2016 UCSF Multidisciplinary Resident Research Symposium

Oral and Poster Presentations, Mentor Awards & Reception

Wednesday, May 25
4:00pm-7:00pm
Mission Bay Campus
Mission Hall
550 16th Street, SF, CA
Rooms MH-1400 and MH-1401/1402
We are pleased to offer a combined clinical and translational, global health, 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. Global Health Sciences is dedicated to improving health and reducing the burden of disease in the world's most vulnerable populations. 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 $1500 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.

UCSF Global Health Sciences (GHS) is dedicated to improving health and reducing the burden of disease in the world's most vulnerable populations. It integrates UCSF expertise in all of the health, social, and biological sciences, and focuses that expertise on pressing issues in global health. GHS works with partners in countries throughout the world to achieve these aims.

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.

Miriam Kuppermann, PhD, MPH  Anna Bakardjieva, MD
Co-Director, RRTP  Co-Director, MMP

Alison Huang, MD, MPhil, MAS  Ben Cheyette, MD, PhD
Co-Director, RRTP  Co-Director, MMP

Paul Volberding, MD
Director of Research, GHS
Schedule of Events

4:00 pm Welcome & Resident Research Program Overview
Miriam Kuppermann and Alison Huang, Co-Directors, CTSI Resident Research Training Program
Paul Volberding, Director, Global Health Sciences
Ben Cheyette and Anna Bakardjiev, Co-Directors, Molecular Medicine Pathway

4:15 pm Resident Oral Papers
Moderated by Miriam Kuppermann

Speaker Name: Kelly E. Huibregste, MD, MS
Title: Secondary Malignancy in Neuroblastoma After 131I-metaiodobenzylguanidine Treatment
Residency Program: Pediatrics
Research Mentor: Kate Matthay, MD

Speaker Name: John K. Lin, MD
Title: Cost-Effectiveness of a Fixed-Dose Combination Pill for Secondary Prevention of Cardiovascular Disease in India, Mexico, Ghana, and South Africa
Residency Program: Categorical Internal Medicine
Research Mentor: Dhruv Kazi, MD, MS

Speaker Name: Ani Kardashian, MD
Title: Morbid Obesity and Diabetes (DM) are Associated with Increased Risk of Death on the Liver Transplant (LT) Waiting List
Residency Program: Categorical Internal Medicine
Research Mentor: Danielle Brandman, MD, MAS

Speaker Name: Scott A. Wilke, MD, PhD
Title: Identifying Prefrontal Cortex Microcircuit Disruptions Underlying Depression
Residency Program: Psychiatry
Research Mentor: Vikaas Sohal, MD, PhD

Speaker Name: Adam K. Lewkowitz, MD
Title: Predictors of undergoing cell-free DNA simultaneously with multiple marker screening or after negative multiple marker screen results
Residency Program: Obstetrics, Gynecology and RS
Research Mentor: Miriam Kuppermann, PhD, MPH

5:30 pm Mentors of the Year Awards
Clinical and Translational Recipient: Danielle Brandman, MD, MAS, Gastroenterology and Hepatology
Global Health Recipient: Dhruv Kazi, MD, MS, Cardiology
Molecular Medicine Recipient: Michael Matthay, MD, Pulmonary and Critical Care

5:45 pm Poster Viewing and Reception
MH-1401/1402
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 three faculty mentors for outstanding excellence in mentoring. This year’s awardees were selected from many outstanding nominations.

Clinical and Translational Mentor
Danielle Brandman, MD, MAS

“Dr. Brandman has served as an incredibly supportive mentor to me during my residency training at UCSF. She was my attending on the inpatient liver transplant service and has served as my clinical research mentor over the past year. Despite her busy schedule, she has made it a priority to nurture my interest in clinical research and to guide me through the many intricate steps to successfully conducting a clinical research project. Additionally, she has gone above and beyond to be accessible to me and to support the development of both my research skills as well as the advancement of my career goals. Perhaps most importantly, she is warm and kind, and her passion for teaching and mentorship has excited my own interest in pursuing a career in academic medicine.”

Nominating Residents' Comments:

Global Health Mentor
Dhruv Kazi, MD, MS

“Kazi is an inspirational researcher and physician as well as an unparalleled mentor. He has taught me from the ground up how to perform cost-effectiveness analyses. He is unfailingly understanding of the challenges of doing research during residency and coaches me through how to surmount them. Though we have substantially changed course twice through the research process, we are well on track to draft a manuscript for publication by year’s end. His enthusiasm is contagious and his example has persuaded me of the feasibility and worth of pursuing a research career. Kazi is well deserving of the Resident Research Mentor Award.”

Nominating Resident’s Comments:

Molecular Medicine Mentor
Michael Matthay, MD

“Dr. Matthay is not only inspirational as a clinician and researcher, but I was impressed by how available he was, despite his very busy schedule. Always responsive and supportive, it's been a treat work with him.”
Abstracts:
Oral Presentations

UCSF Multidisciplinary Resident Research Symposium

Wednesday, May 25th, 2016

Mission Bay, Mission Hall, MH-1400
Abstract title: Secondary Malignancy in Neuroblastoma After 131I-metaiodobenzylguanidine Treatment

Resident’s name: Kelly E. Huibregtse, MD, MS

Name of program: Pediatrics

Purpose: 131I-MIBG is a highly active form of tumor-targeted radiotherapy in patients with relapsed neuroblastoma, with response rates of 30% to 40%. Several reports of second malignant neoplasm (SMN) in patients after treatment with 131I-MIBG suggest the possibility of increased risk, particularly myelodysplasia and leukemia. Incidence of and risk factors for SMN after 131I-MIBG have not been defined.

Methods: This is a multi-institutional retrospective review of patients with neuroblastoma treated with 131I-MIBG therapy at four institutions. A competing risks approach was used to calculate the cumulative incidence of SMN from time of first exposure to 131I-MIBG. Competing risks regression using the Fine-Gray method was used to identify potential risk factors for secondary malignancy.

Results: The analytical cohort included 644 patients treated with 131I-MIBG. The cumulative incidence of SMN was 7.6% (90% CI 4.8-11.9%) and 14.3% (90% CI 9.1-22.1%) at five and ten years from first 131I-MIBG, respectively. No increase in SMN risk was found with increased number of 131I-MIBG treatments or higher cumulative activity per kilogram of 131I-MIBG received (p=0.72 and p=0.84, respectively). An increased risk of SMN was found in patients who had bone disease at the time of first 131I-MIBG therapy. In a multivariate analysis controlling for variables with p<0.1 (stage, age at first 131I-MIBG, bone disease, disease status at time of first 131I-MIBG), patients with relapsed/progressive disease had significantly lower risk of SMN (Subdistribution Hazard Ratio 0.3, 95% CI, 0.1-0.8, p=0.023) compared to patients with persistent/refractory neuroblastoma.

Conclusions: The cumulative risk of SMN after 131I-MIBG therapy for patients with relapsed or refractory neuroblastoma is similar to the published incidence for high-risk neuroblastoma overall. We found no dose-dependent increase in SMN risk. As the number of patients treated with 131I-MIBG earlier after diagnosis and length of follow up time from 131I-MIBG therapy increases, it will be important to reassess this risk.
Abstract title: Cost-Effectiveness of a Fixed-Dose Combination Pill for Secondary Prevention of Cardiovascular Disease in India, Mexico, Ghana, and South Africa

Resident’s name: John K. Lin, MD

Name of Program: Categorical Internal Medicine

Purpose: Cardiovascular disease (CVD) is the leading cause of death worldwide, with low- and middle-income countries (LMIC) facing more than 75% of the global burden. Although evidence-based medications for secondary prevention of CVD are effective and relatively inexpensive, less than a quarter of eligible patients in LMICs receive these drugs. The fixed-dose combination pill (“polypill”) improves patient adherence to evidence-based medications and costs less than the individual components separately. The polypill is currently being evaluated for inclusion in the WHO’s essential medicines list for its potential impact in LMICs. We aim to assess whether the polypill is cost-effective in four LMICs with a large burden of CVD: India, Mexico, South Africa, and Ghana.

Methods: We developed a microsimulation model of 100,000 adults aged 30 to 80 years with prevalent CVD (prior myocardial infarction or stroke) in each of India, Mexico, Ghana, and South Africa. In each setting, we evaluated two treatment strategies: (1) Usual care: monocomponents (ACE inhibitor, aspirin, beta-blocker, and statin) at real-world levels of prescription and adherence (2) Polypill containing aspirin 75 mg, simvastatin 40 mg, lisinopril 10 mg, and atenolol 50 mg at real-world levels of prescription. We assumed the polypill would be as efficacious as its individual components, but would be associated with increased adherence as observed in randomized controlled trials. We derived country-level demographics from UN Population data and age- and gender-specific estimates of prevalent CVD from nationally representative surveys. We used an ingredients approach to costing acute and chronic CVD care, using data from WHO CHOICE 2013 and the International Drug Price Indicator Guide 2014. We assumed the cost of the polypill was 80% of the sum of its individual components (e.g., $1 21.16 in India). We derived effectiveness estimates from GBD 2010. We adopted a health system perspective and a 10-year analytic horizon. Our main outcomes are healthcare costs in international dollars ($I), disability-adjusted life years (DALY), and incremental cost-effectiveness ratio (ICER) of the polypill compared with usual care. We defined an ICER < GDP per capita as very cost-effective. We performed two sensitivity analyses: (1) Increasing the polypill prescription rate to 80% of all eligible patients (per WHO 25x25 target); and (2) Increasing the cost of the polypill to twice as much as the individual components.

Results: At real-world levels of adoption of evidence-based medications, the use of the polypill instead of monocomponents would avert 710-2685 deaths per 100,000 people with CVD in the countries studied. The polypill strategy was very cost-effective among patients with preexisting CVD in India, South Africa, and Ghana (ICER ranging $I 23.04-$I 77.05 per DALY averted). In Mexico, the polypill strategy was dominant, i.e., the polypill strategy cost less than usual care and produced better outcomes. If 80% of eligible patients were to receive the polypill, it would save substantially more lives relative to usual care (6500-10,500 deaths averted per 100,000 people with CVD), and the polypill would become even more cost-effectiveness (ICER = $I 40.31 per DALY averted in India, $I 50.31 per DALY averted in Ghana, and dominant in Mexico and South Africa). Even if the polypill were to cost twice as much as the individual components, it would remain very cost-effective in all countries (ICER ranging $I 136.75-$I 273.20 per DALY averted). A limitation of the analysis was that we did not capture programmatic costs that may be incurred in increasing levels of prescription.

Conclusions: In our microsimulation-based analysis, the polypill is a highly cost-effective approach compared with usual care in India, South Africa, and Ghana, and is cost-saving in Mexico. Addition of an appropriately priced polypill to the WHO essential medications list has the potential to avert a large number of deaths from CVD in LMICs.
**Abstract title:** Morbid Obesity and Diabetes (DM) are Associated with Increased Risk of Death on the Liver Transplant (LT) Waiting List

**Resident’s name:** Ani Kardashian, MD

**Name of program:** Categorical Internal Medicine

**Purpose:** Obesity is a growing problem in LT candidates, paralleling the US obesity epidemic and the increase in LT for nonalcoholic steatohepatitis (NASH). While post-LT survival appears to be similar in obese and non-obese patients, data is scarce regarding risk of waitlist dropout in morbidly obese patients. We aimed to determine the impact of obesity on waitlist outcomes and evaluate predictors of dropout in those with morbid obesity or NASH.

**Methods:** We retrospectively evaluated LT candidates listed between 3/02-12/13. We performed a competing risk analysis to evaluate predictors of removal or death on the waitlist. Variables with p-value.

**Results:** 84,511 patients (34% female, median age 55, 15% Hispanic) were included. 10,001 (12%) had NASH and 3,159 (4%) had BMI>40. Compared with BMI 25-29.9, patients with BMI≥40 were more likely to be female (46% vs 28%), diabetic (25% vs 18%), have NASH (35% vs 13%), and have shorter median waitlist times (161 vs 208 days); all p40, DM was associated with higher dropout risk but was not significant (HR=1.12, CI 1.0-1.26).

**Conclusions:** Patients with morbid obesity or DM are less likely to undergo LT due to death or removal from the waitlist. Interventions to improve waitlist outcomes and access to LT in this growing patient group should be explored.
**Abstract title:** Identifying Prefrontal Cortex Microcircuit Disruptions Underlying Depression

**Resident's name:** Scott A. Wilke, MD, PhD

**Name of program:** Psychiatry

**Purpose:** The prefrontal cortex (PFC) and the neurotransmitter dopamine have been centrally implicated in depression. In animal models, prefrontal neurons expressing dopamine D2 receptors (D2Rs) project subcortically to regulate depression related behaviors. However, it is not known how manipulations that either contribute to or treat depression affect the responses of local prefrontal microcircuits to dopaminergic input.

**Methods:** Our lab has recently developed a novel assay, using live brain slices to image patterns of neural activity in isolated prefrontal microcircuits. A fluorescent reporter of neural activity, GCaMP6 is stereotactically targeted to medial PFC (mPFC) in mice. Subsequently, live slices are cut and activity is imaged simultaneously from 70-100 prefrontal neurons during a baseline period and after exposure to a D2R agonist (quinpirole, 10 μM).

**Results:** I have imaged the response of prefrontal microcircuits to D2R stimulation in two manipulations related to depression. First, using an established mouse model of genetic risk for depression, a Disc1 mutant mouse and second looking at mice treated with the rapid acting antidepressant ketamine. In control slices, mean network activity increases nearly 2-fold in response to D2R stimulation. This response is significantly blunted in slices from Disc1 mutant mice and is preserved or possibly enhanced in mice treated with ketamine. During the baseline period, Disc1 mutants exhibit an altered organization of network activity, shifted towards more negative pairwise correlations. Intriguingly, mice treated with an antidepressant dose of ketamine show an opposing effect on the organization of network activity.

**Conclusions:** This novel assay allows an unbiased approach to discovering prefrontal microcircuit endophenotypes in psychiatric disorders. I have used this technique to identify altered activity in local networks which may be important in depression.
Abstract title: Predictors of undergoing cell-free DNA simultaneously with multiple marker screening or after negative multiple marker screen results

Resident’s name: Adam K. Lewkowitz, MD

Name of program: Obstetrics, Gynecology and RS

Purpose: The American Board of Internal Medicine has partnered with the Society of Maternal Fetal Medicine to create a Choosing Wisely campaign to encourage high-value care in obstetrics. One of the ten proposed clinical guidelines is to avoid simultaneous testing with cell-free DNA (cfDNA) and multiple marker screening (MMS) due to the limited clinical value of dual screening. Despite these recommendations, many women are obtaining dual screening. Our objective is to identify predictors of simultaneous MMS and cfDNA screening or cfDNA screening after negative MMS results among women seeking testing who will be at least 35 years old at the time of delivery.

Methods: Women of advanced maternal age carrying a singleton pregnancy were recruited at the University of California, San Francisco, Prenatal Diagnosis Center. Participants completed a sociodemographic and attitudinal questionnaire, which included items related to knowledge about testing, pregnancy worry, and, attitudes toward potential testing outcomes. Data on prenatal test use was obtained via medical record review. Multivariate analysis with logistic regression using backward elimination was used to identify factors associated with dual screening.

Results: Of the 164 participants, 47 underwent MMS alone, 15 had cfDNA alone, 80 had both MMS and cfDNA, and 22 had invasive testing with or without MMS. Compared to the 46 MMS-negative women who did not undergo further testing, those who underwent cfDNA simultaneously with MMS (n=15) or after negative MMS results (n=57) were more likely to feel that having a miscarriage would be worse than having a child with an intellectual disability (adjusted odds ratio (aOR) 4.59 for every 1-point increase on a 4-point scale, 95% confidence interval (CI) 1.11-19.10; p 0.04); to desire comprehensive testing for intellectual disability (aOR 6.06 for every 1-point increase on a 4-point scale, 95% CI 1.84-19.97; p 0.003); and to have greater pregnancy worry (aOR 3.16 for every 1-point increase on a 4-point scale, 95% CI 1.17-8.51; p 0.02, respectively). They were also more likely to be nulliparous (aOR 2.91, 95% CI 0.99-8.58; p 0.05) and older (aOR 1.29 for every one-year increment in age, 95% CI 1.00-1.66; p 0.05).

Conclusions: Most women who initially opted for screening rather than diagnostic testing underwent cfDNA simultaneously with MMS or after negative MMS results. These women were more likely to have higher scores on the pregnancy worry scale, view miscarriage as a worse outcome than having a child with an intellectual disability, and to more highly desire comprehensive testing for intellectual disability. These findings suggest that women who are particularly concerned about intellectual disability but are not willing to incur miscarriage may be more likely to undergo dual screening. Patients should be counseled more effectively regarding the appropriate sequencing of these tests to avoid unnecessary tests and reduce costs.
## CTSI Resident Research Funding Award 2015 Recipients

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Abstracts:
Poster Presentations

UCSF Resident Research Symposium

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Abstract title: Coarctation Index Predicts Recurrent Aortic Arch Obstruction Following Coarctation Repair in Infants

Resident’s name: Gregory Adamson, MD

Name of program: Pediatrics

Purpose: 1. Assess the predictive value of the echocardiogram measured Coarctation Index on Recurrent Aortic Arch Obstruction (RAAO) after repair of coarctation of the aorta (CoA) in infants with biventricular circulation.

2. Screen or other anatomic, clinical, surgical, and echocardiographic factors associated with RAAO.

Methods: A retrospective cohort study was performed in infants less than 90 days of age who underwent surgical repair of CoA at UCSF from 2010 to 2014. We included infants with biventricular circulation following repair (n=74). We then excluded patients with interrupted aortic arch (n=2), congenital diaphragmatic hernia (n=3), and those lose to follow-up within 3 months of surgery (n=1), leaving a cohort of 68 patients. Anatomic, clinical, and surgical variables were collected via manual review of the electronic medical record. Preoperative (nearest to surgery) and postoperative (pre-discharge) two-dimensional and Doppler echocardiographic images were reviewed, and measurements were made three times and averaged by a single reviewer. Inter-reader reliability measurements were performed. Coarctation Index, our primary predictor variable, was defined as the diameter of the narrowest aortic arch segment divided by the diameter of the aorta at the level of the diaphragm by echocardiography. Outcome variable was RAAO up to 2 years postoperatively, defined as an upper to lower limb blood pressure gradient > 20 mmHg, a peak aortic arch velocity > 3.5 m/s by echo, or a catheter measured peak-to-peak gradient > 20 mmHg (with EF > 55%). Standard descriptive statistics described the distribution of variables. Coarctation Index was grouped into quartiles and also dichotomized based upon an empiric threshold. Univariable and multivariable logistic regression models elucidated determinants of RAAO.

Results: 15 out of 68 subjects (22%) met criteria for RAAO. In the univariable analyses, Coarctation Index, use of patch material, and discharge BP gradient were significantly different in those with and without RAAO. In the multivariate analysis, increasing quartiles of Coarctation Index were protective against RAAO, p=0.001 (OR 0.07; 95% CI 0.02–0.36). Additionally, patch aortoplasty was associated with an increased risk of RAAO, p=0.013 (OR 9.5; 95% CI 1.6–55.8). The multivariate analysis also showed that a Coarctation Index threshold of < 0.7 was highly predictive of RAAO, p=0.0001 (OR 33.8; 95% CI 5.7-199.5). Looking only at patients with autogenous repair (n=43), a Coarctation Index of < 0.7 remained predictive of RAAO, p=0.017 (OR 19.8; 95% CI 1.7-229.6).

Conclusions: Postoperative coarctation index may be used to predict recurrent aortic arch obstruction in patients with biventricular circulation after repair of coarctation of the aorta. Patients with a coarctation index < 0.7 or with a patch aortoplasty warrant close follow-up.
Abstract title: Acute respiratory distress syndrome does not independently predict mortality among all critically ill patients with sepsis

Resident’s name: Catherine L. Auriemma, MD

Name of program: Categorical Internal Medicine

Purpose: Sixty-day hospital mortality is commonly selected as an end-point for ARDS clinical trials. We assessed whether the development of ARDS is independently associated with 60-day in-hospital mortality among septic medical intensive care unit (ICU) patients beyond baseline severity of illness.

Methods: We prospectively enrolled 424 critically ill adult patients with sepsis as part of the Early Assessment of Renal and Lung Injury (EARLI) study. ARDS was defined by the Berlin criteria in mechanically ventilated patients and adjudicated by two board-certified critical care physicians. Patients were followed for 5 days for ARDS development and 60 days for in-hospital mortality. Severity of illness was assessed using the APACHE III score and a modified APACHE III that excluded points related to oxygenation. Unpaired student’s t-tests and chi-square tests were used to compare baseline variables. Multivariate logistic and linear regression models were used to adjust for potential confounding.

Results: Of 424 patients, 235 (55.4%) required mechanical ventilation, and 120 (28.3%) developed ARDS. The unadjusted mortality rate was 45.8% with ARDS vs. 23.8% without (OR = 2.71; 95% CI 1.74-4.24; p<0.001). However, after controlling for baseline severity of illness using the modified APACHE III score, ARDS was not an independent risk factor for hospital death among all patients (OR = 1.33; 95% CI 0.78-2.78; p=0.295). This finding persisted in sensitivity analyses restricted to patients with sepsis from a pulmonary source, those with a non-pulmonary source, patients with shock, and patients with no limitations on code status at the time of ICU admission. Severe ARDS (PaO2/FiO2<100 mm Hg; n=51) remained a significant predictor of 60-day in-hospital mortality even after adjusting for modified APACHE III score, limitations of code status, and presence of shock (OR = 2.30; 95% CI 1.05-5.01; p=0.037). In both unadjusted and adjusted models, development of ARDS did confer prolonged hospital and ICU length of stay (LOS) as well as increased ventilator days among survivors (Table).

Conclusions: Development of ARDS in patients with sepsis was not associated with increased risk for 60-day in-hospital mortality after adjusting for severity of illness. However, ARDS was associated with increased LOS and time on mechanical ventilation among survivors. These data suggest that while 60-day in-hospital mortality may remain a valuable outcome among patients with severe ARDS, alternative outcomes should be considered in the design of clinical trials for patients with mild or moderate ARDS.
Abstract title: Global Burden of Urolithiasis: Mortality inequality

Resident’s name: David B. Bayne, MD

Name of program: Urology

Purpose: The Global Burden of Diseases, Injuries, and Risk Factors Study 2010 assembled data on causes of death and disability from 187 countries. We analyzed this data with a specific interest in urolithiasis. Our objective is to describe global trends in disability and mortality attributed to urolithiasis and identify factors associated with changes over 20 years.

Methods: Age-adjusted sex-specific mortality rates and disease burden for 187 countries were obtained from the 2010 Global Burden of Disease Project for three time points (1990, 2005, 2010). Countries were classified into income groups based on World Bank categorizations. Gross Domestic Product (GDP) per capita, Gini Index, Human Development Index, Body Mass Index, and climate data were all compared.

Results: Between 1990 and 2010, population weighted global mortality from urolithiasis decreased from 0.51 to 0.37 per 100,000 people. When comparing mortality based on World Bank Income Group, high and upper-middle income countries had dramatically larger reductions in mortality relative to lower-middle and low income countries. Multivariate analysis showed that mean annual temperature, HDI, GDP, and national income inequality were associated with statistically significant changes in urolithiasis mortality.

Conclusions: Although urolithiasis mortality has declined over time, there is tremendous variation between high and low income countries. Mortality is higher in low income countries, although disability does not change relative to country GD. Lower mean annual temperature, high HDI, and decreased income inequalities were associated with greater decrease in urolithiasis mortality.
Abstract title: Clinical Factors Related to Neonatal Growth in Congenital Diaphragmatic Hernia

Resident’s name: Rachael H. Beckert, MD, RD

Name of program: Pediatrics

Purpose: Children with congenital diaphragmatic hernia (CDH) are at risk for failure to thrive post neonatal discharge, which is associated with worse respiratory and neurodevelopmental outcomes. This study aims to characterize the growth of CDH infants during their initial hospitalization.

Methods: We performed a retrospective study of 162 newborns with CDH at UCSF Children’s Hospital (2000–2013), excluding those who died prior to repair or had other congenital anomalies. Weight gain (g/day), head circumference (HC) and length growth (cm/week) were calculated. Bivariate and multivariate analyses were used to identify factors associated with growth parameters. A p-value less than 0.05 was considered significant.

Results: Infants were 57% male with a mean gestational age (GA) of 37.7±2.7 weeks, a mean birth weight of 3.0±0.6 kg, and 85% had left-sided defects. Weight gain was sub-optimal for all infants, regardless of disease severity Growth improved with increasing length of stay (LOS), but stayed below normal (25g/d) newborn rates. At discharge, length growth was at expected (0.5cm/wk) newborn rates but HC growth did not meet expectations (0.5cm/wk). At discharge, infants requiring non-primary surgical repair or prolonged ventilation (>14 days) had significantly higher weight gain, but also had longer hospitalization. After adjustment for GA, gender, duration of ventilation, and repair type in a multivariate model, LOS was the most predictive of weight gain at discharge (p <0.001).

Conclusions: Growth failure in infants with CDH begins in the neonatal hospitalization, regardless of disease severity. Weight is more affected than HC or length. These findings reinforce the need to attend to neonatal nutritional management, particularly nutritional support at discharge.
Abstract title: Sex-Specific Genetic Effects in Neuropsychiatric Disease: Proof-of-Concept Using Anthropometric Traits

Resident’s name: Aaron D. Besterman, MD

Name of program: Psychiatry

Purpose: A significant proportion of the overall genetic risk for neuropsychiatric disorders and other common human diseases come from Single Nucleotide Polymorphisms (SNPs). Each SNP confers only a small amount of risk towards any specific disease or trait, but cumulatively they exert a large effect. A calculated cumulative risk score of risk-associated SNPs is called a Polygenic Risk Score (PRS), which may be used to predict clinical outcomes. Currently, PRS are calculated for both males and females using risk SNPs identified through Genome-Wide Association Studies (GWAS) that include individuals of both sexes (combo-PRS) in order to optimize power. However, it is currently unknown whether or not calculating sex-specific PRS will improve predictions of outcomes. Given their sexually dimorphic nature and high heritability, we decided to use anthropometric traits (e.g. height, weight, BMI) to investigate whether sex-specific PRS are superior to combo-PRS and whether within-sex PRS (e.g. male-male or female-female) are superior to across-sex PRS (e.g. male-female or female-male) in trait prediction.

Methods: Autosomal risk SNPs identified through sex-specific meta-analyses of GWAS for height, weight and BMI from the GIANT Consortium were used to calculate PRS in Male (N=1614) and Female (N=1589) parents from the Simons Simplex Collection (SSC). The two data sets were harmonized by removal of ambiguous SNPs and strand-flipping. Standard genomic quality control metrics were also applied. PRS were calculated under an additive model, with each SNP effect being weighted by their degree of association with the specific anthropometric trait. Linear regression was performed to assess the degree of association of the PRS with measured traits (adjusted-R^2), including the first ten principal components in the model. Lastly, binomial analysis was performed to compare the different prediction models.

Results: Combo-PRS accounted for a greater percentage of the variance of all measured traits (height, weight, and BMI) than did sex-specific PRS (Combo adjusted-R^2 of 0.1, 0.02, 0.02; Male-specific adjusted R^2 of 0.06, 0.01, 0.005, Female-specific adjusted R^2 of 0.08, 0.01, 0.01, respectively). This difference was statistically significant (p<0.01) for height but not for weight or BMI. Within-sex PRS (e.g. male-male or female-female) did not account for a significantly higher percentage of the variance than did across-sex PRS for height, weight or BMI (p = 0.1, 0.6; p= 0.3, 0.9; p=0.01, 0.2; with vs. across female and male, respectively).

Conclusions: Predicting anthropometric traits using combo-PRS were superior to sex-specific PRS as expected based on their higher number of individuals included in the initial GWAS (males and females combined). However, within-sex PRS were not superior to across-sex PRS, suggesting that for height, weight and BMI, calculating PRS for an individual from GWAS data of the same sex is not superior to calculating PRS from GWAS data of the opposite sex. Therefore, our results suggest that the optimal method of calculating PRS for height weight and BMI is to use combo-PRS that have additional power based on the higher number of included individuals in the GWAS. Further, our results suggest that autosomal SNPs do not account for the sexually-dimorphic nature of height, weight or BMI. It is unknown whether similar patterns will be observed in common neuropsychiatric disorders with sexually dimorphic features such as psychotic disorders or mood disorders.
Abstract title: A Qualitative Study Exploring the Impact of a Community Choir Intervention on Mood in Diverse Older Adults with Depressive Symptoms

Resident’s name: Christine C. Chiu, MD

Name of program: Psychiatry

Purpose: The Community of Voices (COV) study is a cluster-randomized trial examining the effect of a community choir intervention on physical, cognitive and psychosocial aspects of health and well-being in large group of racially/ethnically diverse older adults. The objective of this qualitative study was to explore the effect of participation in the choir intervention on the mood and emotional well-being of diverse older adults who reported clinically significant depressive symptoms at baseline.

Methods: For the parent study, older adults were recruited from 12 Administration on Aging (AoA) senior centers in San Francisco. Ninety-minute choir rehearsals, led by professional choir directors, took place weekly at senior centers for 44 sessions. The choir repertoire was culturally tailored for each senior center. Inclusion criteria for the parent study included being 60 years old or higher, having adequate visual and hearing acuity and adequate fluency in English or Spanish. Exclusion criteria included having dementia or a severe mental or medical illness that would prevent participation in weekly rehearsals, and current participation in a choir.

Eligibility criteria for the qualitative study were: English-speaking; scoring 8 or higher on the Patient Health Questionnaire (PHQ-8) depression scale at baseline; having completed at least 24 COV choir rehearsals. COV researcher (CC) conducted the individual interviews at senior centers and provided $35 reimbursement for each interview. Semi-structured interviews asked about changes in participants’ mood across three domains (physical, social and psychological) and the perceived relationship of any changes to participation in various aspects of the COV program. Interviews were digitally recorded and transcribed verbatim. Transcripts were analyzed according to the principles of grounded theory using atlas.TI software. Coding and category identification were reconciled by two researchers. Senior researchers reviewed and confirmed the categories and framework.

Results: 10 participants were interviewed (4 African-Americans, 2 Asian-Americans and 4 Caucasians). Mean age was 70 years; mean PHQ-8 score was 12. Four main themes relating to participation in the COV choir intervention were identified: 1) uplifts spirits, 2) provides a safe environment, 3) helps foster trust and friendship, and 4) empowers participants to pursue other activities in their lives. In the emotional domain, participants identified the choir as an escape from their worries and appreciated having the choir as a constant activity in their lives. They described having fun and feeling joyful with listening and learning music in a group. Most participants also alluded to having music linger in their mind long after rehearsals and feeling motivated to listen to music on their own. For many, singing in a weekly choir provided a non-threatening way to practice vulnerability, engage with others as a team, and form meaningful friendships. During rehearsals, many participants felt heard and respected and were comfortable voicing their opinions and finding ways for creative expression. Since starting the choir, some chose to become involved in other community activities and felt less socially isolated.

Conclusions: Participating in a community choir had a positive impact on mood and emotional well-being. Singing and listening to music generated positive emotions and served as a source of distraction from day-to-day worries. Socially, the choir’s supportive environment was conducive for social bonding and creative expression among participants. Improvements in participants’ sense of self efficacy were also evident as they felt more empowered to form new relationships and pursue other activities.
Abstract title: Population-based study to determine prevalence of hypertension and other cardiovascular risk factors in a rural region of Kenya

Resident’s name: Brian K. Cogburn, MD, PhD

Name of program: Preventive Medicine

Purpose: Cardiovascular disease is the leading cause of death in Africa. Hypertension, with a high prevalence in sub-Saharan Africa, appears to be a major contributory factor. Little is known about the prevalence of or risk factors for hypertension in rural areas of sub-Saharan Africa. We propose to estimate the prevalence of hypertension in adults in rural southern Kenya.

Methods: We will conduct the survey in Kaloleni district using randomized two-stage cluster sampling. We will use the validated WHO STEPwise approach to chronic disease questionnaire with additional questions for non-traditional risk factors and collect baseline blood pressure, basic demographic/anthropometric and spot urine from 660 non-pregnant adults over the age of 20 years old.

Results: Our research group conducted a preliminary assessment of hypertension prevalence in the same district during a health fair for a total of 740 residents. The prevalence of hypertension among 91 participants aged >18 years was high (31%). This current study will report prevalence of hypertension and its traditional risk factors, in addition to non-traditional risk factors such as kidney disease from chronic Schistosomaisis infection, indoor smoke exposure, or consumption of “miraa” (a plant-based stimulant). The data collection and analysis will take place November 2015.

Conclusions: Our study will provide epidemiological data critical for mapping and surveillance of hypertension and associated cardiovascular risk factors crucial for curbing the cardiovascular disease pandemic that is emerging in rural Kenya and other parts of East Africa. This will be the first study of nontraditional cardiovascular risk factors in a rural Kenya that has the potential to uncover interventions that can particularly impact rural populations in LMICs. Findings from this study will lead to the development of a team-based health intervention that addresses hypertension in rural populations in low and middle income countries.
Abstract title: Conditional Survival and Predictors of Late Death in Patients with Ewing Sarcoma

Resident’s name: Jillian R. Davenport, MD

Name of program: Pediatrics

Purpose: Long term survivors of Ewing sarcoma (EWS) are at considerable risk for future complications, including late relapse and death. Data on prognostic factors for late death in those who have survived beyond five years are lacking.

Methods: We conducted a retrospective cohort study using the Surveillance, Epidemiology, and End Results (SEER) database. We obtained clinical features and outcome data on 1,351 patients with EWS who had survived 60 months or greater. From these data, we performed univariable and multivariable analyses of overall survival using log-rank tests and Cox proportional hazards models.

Results: Of 1,351 patients in the cohort, there were 209 deaths, 144 (69%) of which were reported to be due to EWS. The OS for five-year survivors at 10 years was 87.5% (95% confidence interval 85.4-89.3%). Univariate adverse prognostic factors for late death in 5-year survivors included age >18 years at initial diagnosis, male sex, and axial/pelvic primary site. Initial stage was not prognostic. Independent adverse prognostic factors for late death included black race [hazard ratio (HR) 2.16, P=0.01], age ≥ 18 years at diagnosis (HR 2.02, P<0.001), male sex (HR 1.43, P=0.01), and axial/pelvic primary site (HR 1.43, P=0.02).

Conclusions: The majority of late deaths in five-year survivors are due to EWS. Black race, age > 18 at diagnosis, male sex, and axial/pelvic primary site (but not stage at diagnosis) are independently associated with increased risk of late death.
**Abstract title:** The Prognostic Value of ST-depression in Lead aVL in Patients with Inferior ST-segment Elevation Myocardial Infarction

**Resident’s name:** Jonathan Fu, MS

**Name of program:** Emergency Medicine

**Purpose:** Inferior ST-elevation myocardial infarctions (STEMIs) with right ventricular (RV) infarct have been shown to have an estimated 2.6-fold increased risk of death. RV involvement is also associated with increased risk of cardiogenic shock, ventricular arrhythmias, and mechanical complications. Some literature suggests that the identification of RV infarct may be done in the conventional 12-lead by specifically looking for ST-segment depression in aVL. The objective of this study is to compare rates of cardiogenic shock in patients with inferior STEMI with and without ST-segment depression >1mm in aVL.

**Methods:** A retrospective secondary analysis was performed on the ACTIVATE-SF registry. Consecutive cases of inferior STEMIs presenting to two hospitals in San Francisco, CA from 2008-2010 were analyzed. Rates of hypotension defined as an SBP.

**Results:** 125 patients with mean age of 60.7 years were included in the study. Rates of hypotension were 12.7% [95% CI 2.9%-22.7%] in those without aVL depressions vs 21.1% [11.7%-30.4%] in patients with aVL depressions, p>0.05. The use of vasopressors was 6.4% [0.0%-13.6%] in those without aVL depressions vs 19.2% [10.3%-28.2%] in those with aVL depressions, p<0.05. Lastly mortality rates differed between those without and with depressions in aVL: 2.1% [0.0%-6.4%] vs 12.8% [5.2% vs 20.4%], p<0.05.

**Conclusions:** In patients with inferior STEMIs, there was a trend towards higher rates of hypotension and statistically significant increased prevalence of ED pressor use and mortality. There is evidence that RV infarct is clinically significant and aVL may predict RV infarct. This study suggests that aVL may have clinically relevant prognostic value.
Abstract title: Characterizing brain metastasis growth before stereotactic radiosurgery

Resident’s name: Michael A. Garcia, MD, MS

Name of program: Radiation Oncology

Purpose: Stereotactic radiosurgery (SRS) precisely targets brain metastases and can be administered in either a frame-fixed or frameless manner. Seymour and colleagues recently showed that patients treated with frameless SRS planned on MRI completed greater than 14 days before SRS delivery have worse local control. An advantage of frame-fixed SRS is acquisition of the SRS-planning MRI on the day of treatment. We sought to describe brain metastasis growth before SRS by comparing the preceding diagnostic MRI (dMRI) and frame-fixed SRS planning MRI scans.

Methods: We reviewed patients treated with frame-fixed SRS for brain metastases at UCSF from 2010-2013. We identified 175 patients (445 brain metastases) with no prior brain treatments who had a preceding dMRI for comparison of brain metastasis size on SRS-planning MRI. All brain metastases were contoured on the dMRI and SRS-planning MRI using MIM software (Version 6.4.1) for volumetric comparison. Factors predictive of brain metastasis growth were investigated using logistic regression analysis. Local control and overall survival (OS) were estimated by Kaplan-Meier method. Multivariable Cox proportional hazard modeling assessed potential risk factors of local control and overall survival.

Results: Median imaging follow up was 10 months. Mean volume of brain metastases was 1.26cc [range 0.01-21.29cc]. Mean volume difference of metastases between dMRI and SRS was 0.40cc (95% CI: 0.05-0.73, p<0.001 by paired T test). Mean time interval between diagnostic MRI and SRS was 23 days, and time interval was strongly associated with brain metastasis growth (Pearson’s r=0.25, p<0.001). If 14 or more days passed between dMRI and SRS, 34% of patients had brain metastasis growth on the SRS planning-MRI per radiology report. The degree of brain metastasis growth between dMRI and SRS was also correlated with size of the initial brain metastasis (Pearson’s r=0.30, p<0.001). Melanoma patients more commonly had brain metastasis growth (p<0.0001), but systemic disease status, concurrent systemic therapy, neurologic symptoms, and dMRI slice thickness or field strength were not associated with growth. Brain metastasis growth (as evaluated by volume thresholds of 0.1cc, 0.25cc, 0.5cc, and 1.0cc) was not associated with worse local control by log rank test. Overall survival was not associated with brain metastasis growth (p=0.47).

Conclusions: Time between diagnostic MRI and SRS is associated with brain metastasis growth, but local control is not compromised when patients receive SRS in a frame-fixed manner. Over a third of patients have clear brain metastasis growth at SRS delivered 14 days or more after diagnostic MRI. For frameless SRS, brain metastasis growth after planning MRI may lead to marginal miss.
Abstract title: Frequent Users to the ED: How Often Do They Go to Another Hospital?

Resident’s name: Delphine Huang, MD, MS

Name of program: Emergency Medicine

Purpose: Background: Frequent emergency department (ED) use, especially at multiple hospitals can be costly, a waste of resources due to redundancy, and a burden on the entire health care system. However, little is known about the rate at which patients use different EDs, as well as the characteristics of these populations.

Objectives: The primary objectives were to 1) identify characteristics of patients who visit the same or different EDs and 2) determine the rates that patients visit multiple hospitals

3) Determine revisits rates and if patients have revisits with similar or different complaints.

Methods: Data were used from 2010 Florida’s Healthcare Cost and Utilization Project (HCUP) State Emergency Department Databases (SEDD). Patients 17 or younger, inter-facility transfers, and patients who were admitted during their index encounter were excluded. Descriptive analyses were performed to compare non-frequent users (<4 visits in 1 year) to both frequent users (≥ 4 but less than 10 visits per year) and super users (≥10 visits per year).

Results: There were 2,698,764 patients who had 4.4 million emergency room visits in Florida in 2010. 6.46% were frequent users, while 0.64% were super users. 67.98% of the frequent and super user cohort were from the ages of 18-44. 32.34% of these patients had Medicaid, and 34.40% were self-pay or were not charged. Most common visits to the emergency room for all groups involved abdominal pain or musculoskeletal/skin complaints. 62.09% of frequent users and 85.73% of super users visited 2 or more hospitals within 1 year, compared with 8.86% of non-frequent users.

Conclusions: ED frequent usage to multiple hospitals is common among patients, but especially among frequent and super users, which can have costly, and resource-efficiency implications for not just individual hospitals, but the entire health care system.
Abstract title: Delays in ACL Reconstruction in Publicly Insured Pediatric Patients

Resident’s name: Krishn Khanna, MD

Name of program: Orthopaedic Surgery

Purpose: Delays in the reconstruction of ACL tears are associated with meniscal and chondral injuries. Obtaining this surgery may be more challenging for patients who are uninsured or publicly insured. The aim of this study was to analyze whether the insurance status of pediatric patients with ACL injuries impacted the time from injury to surgery, and consequently led to a difference in the incidence of secondary meniscal and chondral injuries.

Methods: The study was designed as a retrospective review. The patients were grouped into those with public (government sponsored) insurance and private insurance. The dates of the injury, initial orthopedic evaluation, MRI scan, and ACL reconstruction surgery were recorded as continuous variables. The presence of chondral injuries or meniscal injuries was recorded as dichotomous variables from the operative report. The Wilcoxon test for continuous variables and the Fisher’s exact test for dichotomous variables were used to determine statistical significance.

Results: A total of 170 patients treated by a single orthopedic surgeon from 2010 to 2015 were reviewed. Time from injury to orthopedic follow-up was 31 days vs. 16 days for publicly vs. privately insurance patient (p=0.007). Time from injury to MRI was 38 days vs. 19 days for publicly vs. privately insurance patient (p<0.001). Time from injury to ACL reconstruction was 96 days vs. 61 days for publicly vs. privately insurance patient (p<0.001). Medial meniscal tears and chondral injuries were trending towards being more common in publicly insured patients (p=0.11 and p=0.087 respectively).

Conclusions: The time from injury to subspecialty follow-up, MRI diagnosis, and surgical treatment was significantly longer in publicly insured patients. The presence of medial meniscal and chondral injuries was trending towards being higher in publicly insured patients. Pediatric orthopedic surgeons should stay vigilant and examine their own practice pathways to minimize such delays.
Abstract title: The Use of Pocket-sized Handheld Ultrasound to Diagnose Distal Radius Fracture and Assess Quality of Closed Reduction

Resident’s name: Brian C. Lau, MD

Name of program: Orthopaedic Surgery

Purpose: Closed reduction of a distal radius fracture is a common procedure, however, particularly with trainees or non-orthopedists, requires repeated radiographs or the use of fluoroscopy to obtain a satisfactory reduction. Repeated radiographs are costly and time intensive and fluoroscopy is not widely available. Additionally, in nontraditional medical settings such as the developing world, disaster areas, or in combat zones radiographs and fluoroscopy are not widely available. A portable pocket-sized handheld ultrasound may be a safe, effective, and efficient method to identify suspected distal radius fractures and assist with adequate fracture reductions. This is the first study to evaluate distal radius diagnosis and assessment of closed reduction with a portable handheld ultrasound.

Methods: Sixteen distal radius fracture patients (average age 49.6; 8 female) and 20 healthy control patients (average age 53.3; 10 female) were enrolled. Distal radius fractures had standard 3-view radiographs and 3-view handheld ultrasound (Mobisante Inc.) exam of the wrist before and after reduction. Control patients had 3-view radiographs and handheld ultrasound exam performed. Radiographs were used as the gold standard. A board-certified orthopedic hand-fellowship trained surgeon and board-certified and musculoskeletal-fellowship trained radiologist were blinded and reviewed the ultrasound images for no fracture, fracture without satisfactory reduction, and fracture with satisfactory reduction.

Results: The sensitivity of distal radius diagnosis on ultrasound was 100%; the specificity was 80%; the positive predictive value was 82%; the negative predictive value was 100%. The sensitivity of identifying an unsatisfactory reduction was 88%; the specificity was 75%, the positive predictive value was 78%, the negative predictive value was 86%.

Conclusions: Pocket-sized portable handheld ultrasound demonstrates excellent accuracy in diagnosing distal radius fractures and assessing satisfactory reduction. Handheld ultrasounds may be an alternative to radiographs in environments without access to radiographs including developing countries, disaster zones, or with emergency personnel.
**Abstract title:** Does the use of a single dose of 4mg IV ondansetron cause clinically prolonged QTc in the undifferentiated nauseated patient in the emergency department?

**Resident’s name:** Kai Li, MD

**Name of program:** Emergency Medicine

**Purpose:** Ondansetron is a commonly used antiemetic in the ED. Recent reports indicate that IV administration of ondansetron may cause a prolongation of the QTc interval causing increased risk of arrhythmias, primarily torsades de points. Interval increases as low as 20 msec are considered clinically significant by expert opinion. Most of the current data supporting QTc prolongation following ondansetron administration comes primarily from the anesthesia literature. These studies are often confounded by the concomitant use of anesthetics and procedure-induced hypothermia, and are not directly applicable to the ED population.

This is the first prospective study examining the risk of QTc prolongation following administration of a single dose of 4 mg IV ondansetron in the undifferentiated nauseated ED patient.

**Methods:** This is a prospective, single-center, observational study. We enrolled a convenience sample of adult patients who were ordered a single dose of IV ondansetron by their provider for the treatment of undifferentiated nausea. Exclusion criteria includes: critically ill, prior ondansetron administration pre-hospital or during ED course, forensic patients, pregnant patients, or patients unable to give consent.

ECGs were obtained prior to and five minutes after ondansetron administration. Primarily endpoint was change in QTc. Secondary endpoints were cardiac arrhythmias or significant cardiac events.

Statistics for the change in QTc will be calculated using a paired, one-sided t-test with the null hypothesis that a single dose of 4mg IV ondansetron will not cause a significant prolongation.

**Results:** A total of 20 patients were enrolled between June through November 2015. The mean increase in QTc post-ondansetron administration was 14.1 msec (95% CI 5.5-infinity), (p= 0.005 for the one tailed test, power 0.87). QTc increased beyond 20 msec in 20% (4/20) of patients.

**Conclusions:** Our preliminary data shows that ondansetron causes a moderate QTc prolongation. No cardiac arrhythmias were noted. Our current data is limited by small sample size. Future data analysis will focus on specific subgroups that may be particularly sensitive to QTc prolongation.
Abstract title: The Effect of Submandibular Gland Preservation During Lymphadenectomy on Postoperative Xerostomia

Resident’s name: Jeffrey D. Markey, MD

Name of program: Otolaryngology

Purpose: Compare the presence and degree of postoperative xerostomia following preservation or excision of the submandibular gland (SMG) during level IB neck dissection (ND) without adjuvant radiation.

Methods: Retrospective review with patient questionnaire administered with inclusion criteria including patients with pT1-2N0 oral or oropharyngeal squamous cell carcinoma (SCC) who underwent resection and ND with SMG preservation or SMG excision without postoperative radiation from 2011 to 2015 and a control group not undergoing ND or oral/oropharyngeal resection. Three questionnaires were administered: University of Michigan Xerostomia Quality of Life (XeQoL), Short Form-8 (SF-8), and a xerostomia severity scale (XSS). Dry mouth severity (DMS) was calculated based on XSS scores among those complaining of any xerostomia. The SMG preservation, SMG excision and control groups were all compared.

Results: Sixteen SMG preservation group, 15 SMG excision group and 15 control group patients completed the survey. Complication and recurrence rates were low and comparable in the SMG preservation and excision groups. No differences were identified between the two experimental groups for the XeQoL, SF-8, and XSS questionnaires (p=0.54, 0.56, 0.79). The SMG excision group had a higher mean DMS score (4.6) compared to the SMG preserved group (2.9) (p=0.22). Control patients reported less xerostomia on XeQoL (p=0.06) and XSS (p=0.020) compared to the experimental groups combined with no statistical difference in SF-8 scores (p=0.46).

Conclusions: SMG preservation, though technically and oncologically safe, doesn’t appear in this study to reduce xerostomia. Oral or oropharyngeal resection with ND may result in some degree of xerostomia.
Abstract title: Differences In Psychological Outcomes in Older Versus Younger Oncology Patients Undergoing Chemotherapy: Does Personality Play a Role?

Resident's name: Stefana Morgan, MD

Name of program: Psychiatry

Purpose: Older oncology patients have been consistently found to exhibit lower levels of depression and anxiety, compared to younger patients. Several possible explanations for this difference have been proposed (e.g., older patients may use more adaptive coping strategies; older adults have fewer competing social and occupational responsibilities; having a chronic or life-limiting illness as an older adults is more expected). However, few studies have examined the wide range of potentially relevant psychological factors that may influence depression and anxiety symptoms in older vs. younger oncology patients. Therefore, among a large sample of patients undergoing chemotherapy, the purpose of this study was to compare older (65 years or older) vs. younger patients (< 65 years) in terms of demographic, clinical, and psychological outcomes, and to evaluate for differences between the two age groups on a range of potentially relevant psychological variables (i.e., coping, resilience, perceived stress, and personality).

Methods: This study used a large, well-characterized dataset of adults (n=1,329) with breast, gastrointestinal, gynecological, or lung cancer. Patients had received chemotherapy in the preceding four weeks and were scheduled to receive at least two additional cycles of chemotherapy. While six timepoints were included in the larger study, this analysis utilized the baseline assessment data. Measures included demographic and clinical variables (e.g., time since diagnosis, number of metastatic sites), and key psychological outcomes (i.e., depression, anxiety, and intrusive thoughts/hyperarousal), which were evaluated using the CES-D, STAI-S, and IES-R, respectively. The following potentially relevant psychological variables were also assessed: general coping (Brief COPE), cancer-specific coping (Mental Adjustment to Cancer scale), perceived stress (Perceived Stress Scale), resilience (Connor-Davidson Resilience Scale), and the “Big Five” personality domains (NEO-FFI). Descriptive statistics, chi-square analyses, and t-tests were used to examine relationships between age group (< 65 vs. ≥ 65 years) and demographic, clinical, symptom-related, psychological, coping, resilience, stress, and personality variables.

Results: About one-quarter (27.5%) of the sample was 65 or older (N=365). Older patients were more likely to be male (31.2% in the older group, vs. 18.6% in the younger group). Older patients were less likely to work for pay (21.4% of the older patients vs. 40.3% of the younger patients) and to have childcare responsibilities at home (5.0% of the older patients vs. 28.8% of the younger patients). Compared to younger oncology patients, older patients reported significantly lower levels of depressive and anxiety symptoms, as well as lower levels of intrusive thoughts and hyperarousal. While scores on the resilience scale did not differ between the age groups, older patients had lower levels of trait anxiety, perceived stress, and anxious preoccupation. Findings were mixed with regard to differences between the age groups in terms of the various subscales of the Brief COPE. On the NEO-FFI, older patients also scored lower on neuroticism and higher on agreeableness.

Conclusions: These findings raise intriguing possibilities regarding the role of coping, stress, and personality in the relationship between age and psychological outcomes (including depression, anxiety, intrusive thoughts and hyperarousal) among cancer patients undergoing chemotherapy. Further, these findings point to the need to study coping, perceived stress, and personality as possible mediators of associations between age and previously reported lower levels of psychological distress in older oncology patients. Our team is examining these possibilities using structural equation modeling. Moreover, interventions with patients at risk for higher levels of distress will also be aided by identifying these potentially modifiable factors (for example, interventions that teach more adaptive coping strategies or ways of perceiving stress could theoretically be useful).
Abstract title: Feasibility of a novel emergency system for island communities in East Africa

Resident’s name: Lily B. Muldoon, MD, MPH

Name of program: Emergency Medicine

Purpose: Pre-hospital emergency care is dramatically absent from many low and middle-income countries. Remote and rural populations face additional barriers to accessing acute care. Here we report the feasibility of a novel, community first-responder and care coordinator network known as Health Navigation (HN). Focusing on the fishing communities of Mfangano Island, Kenya, the HN program aims to improve access to acute care services in the Lake Victoria region through emergency transportation, care coordination, and patient advocacy.

Methods: In 2014, a group of ten Community Health Workers were trained on basic first-aid, triage, and care coordination during a week-long intensive training program with monthly advanced education seminars. When called to an emergency, these Health Navigators (HNs) ensure patient safety, coordinate emergency referrals, activate off-island transportation with an emergency boat, and complete in-person follow-up.

Results: From August 2014 to February 2016, HNs responded to a total of 254 emergency cases. Most patients (70.2%) were female, the majority (55.1%) were pediatric medical emergencies, and 19.3% were obstetric patients. The observed incidence of trauma was low (2.4%).

The HNs consistently utilized and adhered to the referral protocol. They responded quickly to patients at the scene (average time to arrival was 16 minutes), and reliably traveled with the patient to the health facility. They provided advanced communication to receiving facilities on 100% of off-island transfers, and provided early, in-person follow-up to 93% of patients.

Conclusions: This evaluation demonstrates adherence to a simple triage and referral protocol, and provides evidence of the feasibility of applying the Health Navigation concept to pre-hospital care for rural populations. Expansion of this program can have enormous implications on health outcomes of the entire Lake Victoria Basin region of 35 million people.
Abstract title: Autoimmune Cytopenias in Pediatric Hematopoietic Cell Transplant (HCT) Patients

Resident’s name: Jessica A. Neely, MD

Name of program: Pediatrics

Purpose: Patients undergoing HCT are at risk for developing autoimmune cytopenias (AIC) in the post-transplant period, but the mechanism by which AICs develop is unclear. We hypothesized that B cell recovery prior to complete T cell recovery would be associated with AICs in this patient population.

Methods: We identified twenty patients age 0-21 who underwent HCT at our institution between 1/1/00 & 7/1/15 and developed AICs, including autoimmune hemolytic anemia (AIHA), immune thrombocytopenia (ITP), autoimmune neutropenia (AIN), or Evans syndrome. A control group was randomly selected at a 2:1 ratio matched for primary disease (malignancy, immunodeficiency/immune dysregulation (ID), or Evans syndrome) & type of transplant (matched related, unrelated, or haploidentical donor). For each patient, we analyzed the snapshot of immune recovery at the time point most proximal to AIC onset but prior to any therapy. B cell recovery was defined as CD19 count >50 cells/uL with IgM & IgA normal for age. T cell recovery was defined as CD4 count >200 cells/uL and PHA >50% of control response. Lineage-specific engraftment was evaluated at the time point most proximal to AIC onset. Median time to B cell and T cell recovery was calculated for cases and controls.

Results: Of cases, 45% (N=9) had AIHA, 30% (N=6) Evans syndrome, 15% (N=3) ITP, and 10% (N=2) AIN. 10 patients had ID, 7 had malignant disease, & 3 had an inborn error of metabolism or thalassemia. Median time to AIC onset was 5.2 mo (range 1.4-15.1 mo). Among ID patients, 56% (5/9) had T cell recovery at AIC onset in contrast to 0% (0/7) of malignant patients (p=0.034). B cell recovery was seen in 67% (6/9) of ID patients at AIC onset, compared to 57% (4/7) of malignant patients (p=1). Compared to a control group, T cell recovery was significantly delayed for all patients who developed AICs (9.3 mos v 6.0 mos, p=0.007), and this difference was most pronounced in patients transplanted for malignancy (p=0.005). Cases and controls were similar except for age (cases 8.2 yr+7.3 v controls 4.0yr+4.7, p=0.03) and incidence of cGVHD, which was higher in controls (5% v 32%; p<0.003). Among cases, 40% had mixed donor chimerism at AIC onset and this was not different among ID and malignant groups (60% v 29%; p=0.33).

Conclusions: The mechanism by which AICs develop may differ based on a patient’s primary disease. In malignant disease, poor T cell recovery may be the primary mediator of autoantibody production by partially-functional B cells. In ID, a number of mechanisms may contribute, including persistence of autoreactive donor lymphocytes, presence of double-negative CD3+ T cells, or delayed T cell recovery in the setting of B cell recovery. Management of post-HCT patients with AICs may need to take into consideration the primary disease and current state of immune recovery to make a mechanism-based decision to use T or B cell directed therapy.
**Abstract title:** Mesenchymal Stem Cells with Antigen Presenting Cell Gene Expression

**Resident’s name:** Matthew H. Schwede, MD

**Name of program:** Categorical Internal Medicine

**Purpose:** Human mesenchymal stem cells (MSCs) have significant therapeutic potential in preclinical models of ARDS, but the ways they produce these benefits aren't fully understood. Cytomix (a mixture of TNF-α, IL-1β, IFN-γ) is often used to model the pro-inflammatory state of ARDS (J Biol Chem, 2010). We used published microarray data to understand the genome-wide expression changes that MSCs undergo in an in vitro model of ARDS.

**Methods:** We downloaded a microarray dataset (GSE68610; J Immuno, 2015) from the Gene Expression Omnibus, which consisted of gene expression data for control MSCs (n=3) and MSCs exposed to cytomix (n=3). We processed the dataset with RMA (J Biostatistics, 2003) and a custom chip description file (Nucleic Acids Res, 2005), resulting in a dataset with 12,067 genes. We performed differential expression analyses using the R package limma (p2). The differentially expressed genes were characterized with gene set enrichment analysis using the Molecular Signature Database, or MSigDB (PNAS, 2005).

**Results:** After cytomix exposure, MSCs up-regulated 652 genes and down-regulated 846 genes. In MSigDB analyses, the up-regulated genes were enriched in hallmark gene sets describing responses to TNF and IFN-γ (FDR-corrected Fisher’s exact p<10^-141). MSCs down-regulated genes that are characteristic of stem cells (p=2.11x10^-45, Cell Stem Cell, 2008). The up-regulated genes included several genes expressed by antigen presenting cells (APCs), such as genes coding for CD40, CD68, CD83, and MHC class II proteins. Complement proteins and anti-inflammatory factors (TSG6, IL-1ra, and prostaglandin E synthase) were also up-regulated. The down-regulated genes included collagen genes and others characteristic of mesenchymal lineages, such as alpha smooth muscle actin, CD285, and laminins. Differential expression patterns were validated with qPCR.

**Conclusions:** MSCs exposed to cytomix transform into cells with APC-like gene expression and lose gene expression patterns associated with a mesenchymal phenotype.
Abstract title: Evaluating smart pump library data to improve safety of intravenous high-risk medications

Resident's name: Murooj Z. Shukry, PharmD

Name of program: Pharmacy

Purpose: Many studies indicate that smart infusion pumps are not used to their full potential and intravenous (IV) administration errors still persist. Infusion pumps are used to administer parenteral medications at precise rates or amounts. Smart pumps have drug library limits and alerts that provide useful information to drive safe practices with use of IV medications, especially high-risk medications. Guardrails® Suite MX software provides drug library for the Alaris® System (smart infusion pump device). The objectives of this study are to evaluate the use of smart infusion pump alerts for IV high-risk medications and to identify opportunities to enhance safe use of the current system.

Methods: This descriptive study evaluates data collected from Guardrails® and Alaris® System for adult patients at UCSF Medical Center during June 2015. A report from Epic (electronic health record) for June 2015 will provide an approximate number for orders of high-risk medications per patient and per patient-visit. The UCSF Institutional Review Board has approved this study. The analysis of this data will help assess clinician use and utility of the drug library. To assess clinician use the following variables will be analyzed: compliance rate of utilizing the drug library, number of alerts, override-to-alert ratio, and clinician response to the alert: override versus cancel versus reprogramming of the pump. To assess the drug library utility the following will be analyzed: frequency of “good catch,” rate of potential nuisance (noise) alerts, rate of averted errors.

Results: Out of 2,534 alerts, 1,954 (77%) were overridden, 498 (20%) were cancelled, and 82 (3%) were reprogrammed to drug library settings. Override action was done within 2 seconds (noise alert) in 772 (40%) of overridden alerts. The top five overridden medications in descending order are: fentanyl, heparin, phenylephrine, magnesium sulfate, and hydromorphone.

Conclusions: Preliminary results indicate that there are potential areas for improvement within the current infusion library.
Abstract title: Association of Gut Microbiota Generated Metabolites and Atherosclerosis in HIV

Resident’s name: Arjun Sinha, MD

Name of program: Categorical Internal Medicine

Purpose: HIV infection is associated with increased atherosclerosis and CVD. This increased risk is partly due to higher levels of inflammation. Changes in gut microbiome and gut mucosa that occur with HIV infection create a “leaky gut syndrome” and are associated with chronic inflammation. This remains true for patients on antiretroviral therapy (ART) with a suppressed viral load. Gut microbiota generated metabolites such as choline, carnitine, betaine, and trimethylamine N-oxide (TMAO), have been associated with increased atherosclerosis in HIV-uninfected individuals. Given the effect of HIV on gut microbiota, we hypothesized that these four metabolites would be associated with subclinical atherosclerosis as measured by carotid artery intima media thickness (cIMT) in HIV-infected individuals.

Methods: IMT was measured in 162 HIV-infected individuals using high resolution ultrasound in the common carotid, bifurcation region, and internal carotid artery. Repeat measurements were done 3.5 ± 1.9 years later to assess IMT progression. Metabolites were measured at Cleveland Clinic using liquid chromatography with mass spectrometry.

Results: The mean age was 49 ± 6 years, 91% were male, 63% were virally suppressed, and 35% were current smokers. After adjusting for demographics and CV risk factors, each doubling of betaine was associated with greater IMT in the common carotid (7%, p = 0.05), bifurcation (9%, p = 0.02), internal carotid (16%, p < 0.01), mean IMT (10%, p < 0.01), and mean IMT progression (1% per year, p < 0.01). Similarly, each doubling of carnitine was associated with greater IMT in the common carotid (9%, p = 0.02), bifurcation (11%, p = 0.04), mean IMT (10%, p = 0.03), and mean IMT progression (1% per year, p = 0.03). In contrast, choline and TMAO levels showed little association with any IMT region. The results were unchanged when the analysis was restricted to the subjects on ART with a suppressed viral load. HIV viral load was associated with higher betaine levels (2% per 10-fold increase in HIV RNA, p = 0.03) while ARV use was associated with 12% lower betaine levels (p = 0.02) and 11% lower carnitine levels (p = 0.02).

Conclusions: Carnitine and betaine are independently associated with higher baseline and yearly progression of carotid IMT in HIV-infected individuals. Unlike studies of HIV-uninfected cohorts, TMAO did not show any association with carotid IMT. This suggests that the pathogenesis of atherosclerosis in HIV-infected individuals is distinct from uninfected individuals. As betaine and carnitine are generated by gut metabolism, restoring the changes in the gut microbiome that occur with HIV may reduce the progression of HIV-associated atherosclerosis.
Abstract title: Capturing Resilience: an examination of adolescent resilience

Resident’s name: Vivien K. Sun, MD, MPhil

Name of program: Pediatrics

Purpose: Depression is the most common mental health problem affecting adolescents nationally, causing significant impairment to their health, development, and well-being. Although depressive symptoms are inversely associated with resilience, relatively little is known about how depressed adolescents experience resilience, particularly in low income, urban environments.

The objectives of the study were: 1. to engage adolescents with depression by reflecting on their everyday realities and 2. to provide a qualitative analysis of how these adolescents experience resilience.

Methods: Photovoice is a widely used research methodology that employs photography to access the experience of individuals and provides them with a voice for expression. Investigators recruited participants aged 13-17 years with a diagnosis of depression from a safety-net primary care clinic in San Francisco, CA. Participants took photographs examining topics such as what defines you, what motivates or inspires you, and how do you envision your past vs. future. Participants met weekly as a group for a total of six guided sessions to discuss their photographs through a consensus-building process. All sessions were audio-recorded, transcribed, and analyzed using a general inductive approach in ATLAS.ti to identify common themes.

Results: Five adolescents participated in this study. The average age was 16.2 years. All participants were low-income, non-white (4 Latino and 1 African-American) urban youth. Three major themes emerged that captured their capacity for resilience: 1) embracing adolescence as a time of positive growth; 2) staying true to one’s self despite feeling misunderstood; and 3) drawing upon the courage and beauty in their external environment. Participants universally reported the photovoice discussion groups to be a positive and enriching experience.

Conclusions: Photovoice offers a unique window into the experience of adolescent resilience in the face of depression. Beyond feeling hopeless or sad, participants described a distinct optimism for their future despite the challenges of being low-income, urban youth.
Purpose: Estimations of blood loss are often inaccurate in surgical procedures. Blood loss is typically estimated at the time of dilation and evacuation (D&E) and it is unclear how accurate those estimations are. We aim to compare the mean measured versus estimated blood loss at the time of D&E.

Methods: Using a standard protocol, we measured blood loss for all D&E procedures between 16-24 weeks at one abortion clinic. The protocol involved weighing all blood-containing items as well as measuring blood captured in the D&E tray. Providers recorded estimated blood loss before weighing or measuring blood. We compared means by gestational age using a t test.

Results: There were 372 eligible procedures from January through September 2015 included in our data analysis. Mean estimated versus measured blood loss was significantly different for each gestational age group: 101ml vs 200ml at 16 weeks, 127 vs 222 at 17 weeks, 134 vs 275 at 18 weeks, 130 vs 302 at 19 weeks, 180 vs 362 at 20 weeks, 179 vs 391 at 21 weeks, 193 vs 406 at 22 weeks, 229 vs 629 at 23 weeks, and 253 vs 715 at 24 weeks (p<0.05 for all comparisons).

Conclusions: Providers consistently and significantly underestimate blood loss at the time of D&E. Based on the above data; we developed two training modules which summarize our findings in this way: At 16 weeks, a D&E has on average 150ml blood loss. Every week thereafter has an additional 50ml of blood loss (200ml at 17 weeks, 250ml at 18 weeks, etc.). Then, at 23 and 24 weeks, average blood loss increases to 600ml and 700ml respectively. Further research is underway to determine the impact of these training modules on providers’ ability to more accurately estimate blood loss.
Purpose: We sought to characterize temporal trends in the use of endovascular treatment (EVT) for acute ischemic stroke at academic medical centers in response to recent clinical trials. Although endovascular devices for stroke were first cleared for marketing in 2004, initial clinical trials in 2013 failed to demonstrate efficacy and subsequent clinical trials beginning in 2014 were strongly positive. The impact of these data on practice patterns at academic medical centers, which perform most EVT, is unknown.

Methods: We identified all acute ischemic stroke hospitalizations at academic medical centers that were members in the University HealthSystem Consortium from October 2009 to July 2015 using International Classification of Disease, 9th revision codes 433.x1, 434.x1, and 436 for stroke and procedure code 39.74 for EVT. We compiled quarterly data on the number and proportion of stroke hospitalizations using EVT and we used segmented log-linear regression to identify temporal trends and to evaluate changes in trends at prespecified time points corresponding to the quarter in which pivotal trials were first reported.

Results: From 2009-15, we identified 357,973 acute ischemic stroke hospitalizations at 161 medical centers. The proportion of stroke hospitalizations using EVT was 1.5% in 2009 and grew by 25% a year (95% CI 21% to 29%) to reach 3.1% in 2013. After negative results from the initial trials were reported in 2013, EVT use hovered between 2.5% and 2.7% (1% relative change per year; 95% CI -9% to +8%; p=0.004 for change in trend) until 2014 when the first positive trials were reported and EVT use jumped at a growth rate of 151% per year (95% CI 101% to 212%; p<0.001 for change in trend) to reach fully 4.7% of all stroke hospitalizations by 2015.

Conclusions: The previously steady growth in EVT flattened in 2013, coincident with the initially negative results from clinical trials, but has dramatically increased since positive trials were first reported in 2014.
Abstract title: Sum of Doppler Tissue Imaging Lateral Mitral Annular Velocities at Peak Systole and Early Diastole Discriminates Diseased from Healthy Hearts

Resident’s name: Jeffrey M. Tyler, MD

Name of program: Categorical Internal Medicine

Purpose: The cardiac cycle is continuous and interconnected but parsed into diastolic and systolic phases for study. A simple measure that integrates these phases of heart function is desirable. Tissue Doppler imaging (TDI) is performed routinely and displays diastolic and systolic wave forms in one tracing. Based on empiric observations, we hypothesized that the sum (sum S'E') of lateral mitral annular systolic (S') and early (E') diastolic velocities predicts global heart function.

Methods: A cross-sectional study was conducted on a sample of echocardiograms at our institution performed either as part of standard of care or as voluntary participation in the Health eHeart Study, an internet-based study. Exclusion criteria included age greater than 75 or less than 30 years, severe mitral regurgitation and non-sinus rhythm. S', E', left ventricle ejection fraction (LVEF), and diastolic function were measured in the standard fashion. A scoring system was used to quantitatively integrate LVEF and diastolic function as an integer with 0-3 points assigned to progressively lower LVEF and 0-3 to degrees of diastolic dysfunction. Using receiver-operator characteristics curve analysis, a cutoff value for sum S'E' was generated.

Results: Ninety-one patients (51 ± 13 years, 46% female) were selected to generate an even distribution across cardiac health as defined by the scoring system (2.4 ± 2.1). Mean sum S'E' was 18 ± 7. After adjusting for age and sex, sum S'E' correlated inversely with points (β=-0.26, 95% CI -0.3 - -0.2, p<0.01). A sum S'E' cutoff of ≥ 20 had a sensitivity of 92% and a specificity of 78% for normal global heart health (0 points). A sum S'E' cutoff of < 15 had a sensitivity of 84% and a specificity of 82% to determine poor global heart health (4-6 points).

Conclusions: TDI lateral mitral valve annular sum S'E' is easily obtained from a single wave form. In particular, a sum of ≥ 20cm/s is a strong indicator of a healthy heart and one < 15 of cardiac impairment. This integrated index may provide a useful echocardiographic screening measure that guides the level of scrutiny of a clinical echocardiogram.
Abstract title: Fertility Preservation Services for Women with Newly Diagnosed Cancer: A National Survey

Resident’s name: William D. Winkleman, MD

Name of program: Obstetrics, Gynecology and RS

Purpose: To more fully understand the resources available for cancer patients seeking fertility preservation.

Methods: An online survey was distributed in January 2015 to 394 IVF clinics affiliated with the Society for Assisted Reproductive Technology.

Results: Responses were received from 84 clinics (21.6% response rate). Most clinics offer oocyte (96%) and embryo freezing (98%) while 22 clinics offer ovarian tissue freezing (26%). Fertility preservation is commonly offered for breast (98%), hematologic (96%) and ovarian cancers (82%). Only 26 clinics (31%) offer fertility preservation for premenarchal cancers. The patient experience and availability of ancillary support varies across clinics. The majority provide financial support and have brochures/web based material (73% and 67% respectively). Half (53%) have a designated patient navigator to coordinate of care. Only one third (33%) of clinics maintain long-term follow up with cancer patients.

The majority of clinics (71%) receive fewer than twenty cancer referrals annually. Compared to the practices with lower oncologic volume, the 28 centers that receive more than twenty referrals annually are more likely to be in the Northeast (X²=8.28, p=0.04) and have an academic affiliation (X²=5.65, p=0.04). These clinics are more likely to provide a patient navigator (X²=13.31, p<0.01), hold educational presentations (X²=17.14, p<0.01), and offer financial support (X²=7.53, p=0.01). These clinics are also more likely to have long-term follow up (X²=5.67, p<0.01) and patients are more likely to return to take advantage of their treatment (X²=11.26, p<0.01). Five centers receive over 100 referrals per year and are all academic centers with high overall patient volume (>700 IVF cycles annually).

Conclusions: While the majority of IVF clinics offer fertility preservation, many may not have sufficient patient resources or support given low clinic volume. Only around a quarter of clinics offer ovarian tissue freezing which is a way to preserve reproductive potential in patients who must urgently undergo aggressive chemotherapy and/or radiation and may be the only option available to premenarchal girls. Additionally, patients are more likely to return to take advantage of their fertility treatment if they are referred to a center with high volume suggesting that through patient education, outreach and support, clinics may ultimately affect the fertility of cancer patients and increase utilization rates after successful cancer treatment.
Thank you all for joining us
and we hope to see you next year!

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