary HPV study was conducted within an existing female sex worker (FSW) cohort in Nairobi. At the baseline visit, type-specific HPV DNA was detected using PGMY09/11 PCR (Roche), and participants were tested for sexually transmitted infections. Demographic and sexual history was also obtained. Exfoliated cervical cells were collected for cytological screening by ThinPrep liquid-based cytology (Cytyc) at baseline and followup visits.

Results: Over half (54%) were infected with a high-risk (HR) HPV type, of which HPV16 and 52 were the most common types. HIV-1 prevalence was 23% and HIV-1 sero-positivity was associated with high-grade cervical lesions, particularly among women with CD4 count less than 500 cells/mm3 (odds ratio [OR] = 6.9; 95% confidence interval [CI]: 1.7--24.9). Most (78%) of the HIV-1 seropositive women were infected with multiple HPV types. Among women who had normal cytology at the time of entry into the study, the risk of having an abnormal Pap smear within one year was significantly elevated for women with multiple HPV types at study entry (adjusted odds ratio [aOR] = 6.0; 95% CI: 2.3--15.7) and with a subset of HR HPV types (aOR = 4.2; 95% CI: 1.6--11.2).

Conclusions: Infection with high risk HPV 52, which is not covered by the current HPV vaccine, is common in this population. Detection of multiple concurrent HPV infections may be a useful marker to identify women at risk of developing precancerous lesions in populations of high HPV prevalence.
Abstract title: Mammographic Changes after Oncoplastic Reduction Mammaplasty

Resident's name: Merisa Piper, MD

Name of program: Surgery, Plastic Surgery & East Bay Surgery

Purpose: Reconstruction of partial lumpectomy defects with reduction mammaplasty techniques can improve aesthetic outcomes. However, the impact of the significant tissue rearrangement on post-operative mammographic findings and subsequent recommendations for biopsy has not been well-studied.

Methods: A retrospective review of 64 patients who underwent partial mastectomy with immediate oncoplastic reduction mammaplasty reconstruction from 2001 to 2008 was performed. Mammography reports at 6 months, 1 year, and 2 years post-operatively were reviewed for Breast Imaging Reporting and Data System (BI-RADS) scores, predominant findings, and recommendations for subsequent imaging or biopsy.

Results: At six months post-operatively, 79% of patients had benign findings of post-surgical changes, while 10% had calcifications on mammography. At one year, 76% of patients continued to have benign mammograms while 15% had calcifications. Five patients had suspicious findings and underwent biopsy. Four patients had benign findings, while one patient had recurrent carcinoma. At two years, rates of fat necrosis increased (3%), while rates of calcifications decreased (9%). 78% of patients had expected post-operative changes. Two patients required biopsies, both of which revealed benign findings.

Overall, 89% of patients required no additional intervention in the two-year period following oncoplastic reduction mammaplasty. Of patients recommended for biopsy, malignancy was discovered in 14%, for an overall recurrence rate of 2% at 2 years. This data is similar to a previously published large study (1841 women) of mammographic surveillance after partial mastectomy without oncoplastic reconstruction at our institution, which found a 6% malignancy rate at 5 years.

Conclusions: Although substantial tissue rearrangement is performed at the time of oncoplastic reduction mammaplasty, our results demonstrate low rates of abnormal post-operative mammograms and subsequent biopsies over the first three years following the procedure. These findings support the use of oncoplastic reduction mammaplasty as a strategy for improving reconstructive outcomes in patients undergoing partial mastectomy.
Abstract title: Creating Microstructured Films for the Treatment of Cutaneous Fibrotic Disorders

Resident’s name: Jubin Ryu, MD, PhD

Name of program: Dermatology

Purpose: Fibroblasts play a critical role in normal wound healing, but pathologic hyperactivity can lead to fibrosis, which causes significant clinical morbidity in nearly all organs, including the lungs, kidneys, heart, and skin. Within dermatology, fibrosis is a central etiologic feature in a wide range of diseases, including hypertrophic scars, keloids, morphea, systemic sclerosis, and pediatric overgrowth syndromes. Interestingly, biophysical cues such as the topography and mechanical stiffness of the surrounding environment have been shown to play a role in this process. In this research project, we aim to create biocompatible thin films with microscale fibers protruding from their surface, and we hypothesize that we can identify specific fiber parameters that reproducibly inhibit fibroblast activity.

Methods: We have developed a series of microstructured films through lamination of medical grade polypropylene through a porous polycarbonate membrane. The fiber length, diameter, and geometry can be reliably controlled during synthesis, allowing us to track and adjust different characteristics that may affect fibroblast activity. To assay for effects of these films on fibroblast morphology and function, we performed both qPCR for TGF beta signaling and immunostaining for actin cytoskeletal proteins in cultured 3T3 fibroblasts. To assess for an in vivo effect, we induced cutaneous surgical wounds in mice and assessed for collagen and scar deposition.

Results: Compared to controls, fibroblasts that were grown on microstructured films appeared much more rounded, with loss of actin stress fibers. There is also a significant reduction in Collagen III, TGFβ1, and TGFβ receptor II (TβRII) gene transcripts in fibroblasts cultured on the microtopography. In vivo, placement of our films led to significant reductions in collagen deposition during cutaneous wound healing.

Conclusions: Microtopography can inhibit myofibroblastic activation both in vitro and in vivo, suggesting that physical cues can be used a new class of therapeutics for cutaneous fibrotic diseases.
Abstract title: Radiation Exposure to Breast Tissue in Female Orthopaedic Surgeons

Resident’s name: Lindsey C. Sheffler, MD, MAS

Name of program: Orthopaedic Surgery

Purpose: Female orthopaedic surgeons have a 3-fold increase in breast cancer risk compared to age-matched controls. Intra-operative fluoroscopy increases the occupational risk of radiation exposure. Whether or not ill-fitting lead aprons adequately protect breast tissue from radiation in female orthopaedic surgeons has, to our knowledge, yet to be studied.

Methods: An anthropomorphic phantom of a pelvis was placed on a standard operating table to scatter radiation. A female torso phantom (size 2-4) was placed opposite a C-arm fluoroscopy machine to mimic surgeon position. A dosimeter (Canberra Dosicard®) was placed on the upper outer quadrant (UOQ) of the breast bilaterally. Lead aprons (0.5 mm pb equivalent) of two types (cross-back, vest) in sizes S-XL were placed on the torso. Radiation exposure was measured over two minutes of continuous fluoroscopy (90 kvp, 5 mA). Two C-arm projections (AP, cross-table lateral) and two surgeon positions (facing the table, 90 degrees to the table) were studied. Descriptive data was obtained.

Results: Larger apron sizes resulted in increased radiation exposure to the UOQ. Lower doses were observed for the vest compared to the cross-back apron type and for AP projections compared to cross-table lateral projections. Highest radiation doses to the right UOQ were observed when the phantom was 90 degrees to the operating table and the C-arm was in an AP projection. Highest radiation doses to the left UOQ were observed when the phantom was facing the operating table and the C-arm was in a cross-table lateral projection.

Conclusions: Ill-fitting lead aprons may not adequately protect the upper outer quadrant of breast tissue in female orthopaedic surgeons. Increased radiation exposure to this area is observed when the UOQ is facing the operating table or adjacent to the xray tube. New lead apron designs may be warranted to better protect female orthopaedic surgeons from intra-operative radiation exposure.
Abstract title: PGE2 Mediated Oligodendrocyte Precursor Arrest

Resident’s name: Lawrence R. Shiow, MD, PhD

Name of program: Pediatrics

Purpose: Neonatal white matter injury (WMI) is associated with poor neurodevelopmental outcomes and occurs in extreme low birthweight (ELBW) premature infants. A feature of WMI is the presence of arrested immature precursors of oligodendrocytes, the cells that myelinate the CNS. Pathologic Wnt signaling has been shown to arrest oligodendrocyte precursor development. Because inflammation is highly associated with WMI and poor neurodevelopmental outcomes in ELBW infants, we hypothesize that a link between inflammation and WMI may involve the inflammatory mediator prostaglandin E2 (PGE2). PGE2 can activate Wnt signaling in other progenitor populations (colorectal cancer and hematopoeitic stem cells).

Methods: Cultured primary oligodendrocyte precursor cells (OPCs) are isolated from postnatal day 6-8 mouse pups. Maturation can be induced by withdrawal of PDGF-AA growth factor and addition of thyroxine hormone. After 60h of this stimuli, the maturation of these OPCs into myelinating oligodendrocytes can be assayed by MBP (myelin basic protein) staining. Cells were co-treated with PGE2 and inhibitors. PGE2 receptor expression was assessed by RT-PCR.

Results: We found that PGE2 induced a dose-dependent inhibition of maturation, as assessed by decreased MBP expression, as well as increased expression of Nkx2.2, a transcription factor expressed in immature cells. Cell death was not different. Similar results also occurred with PGE1. We also find that this effect is reversed by the Wnt inhibitor XAV-939. Expression analysis by RT-PCR shows that OPCs express EP1, EP2, and EP4 receptors. EP1 expression was robust and we tested an EP1-specific inhibitor ONO-8711, which also reversed the effects of PGE2.

Conclusions: Based on our results, we conclude that in vitro cultured primary OPCs are sensitive to the inflammatory mediator PGE2 and arrest in maturation. This appears to occur through Wnt signaling, a pathway that is activated by PGE2 in other progenitor populations and can arrest OPCs when dysregulated.

Future studies will continue to investigate the signaling requirements for PGE2-mediated OPC arrest, and will explore the role of PGE2 in mouse models of inflammation-induced WMI.
Abstract title: The Effects of Intranasal Oxytocin and Attachment Avoidance on Response to Social and Drug-Related Stimuli in Patients with Opioid Use Disorder Receiving Opioid Replacement Therapy

Resident's name: Christopher Stauffer, MD

Name of program: Psychiatry

Purpose: This pilot study aims to examine the effects of intranasal oxytocin and attachment avoidance on response to drug-related stimuli in patients with opioid use disorder (OUD) receiving opioid replacement therapy (ORT). ORT, the current OUD standard of care, effectively treats withdrawal and craving; however, physiological dependence on opioids persists, and relapse rates remain high. OUD treatment programs also rely heavily on the relative effectiveness of psychosocial interventions. For example, a recent meta-analysis found that the most important components of Alcoholics Anonymous are the reparation and maintenance of supportive social networks. Attachment avoidance, “the tendency to fear interpersonal dependency and closeness”, has been linked to OUD and may impair engagement in crucial psychosocial treatments. The hypothalamic neuromodulatory peptide, oxytocin, has well-demonstrated anti-addiction effects in animals. In humans, oxytocin has been shown to increase trust and cooperation in individuals with high attachment avoidance and is safely administered intranasally, making it a novel pharmacological treatment candidate for OUD.

Methods: 26 male patients with OUD receiving ORT at the SFVAMC received oxytocin 40-IU or placebo at each of two testing sessions =1 week apart in a double-blind, placebo-controlled, cross-over study. We examined oxytocin’s effects on: 1) impulsivity toward drug-related stimuli using a Delayed Discounting (DD) task and 2) the relationship of drug images to “self” words or “other” words using an Implicit Association Test (IAT). Attachment avoidance was measured as a possible moderating variable using the Relationship Structures (ECR-RS) questionnaire.

Results: We found that oxytocin: 1) reduced impulsivity toward hypothetical heroin rewards [DD k-score, M±SE: oxytocin = .99±.29, placebo = 1.72±.37; t(17) = 2.11, p = .05, d = 0.52] and 2) that attachment avoidance moderated oxytocin’s effect on IAT scores. Specifically, after receiving oxytocin, “low avoidance” participants associated drugs with self (M±SE = -.25±.20) while “high avoidance” participants associated drugs with others (.29±.11), t(10) = 2.23, p = .02, d = 1.02. This is a change from the placebo condition, in which “low avoidance” participants slightly associated drugs with others (.18±.13, compared to OT group, p = .09) and “high avoidance” participants showed no significant association of drugs to either self or others (.06±.12, compared to OT group, p = .04).

Conclusions: Oxytocin may attenuate impulsivity toward, and shift implicit self-associations with, opioids in OUD patients receiving ORT. Patients with high attachment avoidance may selectively benefit from oxytocin. Further investigation into the role of oxytocin in OUD treatment is warranted.
Abstract title: Tuberculosis Screening for Diabetic Patients in Community Clinics in Kunming, China

Resident's name: Alanna Stone, MD, MPH

Name of program: Internal Medicine

Purpose: China has a rising epidemic of diabetes mellitus with a prevalence of 11.6%, representing up to 113.9 million people. China also has an estimated 1.4 million cases of tuberculosis (TB). Diabetic patients have a 3-fold increased risk of developing active TB in addition to higher risk of TB treatment failure and even death.

Primary Aim: To build health workforce capacity in the region to improve diagnosis and treatment of TB among high risk groups.

Secondary Aim: To determine whether TB screening in diabetic patients should be recommended in China.

Methods: Physicians and nurses at 5 designated district health centers and 5 sub-centers in the Xishan District of Kunming, Yunnan Province, China were trained to screen diabetic patients for TB. A symptom questionnaire was used at each clinic visit: cough for >2 weeks, night sweats for =4 weeks, fever for =4 weeks, weight loss over the previous 4 weeks, and symptoms of extra-pulmonary TB. A “yes” answer to any of these questions generated a referral for evaluation in the district TB clinic. Data were then collected on number of diabetic patients screened, number of positive screens, patients referred to and seen at the district TB clinic, and the number of patients diagnosed with TB.

Results: From June to November of 2013, 2136 diabetic patients were screened in the designated clinics. Of these, 129 patients screened positive and 104 patients arrived at TB clinic for diagnostic testing resulting in 7 confirmed cases of TB. The case notification rate was 327 per 100,000 screened.

Conclusions: Providers at health centers in Kunming, China are able to enact a simple protocol integrating TB screening into diabetes care. However, while many diabetic patients were screened, few screened positive resulting in a relatively low case notification rate. Poor provider understanding of reasons for screening, including risk factors for and symptoms of TB, was a barrier to successful detection. Other barriers included poor integration of screening into provider workflow and patient resistance to referral for diagnosis. Screening for TB in diabetic patients in areas of high prevalence of both diseases is likely an important step in decreasing the incidence of TB. There will also need to be ongoing provider and patient education about TB and reasons for screening to maintain timely diagnosis and treatment of this disease.
Abstract title: Lupus Risk Alleles with High Ethnic Variability Worldwide

Resident’s name: Belinda A. Waltman, MD

Name of program: Internal Medicine

Purpose: Systemic lupus erythematosus (SLE) disproportionately affects minority patients. Non-European ancestry is associated with more severe disease, and conversely, European ancestry is associated with a lower risk of developing renal disease in SLE. Large genetic studies have identified 58 single nucleotide polymorphisms (SNPs) that influence risk of SLE. Separately, the Human Genome Diversity Project (HGDP) has characterized the allele frequency of 650,000 SNPs in 938 people from 53 different populations worldwide. We hypothesized that SLE SNPs with the greatest allele frequency differences across populations compared to Europeans could identify risk alleles that are associated with severe disease manifestations.

Methods: We analyzed the frequency distribution of the 58 SLE SNPs across populations in the HGDP database grouped into 6 geographic regions; 50 SNPs or proxies had available data. For each SNP, we determined the maximum absolute difference (max diff) in mean frequency between each region and Europe. SNPs were selected whose max diff was greater than 4 standard deviations of the distribution of intra-European frequencies. We tested these SNPs in our multiethnic cohort of 1588 SLE patients for severe disease outcomes (renal disease by ACR renal criterion, severe renal disease including severe forms of lupus nephritis on biopsy or end-stage renal disease, and production of double-stranded DNA antibodies) stratified by ethnicity: Caucasian, African American, Hispanic, and Asians. Logistic regression was performed for these 3 outcomes, adjusting for disease duration and gender.

Results: The max diff approach identified 19 SNPs; 13 had been genotyped in our SLE collection. Analysis identified a strong association between renal disease and Hispanic ethnicity: the number of these 13 risk alleles cumulatively increased the risk of renal disease among Hispanic patients (OR=1.2 per allele, p=0.006). Three of the 13 SNPs were individually associated (p = 0.05) with renal disease or severe renal disease. The strongest single allele associations were rs2205960/TNFSF4 (OR=2.2, p=0.0014 for renal disease), rs2736340/BLK (OR 2.1, p=0.006 for severe renal disease and OR 1.6, p=0.05 for renal disease) and rs9888739/ITGAM (OR 1.8, p=0.04 for renal disease).

Conclusions: Using publically-available worldwide genetic ancestry data from the HGDP, we identified SLE risk SNPs with high allele frequency variability across populations, postulating that these variants might influence severe disease phenotypes. Indeed, in a multiethnic SLE cohort, these 13 SNPs cumulatively increased the risk of renal disease in Hispanics, and 3 of these 13 alleles were individually associated with renal disease outcomes. This study supports that genetic ancestry may contribute to different disease outcomes seen in SLE across ethnicities. This method represents a rational approach to identify relevant genetic risk variants that influence disease severity in SLE.
Abstract title: Impact of Comorbidity and Age on Survival among Older Veterans with Early Stage Non-Small Cell Lung Cancer (NSCLC)

Resident's name: Melisa L. Wong, MD

Name of program: Internal Medicine

Purpose: Older age has been shown to be a stronger predictor of treatment receipt than comorbidity for NSCLC of all stages. We hypothesized that comorbidity would be a stronger predictor of survival than age among veterans with early stage NSCLC.

Methods: We obtained first-line treatment and overall survival to 5 years from the Veterans Affairs Central Cancer Registry for 6,361 veterans age > 65 diagnosed with stage I-II NSCLC from 2003-2008. Veterans were grouped by age (65-74, > 75), Charlson comorbidity index (CCI 0, 1-3, > 4), and stratified by first-line treatment. Log-rank tests and Cox proportional hazards models were used to identify differences in 5-year survival according to comorbidity and age.

Results: Median age at diagnosis was 74 and median CCI was 2 (range 0-13). 2,840 (45%) patients received surgery: 2,219 lobectomies (includes 135 pneumonectomies) and 621 sublobar resections. 1,645 (26%) patients received radiation and 1,876 (29%) received other/no treatment. When stratified by age and comorbidity, veterans with CCI 0 who underwent surgery had similar 5-year survival regardless of age and veterans with CCI > 4 had the worst 5-year survival across all treatment groups. In the lobectomy group, 5-year survival for veterans with CCI 0 was 64% for age 65-74 and 59% for age > 75; for veterans with CCI > 4, 5-year survival was 49% for age 65-74 and 50% for age > 75 (log-rank test, p = .002). In multivariable analysis, severe comorbidity was one of the strongest predictors of 5-year survival for all treatment groups along with stage and geographic region. The hazard ratio for 5-year mortality for CCI > 4 was 1.45 (95% CI 1.16-1.83) in the lobectomy group and 1.75 (95% CI 1.11-2.75) in the sublobar resection group. Age had only a modest effect on mortality in the lobectomy group (HR 1.16; 95% CI 1.01-1.34) and radiation group (HR 1.15; 95% CI 1.01-1.31) but was not prognostic in the other treatment groups.

Conclusions: Severe comorbidity is a much stronger predictor of overall survival than age in early stage NSCLC. Therefore, elderly patients with minimal comorbidity should be considered for surgical evaluation.
Abstract title: Decompressive Hemicraniectomy and Contusion Expansion in Traumatic Brain Injury

Resident’s name: Lara Zimmermann, MD

Name of program: Neurology

Purpose: Traumatic brain injury affects ~1.7 million Americans and costs ~$60 billion in the United States annually. A common and severe type of primary brain injury is a cerebral contusion: a hemorrhagic lesion where blood is intermixed with brain tissue. A common type of secondary brain injury is hemorrhagic enlargement of a contusion, which occurs in about 50% of cases and increases morbidity and mortality. In severe brain injury, hemicraniectomy or hemicraniotomy may be indicated for hematoma evacuation or management of elevated intracranial pressure. We investigated the relationship between decompressive hemicraniectomy and contusion expansion in traumatic brain injury.

Methods: A retrospective analysis was performed on a prospective observational database of patients with severe traumatic brain injury who were admitted to the neurosurgical intensive care unit at one university hospital from 2004-2010. We identified 237 patients with traumatic cerebral contusions. Currently, 116 cases have been fully analyzed (analysis ongoing).

Results: We identified 237 patients with traumatic cerebral contusions. Currently, 116 cases have been analyzed (analysis is ongoing). Hemicraniectomy or hemicraniotomy was required in 46 / 116 (40%) patients. Contusion expansion (defined as >30% volume increase) occurred in 85 / 116 (73%) patients. Of these, 35 / 85 (41%) underwent decompressive hemicraniectomy prior to contusion expansion and 50 / 85 (58%) did not (Chi-square 0.3076, p = 0.58).

Conclusions: This project is ongoing, and further data analysis is required to determine if decompressive hemicraniectomy is associated with increased risk for contusion expansion or not. Importantly, we still need to control for confounding variables including patient age, sex, initial GCS and Rotterdam CT score.
Abstract title: Infections, Interventions, and Mortality of Pediatric Bone Marrow Transplant Patients in the Intensive Care Unit

Resident’s name: Matt Zinter, MD

Name of program: Pediatrics

Purpose: Over 2,300 children undergo bone marrow transplantation in the United States each year, and up to 44% require PICU support for life threatening complications. PICU mortality has dropped from 85% to below 44% but current rates of infection and interventions are poorly defined. We aim to (1) describe admission characteristics, infections, critical care interventions, and outcomes of BMT patients requiring PICU support, and (2) identify risk-factors for mortality.

Methods: This is a retrospective multicenter cohort analysis of 246,346 PICU admissions for patients ≤21 years old between 1/1/2009 and 6/30/2012. Data were extracted from 112 sites nationwide through the Virtual PICU Systems database. BMT patients were identified through ICD-9 codes. Infections, interventions, and mortality were recorded from admission through PICU death or discharge. Non-invasive positive pressure ventilation (NIPPV) was defined as CPAP or BiPAP.

Results: Patients with a history of BMT comprised 0.7% of all PICU admissions (1,782/246,346) and had 16.2% mortality compared with 2.4% mortality for non-BMT admissions (RR 6.7, 95% CI 6.0-7.5, p<0.001). Median time to meeting discharge criteria for survivors was 2.5 days (IQR 1.0-5.7, skew 5.2). Median PRISM3 score was 8 (IQR 3-13, skew 1.1). Leading BMT indications were hematologic (41.5%) or solid cancer (18.6%) and non-malignant hematologic (12.7%), immunologic (9.5%), and metabolic disease (5.3%).

No infections were documented in 53.1% of admissions; mortality for these admissions was 11.2%.* Sepsis was present in 24.4% of admissions, with 22.2% mortality (RR 2.0, 95% CI 1.5-2.6, p<0.001). Gram-positive, gram-negative, fungal, and viral infections were present in 7.0%, 8.9%, 9.1%, and 19.9% of admissions, with mortality rates of 17.6% (RR 1.6, 95% CI 1.03-2.4, p=0.023), 22.0% (RR 2.0, 95% CI 1.4-2.8, p<0.001), 33.7% (RR 3.0, 95% CI 2.3-4.0, p<0.001), and 28.5% (RR 2.5, 95% CI 2.0-3.2, p<0.001), respectively.

No critical care interventions (NIPPV, intubation, RRT, or ECMO) were used in 58.1% of admissions; mortality for these admissions was 1.9%. NIPPV without intubation was used in 7.2% of admissions, with 4.7% mortality rate (RR 2.4, 95% CI 0.99-5.9, p=0.025). Endotracheal intubation and RRT were used in 34.6% and 11.2% of admissions, with mortality rates of 42.5% (RR 22.0, 95% CI 14.1-34.3, p<0.001) and 51.3% (RR 26.6, 95% CI 16.9-41.8, p<0.001), respectively. ECMO was used in 0.2% of admissions, with 100% mortality (RR 51.8, 95% CI 33.6-80.0, p<0.001).

* reference groups for infection* and intervention comparisons

Conclusions: Mortality for pediatric BMT patients in the PICU may be as low as 16.2%, but higher for those receiving intubation (43%) or RRT (51%). ECMO is rarely attempted and even more rarely successful. Greater understanding of other risk-factors affecting mortality and the need for critical care support is needed.