

ChemDraw version 17.1 was used to qualitatively compare the antibiotic chemical structures in question.

**Summary of results** The R1 side chain of penicillin and cefazolin was found to be significantly different. This finding suggests that cefazolin can be administered in select patients with a history of penicillin allergy. We propose recommendations and specific situations where it is appropriate to do so.

**Conclusions** These guidelines contribute to current antibiotic stewardship practices and address unnecessary substitution of cefazolin for later-generation antibiotics, which are associated with higher costs, increased risk of complications, and the potential for emergence of multidrug resistant organisms.

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### DYSPHAGIA IN CHILDREN AFTER CONGENITAL CARDIAC SURGERY: A SYSTEMATIC REVIEW

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**Purpose of study** As the morbidity and mortality of congenital cardiac surgery has improved, attention to postoperative feeding outcomes has become increasingly important[Sf1]. While centers have embarked on various strategies to achieve oral feeding postoperatively, there is still wide variability in common practice.

**Methods used** The literature was searched using the MEDLINE, EMBASE, and CINAHL databases for publications up to March 2018. All papers discussing pediatric patients with congenital heart defects, surgical intervention, and swallowing dysfunction were reviewed in a systematic fashion. Exclusion criteria were non-English publications, only >18 year old patients, and no outcome data regarding feeding or swallowing.

**Summary of results** In total, 19 studies were included[Sf1]. Of these, 6 studies focused on dysphagia specifically, but notably included heterogenous assessment methods and outcomes. 9 studies discussed vocal fold dysfunction (VFD). Among those, only 5 assessed swallowing function discreetly and none found dysphagia in more than half of the patients with VFD. There were 5 studies evaluating feeding disorders in general, and only 1 study evaluated long-term results greater than 2 years.

**Conclusions** The available data on dysphagia after congenital cardiac surgery is heterogenous and sparse. In particular, there is a lack of common outcomes that are reported. Additional studies that focus on dysphagia in this population are needed to better isolate the risk factors and to develop comprehensive postoperative feeding strategies. A consensus of standardized, trackable outcomes will provide the basis for evidence driven feeding programs in this fragile population.

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### SHOULDER AND ELBOW FUNCTION FOLLOWING THE SUPINATION-EXTERNAL ROTATION PROTOCOL IN CHILDREN WITH BIRTH RELATED BRACHIAL PLEXUS INJURIES: A PILOT STUDY

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**Purpose of study** Birth-related brachial plexus injuries (BRBPI) occur in approximately 1 of 1000 live births. Consensus

regarding the optimal management of birth-related brachial plexus injuries (BRBPI) has not been achieved with various treatments including physiotherapy, occupational therapy, and surgery. Our group developed a protocol that repositions the shoulder into supination and external rotation (Sup-ER), which restores supination and external rotation by two years of age. However, the longer-term outcomes of the Sup-ER splint have not been reported.

**Methods used** This cross-sectional cohort study examined 16 children older than 4 years of age with severe BRBPI who were treated with the Sup-ER splint. Shoulder and elbow function were measured by the Axillary, Back, and Cranial loops and a modified Mallet scale. Additionally, the passive and active range of motion of internal rotation, external rotation, supination, pronation, elbow flexion and elbow extension, as well as internal and external rotation strength were examined.

**Summary of results** All functional and active movements were statistically significantly lower in the affected arm compared to the unaffected arm, except for elbow flexion. Passively, there were statistically significant differences between the affected and unaffected arms in all movements except for internal rotation and supination. Strength in internal and external rotation was weaker in the affected arm, with internal rotation having a relatively larger strength deficit.

**Conclusions** Despite statistical differences in the anatomic ranges of motion between the affected and unaffected arms, the ranges in both arms were within functional limits. Overall, the Sup-ER protocol has been effective in restoring elbow and shoulder function in children with BRBPI.

## Adolescent Medicine and General Pediatrics II Concurrent Session

8:00 AM

Friday, January 25, 2019

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### ASSESSING NUTRITIONAL INTAKES IN CHILDREN WITH NEPHROTIC SYNDROME

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10.1136/jim-2018-000939.223

**Purpose of study** Information regarding nutrition management of childhood nephrotic syndrome (NS) is limited. Based on risks of disease-related edema and corticosteroid side-effects, our NS clinical pathway incorporates standardized recommendations for daily energy, sodium (Na), calcium (Ca) and Vitamin D (VitD) along with food intake records. This study compares actual dietary intakes of patients with NS to our pathway's nutrition recommendations.

**Methods used** Our retrospective study included incident NS patients (1–17 years) treated with prednisone (60 mg/m<sup>2</sup>/day) seen from Feb 2013-May 2018 who completed a valid 3 day food record 4 weeks post-diagnosis. Intake information was analyzed using esha™ Food Processor program. Pathway recommendations for daily energy requirements were based on height, weight, age and gender using a sedentary activity factor. We recommended a daily Na intake of 1 mg/1 calorie of

energy with 500 mg Ca and 1000 IU VitD supplementation daily. Actual daily energy, Na, Ca and VitD intakes were compared to pathway recommendations and age-appropriate daily recommended intakes (DRIs).

**Summary of results** Thirty-six of 76 children (47%) completed food records. Actual and recommended energy intakes were similar across all age groups (median 1169 and 1275 kcal,  $p=0.52$ ). Seventeen of 36 patients (47%) consumed extra energy with only 4/36 (11%) exceeding recommendations by >30%. Twelve (33%) children exceeded suggested daily Na intakes with 4/36 (11%) exceeding Na recommendations by >50%. Across all age groups, mean dietary Ca intake was  $75\% \pm 33\%$  of DRI. Of 22 (61%) patients who reported Ca supplementation, 16 (73%) had total Ca intakes achieving DRI. Children age 1–3 years were more likely (77%) to meet DRI vs 4–8 years (33%) and 9–18 years (38%). None of the children met DRI for VitD through diet alone. With VitD supplementation, 24 (66%) met DRI with younger children 1–3 years (81%) more likely to achieve DRI.

**Conclusions** Based on intake data, our energy and Na recommendations are reasonable and attainable for most patients. Overall low intakes of Ca and VitD justify our pathway's recommendation for daily supplementation. Ongoing individualized nutrition assessment and age-appropriate supplementation are warranted given the effects of corticosteroid burden on bone health in these patients.

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#### SUMMARY OF ONLINE PARENTING RESOURCE RECOMMENDATIONS FOR CHILDREN'S MEDIA USE

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10.1136/jim-2018-000939.224

**Purpose of study** The purpose of this study is to summarize the information presented in popular websites as they pertain to media use in children and parenting methods concerning media.

**Methods used** A list of 32 websites was compiled by performing a Google search with the following search parameters: parenting, parenting advice, parenting resources, parenting website, effective parenting, parenting media use, parenting social media, parenting technology. Websites needed to meet the following criteria: US-based, not forum-based, included a search bar, and covered topics pertaining to parenting and technology. The websites were then evaluated for appropriate topics, and only articles posted within the past 5 years were evaluated.

**Summary of results** Of the 32 online sources that were evaluated, there was significant variability in the information they provided (table 1). Of the 28 questions asked, only 12 had a majority (>50%) agreement on recommendations, and there were no topics that had complete agreement. There was also a certain degree of discrepancy between the suggestions of the online sources and the recommendations in the American Academy of Pediatrics (AAP) Bright Futures. For 14 questions, many online sources did not discuss the topic, or if they did discuss it, they did not give specific recommendations (>50% of sources did not discuss the topic or did not give specific recommendations). The AAP does not provide specific recommendations regarding some of the topics we evaluated.

**Conclusions** While certain topics are addressed in a consistent manner, there is still a large degree of discrepancy in advice given to parents regarding children's media use. Pediatricians should be aware of the variability in information provided to parents on the internet and be able to provide them with reliable sources.

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#### ASSESSMENT OF PROVIDERS' BASELINE KNOWLEDGE TO DESIGN AN EFFECTIVE CURRICULUM ON LGBTQ HEALTH FOR PEDIATRIC RESIDENTS

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10.1136/jim-2018-000939.225

#### Abstract 225 Table 1

At what age should you start introducing media to children?

1 year (3%), 1.5 years (41%), 2 years (16%), discussed but no age given (19%), not discussed (22%)

Primary reason for giving cell phone to child?

Safety/emergency (59%), necessity (50%), child desire to have phone (0%), not discussed (38%)

What cautions about social media are covered?

Privacy (53%), cyberbullying (59%), parental supervision (6%), content control (44%), depression (31%), addiction (41%), oversharing/inappropriate sharing (31%), negative body image (28%), anxiety (9%), other (28%), not discussed (16%)

What benefits about social media are covered?

Strengthen social connections (47%), building an identity (25%), connecting with others with similar interests (47%), creative expression (25%), getting involved (9%), other (25%), not discussed (19%)

What solutions to cyberbullying were presented?

Have open conversations with child (41%), discuss proper online behavior (28%), document/report the incident (13%), block cyberbully (13%), educate children to identify bullying (25%), take an active role in child's social media account (38%), find adult/school resources (9%), decrease social media time (6%), teach social media literacy (9%), know the warning signs of children being cyberbullied (6%), ignore it (6%), communicate with cyberbully directly (6%), not discussed (22%)

Should media use be limited to certain parts of the house?

Yes (81%), no (0%), discussed, but no specific recommendations given (3%), not discussed (16%)

Should screen time be allowed during meals?

Yes (0%), no (75%), yes but limited (3%), not discussed (22%)

Should children be supervised while using media?

Yes (94%), no (0%), not discussed (6%)

Does the media (tv, movies, video games) promote violence?

Yes (72%), no (3%), discussed, but no conclusion (6%), not discussed (19%)

To meet the character count, all results are not included in this table.

**Purpose of study** LGBTQ individuals face significant health disparities, in part due to medical providers' discomfort with addressing health needs specific to the LGBTQ population. Prior studies in this field showed that education sessions targeted at medical students increased their comfort and competency. This study aims to measure the effect of a weeklong resident-led curriculum about LGBTQ healthcare on self-reported knowledge and comfort among residents and attending physicians on this topic.

**Methods used** Providers' knowledge and comfort in providing care for LGBTQ patients was assessed with a 7-question anonymous cross-sectional survey (Qualtrics®) prior to and after a weeklong curriculum composed of case-based discussions, didactics, videos, and resident testimonials of their experiences caring for LGBTQ patients in Fresno, CA. The pre and post surveys interrogated each provider's understanding of 13 terminologies specific to LGBTQ youth as well as self-reported comfort and knowledge of LGBTQ health needs.

**Summary of results** The pre-curriculum survey was completed by 29 residents and 13 attendings while the post-curriculum survey was completed by 18 residents and 3 attendings. Seven complete pre/post-curriculum matched assessments were completed. Participants reported either no prior LGBTQ training or found their prior training unhelpful. Providers were overall unfamiliar with most transgender related terminology and care. Their perceived preparedness and comfort in providing LGBTQ-specific care improved. Providers also conveyed interest in further education regarding hormone replacement therapy and other transgender-specific care.

**Conclusions** This preliminary study reveals a need for improvement in LGBTQ training among pediatric providers. The positive response to the curriculum points to its potential usefulness. Implementation of a formal LGBTQ curriculum within residency training can improve pediatric providers' confidence in their ability to provide care to LGBTQ patients.

## 227 INVESTIGATING PARENTAL CONCERNS AT THE FIRST WELL CHILD VISIT

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**Purpose of study** Anticipatory guidance is a valuable component of the newborn well child visit; however, little research exists describing what topics are most important for each family. This study aims to identify common parental concerns at the newborn visit and to highlight sociodemographic characteristics that predict number of concerns and common themes in order to tailor anticipatory guidance.

**Methods used** A retrospective chart review of 300 newborns examined number of parental concerns and common themes at the first well child visit. Sociodemographic and health characteristics were recorded. Nonparametric tests and chi-squared analyses identified differences between groups.

**Summary of results** 35 parental concern themes were identified; most common concerns included feeding (42%), jaundice (23%), and sleep (8%). Elevated bilirubin was associated with more questions about jaundice (OR 3.8, CI 2.2, 6.7). 26% of families expressed no concerns. The families who expressed no concerns (n=224) were similar in terms of maternal age, race, ethnicity, primary language and gestational age at birth

compared to families who expressed no concerns (n=76). First-time parents and those with private insurance were more likely to express concerns than their counterparts (82% vs. 70%, 81% vs. 66%, p<0.05, respectively).

**Conclusions** A tailored approach to anticipatory guidance is warranted. Some families may not express concerns and the reasons are likely multifactorial- experience with a prior child, socioeconomic stressors or health illiteracy. Developing a greater understanding of parental concerns fosters collaborative discussions between parents and providers.

## 228 THE FRESNO FIT PROJECT: BRINGING HEALTHY EATING INSIDE THE INNER-CITY CLASSROOM

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10.1136/jim-2018-000939.227

**Purpose of study** About a third of adolescents in Fresno are overweight or obese. Access to healthy food and health care is a challenge in the inner city. Changing eating habits in the pediatric clinic is also a challenge. Therefore, pediatric trainees arranged to bring a healthy lifestyle project 'Fresno Fit' to an inner-city classroom. The aim was to take the youth as partners to work to identify and overcome barriers to eating healthy. Community leaders also spoke to the class about living healthy lives and building their careers.

**Methods used** 20 inner-city high school students who were enrolled in an elective program (Women's Alliance) and their teacher partnered with pediatric residents. Together, they recruited community leaders (CL) who gave 1 hour mentoring sessions over healthy snacks. Also, residents taught sessions on nutrition and supported students in growing their own classroom garden. Students provided their perspective of barriers to implementing dietary changes using student-led focus groups with residents.

**Summary of results** Students participated in 24 mentoring sessions (14 with CLs and 10 with residents). Reported barriers to health included the unwillingness to try new things, and that junk food is cheap and tasty. Changes reportedly implemented by students included stopping soda, removing junk food from home and reducing portion sizes. Students felt that games and competition would improve participation.

**Conclusions** Residents, medical students, and community members can collaborate with students and schools using a 'Youth-as-Partner' approach to build knowledge on nutrition and identify barriers to nutritious eating. Further study on clinical and classroom collaboration is warranted in developing strategies to overcome barriers to maintaining a healthy diet for adolescents.

## 229 EDUCATIONAL IMPACT OF RESTRICTING RESIDENT WORK HOURS: A COMPREHENSIVE LITERATURE REVIEW

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10.1136/jim-2018-000939.228

**Purpose of study** In 2011, the residency work-hour regulations were revised to improve resident well-being and patient care

**Abstract 229 Table 1** Educational impact of pre- and post-2011 ACGME work-hour guidelines

| First Author, Year Published | Location of Study and Specialty                               | Participants   | Educational Impact   |
|------------------------------|---|--|--|
| Schumacher DJ, 2014          | US (National Survey) Pediatric Residents                      | 634, all subjects worked both pre and post 2011 guidelines                         | 9% reported improvement; 60% no change; 31% worse education impact after 2011 guidelines   |
| Nevin CR, 2014               | U Alabama, Internal Medicine Residents Focus Groups           | 34 residents who worked during both pre and post 2011 guidelines                   | 75% PGY-1% and 94% senior residents expressed negative impact on education of interns  |
| Lindeman BM, 2013            | Johns Hopkins, Survey of Surgical Residents                   | 30 residents pre 2011 guidelines and 36 residents post 2011 guidelines             | Satisfaction with quality of operative experience 27 (90%) of 30 satisfied in 2011 vs 28 (78%) out of 36 in 2012; p=0.03   |
| Wolf SJ, 2018                | US National Survey of Educators, Emergency Medicine           | 157 Program Leaders  | Average satisfaction rating of 2.58 out of 5. Majority of educators reported negative impact   |
| DeLaroché A, 2013            | US (National Survey) Neonatology Interns                      | 316 participants followed pre 2011 guidelines; 509 participants followed post 2011 | Lecture attendance (83.9% vs. 70.5%) comparing 2011 group to 2012; p   |
| Garg M, 2014                 | US (National Survey), Internal Medicine Directors             | 237 Internal Medicine Program Directors  | 60% believe education is worse after 2011 changes. 30% believe it is unchanged and 10% has improved.   |
| Vucicevic D, 2014            | Mayo Clinic Arizona, Internal Medicine Residents              | Internal Medicine Residents  | In-training exam (ITE) scores no statistical difference. Number of patients seen decreased by 16.36% (p<0.001) after 2011 guidelines.  |
| Auger KA, 2014               | Cincinnati Children's, Pediatric Residents                    | 23 Residents followed post 2011 and 26 followed pre-2011 guidelines                | Discussion of patients during morning rounds 87% for pre-2011 guidelines vs. 46% for post-2011 guidelines (p<0.05)   |
| Desai SV, 2018               | US (National Survey), Internal Medicine Residents and Faculty | 32 Program pre-2011 and 31 Programs post-2011                                      | Average scores on in-training exams were not different. Interns satisfaction with education was not different in the 2 groups but the faculty were more satisfied with the educational experience during the pre-2011 guidelines |
| Bilimoria KY, 2016           | US (National Survey), Surgery Residents                       | 2110 in pre-2011 group and 2220 in post-2011 group                                 | Dissatisfaction with overall quality of resident education was not different but pre-2011 residents were significantly less likely to leave during an operation (7.0% vs. 13.2%, p<0.001)  |
| Saadat LV, 2016              | US (National Survey), General Surgery Directors               | 59 Directors of the Standard (post-2011) and 58 Directors of Flexible (pre-2011)   | Attending educational activities: 74.1% pre-2011 vs 3.4% post-2011; p<0.001.   |

but the educational impact remains unclear. Our study aims to evaluate the impact of the Accreditation Council for Graduate Medical Education's (ACGME) 2011 duty hour regulations on residents' education.

**Methods used** We performed a literature review through Pubmed, Cochrane and Google Scholar to find scholarly articles that evaluated the educational impact of the 2011 ACGME changes. Only articles which included perspectives from residents or program leaders who worked during both time periods were included.

**Summary of results** We found 11 studies that met our inclusion criteria. The studies were survey based and compared the pre-2011 (AKA 'Flexible' in some studies) and post-2011 (AKA 'Standard' in some studies) guidelines. As a result of the 2011 more restrictive hours, majority of the studies reported a negative impact, especially on the education of more junior residents in terms number of patients cared for or time spent on patient cases as well as lecture attendance by the group. In one large study, the educators and program directors of programs were dissatisfied with the educational impact of restricted duty hours post 2011 changes but the residents were not as dissatisfied.

**Conclusions** After the implementation of ACGME's 2011 duty hour restrictions on residents, resident education has been negatively impacted. Residency programs should be allowed to have the flexibility to implement schedules that best supports the structure of their staffing and educational needs.

## Cardiovascular III

### Concurrent Session

8:00 AM

Friday, January 25, 2019

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#### MECHANICAL CIRCULATORY SUPPORT PATIENTS AWAITING HEART TRANSPLANTATION WITH POSITIVE AT1R ANTIBODIES HAVE ACCEPTABLE OUTCOME POST-HEART TRANSPLANT

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10.1136/jim-2018-000939.229

**Purpose of study** Angiotensin type 1 receptor (AT1R) antibodies (abs) are known to occur in patients (pts) with congestive heart failure and pts on mechanical circulatory support (MCS). When AT1R Abs are noted at high levels in MCS pts, MCS mortality is increased. AT1R has also been associated with the development of an inflammatory state inciting thrombosis. Furthermore, it is not clear whether these patients with MCS and AT1R antibodies are at increased risk for post-heart transplant complications such as primary graft dysfunction

Abstract 230 Table 1

| Endpoints                                       | MCS+AT1R (n=76) |                              | MCS w/o AT1R (n=92) | P-Value |
|---|-----------------|------------------------------|---------------------|---------|
|   | Binding Level   | Binding Level>40 U/ml (n=52) |                     |         |
| Incidence of PGD, %                             | 0.0% (0/24)     | 7.8% (4/52)                  | 6.5% (6/92)         | 0.396   |
| 1 Year Survival                                 | 90.5%           | 90.2%                        | 92.8%               | 0.780   |
| 1 Year Freedom from CAV                         | 89.7%           | 93.8%                        | 94.1%               | 0.858   |
| 1-Freedom from NF-MACE                          | 87.0%           | 91.9%                        | 84.0%               | 0.432   |
| 1-Freedom from Any-Treated Rejection            | 94.4%           | 85.5%                        | 81.4%               | 0.344   |
| 1 Year Freedom from Acute Cellular Rejection    | 100.0%          | 98.0%                        | 95.2%               | 0.492   |
| 1 Year Freedom from Antibody-Mediated Rejection | 100.0%          | 91.5%                        | 94.3%               | 0.387   |

(PGD) due to the recipients' highly inflamed state while undergoing heart transplant. We sought to pursue this question.

**Methods used** Between 2011 and 2016, we assessed 168 MCS pts with (n=76) and without (n=92) circulating AT1R abs who were bridged to heart transplantation. Endpoints included: moderate-severe PGD, 1 year survival, rejection, CAV (as defined by  $\geq 30\%$  stenosis via angiography), and non-fatal major adverse cardiac events (NF-MACE: MI, new CHF, PCI, ICD/pacement, or stroke). The degree of AT1R ab binding was also assessed. Binding level was stratified by  $< 40$  U/ml (low-binding, n=24) and  $\geq 40$  U/ml (high-binding, n=52).

**Summary of results** MCS pts with and without AT1R abs who were bridged to HTx had similar rates of moderate-severe PGD, survival, CAV, NF-MACE, and rejection in the first-year post-transplant. None of the MCS pts with a binding level  $< 40$  U/ml developed PGD. 4 MCS patients with a binding level  $\geq 40$  U/ml developed moderate-severe PGD (see table 1) but this did not reach statistical significance.

**Conclusions** AT1R antibodies do not appear to confer increased risk in post-heart transplant outcomes for MCS patients. In addition, higher AT1R antibody levels did not appear to be associated with PGD or other worse outcomes. Further studies need to be performed to confirm these observations.

**231 DO PATIENTS WITH PERIPHERAL ARTERIAL DISEASE UNDERGOING HEART TRANSPLANTATION HAVE ACCEPTABLE OUTCOME POST-TRANSPLANT?**

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10.1136/jim-2018-000939.230

**Purpose of study** Peripheral arterial disease (PAD) is a known risk factor for patients undergoing heart transplantation (HTx). Diabetic patients with PAD tend to have small vessel disease and hence, non-healing ulcers which would preclude their candidacy for HTx. However, there are many non-diabetics that tend to develop PAD. These patients may have proximal vessel disease that can be bypassed or undergo vessel angioplasty with stents. It has not been firmly established

Abstract 231 Table 1

| Endpoints                   | HTx Patients with PAD (n=26) | No PAD (n=322) | P-Value |
|-----------------------------|------------------------------|----------------|---------|
| 5 Year Survival             | 69.2%                        | 81.4%          | 0.220   |
| 5 Year Freedom from CAV     | 88.5%                        | 84.5%          | 0.557   |
| 5 Year Freedom from NF-MACE | 73.1%                        | 78.3%          | 0.673   |

whether patients with significant PAD can undergo HTx with acceptable outcomes.

**Methods used** Between 2010 and 2013, we assessed 26 HTx patients with established PAD. The criteria for PAD included:  $\geq 50\%$  stenosis in a major non-cardiac vessel. Patients with non-healing ulcers were excluded from the study. Outcomes included 5 year survival, 5 year freedom from cardiac allograft vasculopathy (CAV) as defined by stenosis  $\geq 30\%$  by angiography, and 5 year freedom from non-fatal major adverse cardiac events (NF-MACE: myocardial infarction, new congestive heart failure, percutaneous coronary intervention, implantable cardioverter defibrillator/pacemaker implant, stroke). These patients were compared to a contemporaneous HTx group without PAD (n=322).

**Summary of results** There was a numerical trend towards decreased survival for patients with PAD compared to the control group but this did not reach statistical significance. Patients with PAD had similar outcomes of CAV or NF-MACE development relative to the control group (see table 1).

**Conclusions** Patients with PAD can undergo HTx with acceptable outcomes. However, a larger number of patients are needed to confirm these findings.

**232 BIOPSY-NEGATIVE REJECTION LATE AFTER HEART TRANSPLANTATION: WHAT IS THE IMPACT ON LONG-TERM SURVIVAL?**

A Lam, S Dimbil, R Levine, E Passano, M Hamilton, J Kobashigawa. Cedars-Sinai Medical Center, Los Angeles, CA

10.1136/jim-2018-000939.231

**Purpose of study** Biopsy-negative rejection (BNR) is an entity where the endomyocardial biopsy (EMB) shows no findings of rejection, but there is proven cardiac dysfunction i.e. low echocardiogram ejection fraction or abnormal hemodynamics. BNR has been noted both early and late after heart transplantation (HTx). Late biopsy-proven acute rejection has been associated with worse outcome. It is not known whether late BNR is associated with long-term adverse events in terms of survival, cardiac allograft vasculopathy (CAV), and non-fatal major adverse cardiac events (NF-MACE).

**Methods used** Between 2008 and 2013, we assessed 33 HTx patients who developed BNR via the following criteria: acute cellular rejection (ACR)  $\leq 1R$ , antibody mediated rejection (AMR) 0, cardiac dysfunction (LVEF  $\leq 40\%$ , CI  $< 2.0$ ). Patients were then divided into those that developed BNR prior to 1 year post-HTx (n=23) and after 1 year post-HTx (n=10). The following 5 year subsequent endpoints were evaluated: survival, CAV as defined by stenosis  $\geq 30\%$  by angiography, and NF-MACE (myocardial infarction, new congestive heart failure, percutaneous coronary intervention, implantable cardioverter defibrillator/pacemaker implant, stroke).

Abstract 232 Table 1

| Endpoints                              | Early BNR<br>(n=23) | Late BNR<br>(n=10) | P-Value |
|--|---------------------|--------------------|---------|
| Subsequent 5 Year Survival             | 87.0%               | 50.0%              | 0.020   |
| Subsequent 5 Year Freedom from CAV     | 82.6%               | 40.0%              | <0.001  |
| Subsequent 5 Year Freedom from NF-MACE | 47.8%               | 30.0%              | 0.369   |

**Summary of results** When patients were divided into early vs late BNR, late BNR appeared to have greater impact on leading to poor outcome relative to early BNR. Late BNR was associated with significantly reduced subsequent 5 year survival and an increase in the development of angiographic CAV. The timing of BNR did not make a difference in the development of NF-MACE. (see table 1)

**Conclusions** Late BNR in HTx is associated with poor long-term outcome. The mechanism of this rejection is not clear but appears to represent a heightened immune response that is being missed on EMB. More aggressive augmentation of IMS and/or immunomodulation are indicated in patients presenting with late BNR.

### 233 CROSSING LOW LEVEL DONOR-SPECIFIC ANTIBODY AT THE TIME OF HEART TRANSPLANTATION: IS IT WORTH IT?

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10.1136/jim-2018-000939.232

**Purpose of study** End-stage heart failure patients awaiting heart transplant (HTx) often have circulating antibodies most commonly against human leukocyte antigens (HLA), termed 'sensitization.' Such antibodies present a challenge if the potential donor has corresponding HLA antigens as donor-specific antibodies (DSA) can result in hyperacute rejection after transplant. However, due to the scarcity of donor hearts, hearts with low-level DSA may be used to expand the donor pool. We reviewed our patient population to assess the long-term outcome of patients who underwent HTx while crossing low-level DSA.

**Methods used** We assessed 355 patients undergoing HTx between 2010 and 2013 at our center. There were 34 HTx patients with a low-level DSA (MFI <5000). Endpoints assessed: 1 year freedom from any-treated rejection (ATR), acute cellular rejection (ACR), antibody-mediated rejection (AMR), 5 year survival, 5 year freedom from cardiac allograft vasculopathy (CAV) defined as stenosis  $\geq 30\%$ , 5 year freedom from non-fatal major adverse cardiac events (NF-MACE: myocardial infarction, heart failure, coronary intervention, defibrillator/pacemaker, stroke). The control group (n=197) was HTx patients without DSA.

**Summary of results** The 34 HTx patients with a low-level DSA had significantly less freedom from first-year AMR. There was no difference in freedom from 1 year ATR or ACR, 5 year CAV and 5 year NF-MACE. 5 year survival was similar between the groups (see table 1).

**Conclusions** Crossing low-level DSA at the time of HTx appears to result in acceptable outcomes despite the increased risk of first-year AMR. Crossing low-level DSA in sensitized patients can expand the donor pool.

Abstract 233 Table 1

| Endpoints                                       | Low-Level<br>DSA,<br>MFI<5000<br>(n=34) | No DSA<br>Pre-HTx<br>(n=197) | P-Value |
|---|---|------------------------------|---------|
| 5 Year Survival                                 | 93.5%                                   | 81.2%                        | 0.072   |
| 5 Year Freedom from CAV                         | 87.1%                                   | 84.8%                        | 0.451   |
| 5 Year Freedom from NF-MACE                     | 87.1%                                   | 78.2%                        | 0.132   |
| 1 Year Freedom from Any-Treated Rejection       | 77.4%                                   | 85.8%                        | 0.236   |
| 1 Year Freedom from Acute Cellular Rejection    | 90.3%                                   | 91.4%                        | 0.898   |
| 1 Year Freedom from Antibody-Mediated Rejection | 83.9%                                   | 97.0%                        | 0.002   |

### 234 THE IMPACT OF COMPLEMENT-BINDING ANTIBODIES ON ADVERSE EVENTS LONG-TERM AFTER HEART TRANSPLANTATION

V Arruarena, S Dimbil, R Levine, E Passano, M Hamilton, J Kobashigawa. Cedars-Sinai Medical Center, Los Angeles, CA

10.1136/jim-2018-000939.233

**Purpose of study** Circulating antibodies after heart transplantation (HTx) place patients at risk for cardiac allograft vasculopathy (CAV) and decreased survival. Circulating antibodies cause injury by activating the complement cascade, the first step of which is binding of the antibody to C1q. The ability of an antibody to bind C1q is therefore a potential marker of cytotoxicity. The purpose of this study was to assess the impact of C1q-binding antibodies on HTx outcomes.

**Methods used** We assessed 23 HTx patients between 2012 and 2015 with C1q donor-specific antibodies (DSA) in the first-year after HTx compared to a control group without DSA (n=360). Endpoints assessed: 5 year survival, 5 year freedom from CAV (stenosis  $\geq 30\%$ ) and non-fatal major adverse cardiac events (NF-MACE: myocardial infarction, heart failure, coronary intervention, defibrillator/pacemaker, stroke). Outcomes were assessed by Class I (n=6) vs Class II (n=17) antibodies.

**Summary of results** C1q DSA in first year after HTx are associated with a lower 5 year freedom from NF-MACE. There was no association between C1q DSA and survival, nor with Class I vs Class II antibodies. (see table 1)

**Conclusions** Complement-binding DSA are associated with the subsequent development of NF-MACE. A larger number of

Abstract 234 Table 1

| Endpoints                   | Complement-Binding DSA<br>(n=23) | No DSA<br>(n=360) | P-Value |
|-----------------------------|----------------------------------|-------------------|---------|
| 5 Year Survival             | 73.9%                            | 86.7%             | 0.145   |
| 5 Year Freedom from CAV     | 95.7%                            | 86.9%             | 0.214   |
| 5 Year Freedom from NF-MACE | 47.8%                            | 79.2%             | <0.001  |

| Complement-Binding DSA (n=23) |                  |                    |         |
|-------------------------------|------------------|--------------------|---------|
| Endpoints                     | Class I Ab (n=6) | Class II Ab (n=17) | P-Value |
| 5 Year Survival               | 100.0%           | 64.7%              | 0.155   |
| 5 Year Freedom from CAV       | 100.0%           | 94.1%              | 0.552   |
| 5 Year Freedom from NF-MACE   | 50.0%            | 47.1%              | 0.473   |

patients are needed to demonstrate whether these complement-binding antibodies require treatment to improve long-term outcomes.

### 235 MEDICAL COMPLICATIONS AT MASTERS GAMES: EXAMINING THE RISK FOR SAFER EXERCISE IN MASTERS ATHLETES

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10.1136/jim-2018-000939.234

**Purpose of study** International ‘masters games’ are gaining global participation. Information pertaining to the prevalence of cardiovascular risk factors and medical complications that occur during these games are limited. This study determined the prevalence of pre-existing cardiovascular disease (CVD) and traditional risk factors and reported the incidence and type of medical complications that occurred during the Pan-American Masters Games held in Vancouver, Canada.

**Methods used** This was a retrospective, cross-sectional study. Masters athletes ( $\geq 30$  year) were offered a voluntary, self-administered questionnaire pertaining to pre-existing CVD and traditional risk factors. The survey was composed of questions from the American Heart Association 14-element recommendations. Medical incidents were evaluated and documented by the medical team utilizing a standard injury reporting form.

**Summary of results** A total of 856 (56% male, mean age  $56 \pm 11$ , range 30–101) athletes (17.1%) completed the survey. CVD was reported by 12.3% ( $n=105$ ; 53% male) athletes. Arrhythmias ( $n=41$ ; 4.8%), heart valve disease ( $n=34$ ; 4.0%), and coronary artery disease ( $n=21$ ; 2.5%) were the most commonly reported forms of CVD. At least one cardiovascular risk factor was present in 413 (48.2%) athletes. Dyslipidemia ( $n=110$ ; 12.9%) and hypertension ( $n=87$ ; 10.2%) were the most prevalent cardiovascular risk factors. A total of 247 (4.9%) complications, including four (0.1%) non-fatal cardiovascular complications, were documented in the 4999 athletes. The most prevalent types of complications were musculoskeletal ( $n=188$ ; 76.1%), dermatological ( $n=37$ ; 15.0%), and concussions ( $n=6$ ; 2.4%). Twenty competitors (0.4%) required hospital care for their complications.

**Conclusions** Masters games participants have known CVD and established risk factors. Musculoskeletal injuries were the most prevalent medical complication. There were few adverse CVD events requiring hospital care and none were fatal. On-site medical treatment and hospital transportation are crucial to providing timely medical care in the case of emergencies.

### 236 10-YEAR OUTCOMES IN HEART-KIDNEY TRANSPLANT PATIENTS

R Sharoff, S Dimbil, R Levine, E Passano, M Hamilton, J Kobashigawa. *Cedars-Sinai Medical Center, Los Angeles, CA*

10.1136/jim-2018-000939.235

**Purpose of study** Combined heart–kidney transplantation (HKTx) has been shown to have successful short-term outcomes. There are an increasing number of patients with end-stage heart failure and concomitant end-stage renal failure that require dual-organ transplantation. We sought to assess the 10 Year outcomes of HKTx patients in our single center.

Abstract 236 Table 1

| Endpoints  | HKTx (n=27)   | HTx Alone (n=496) | P-Value |
|--|---------------|-------------------|---------|
| 10 Year Survival                                 | 64.4%         | 62.4%             | 0.856   |
| 10 Year Freedom from CAV                         | 91.7%         | 75.3%             | 0.176   |
| 10-Freedom from NF-MACE                          | 69.8%         | 65.0%             | 0.758   |
| 10-Freedom from Any-Treated Rejection            | 87.7%         | 79.8%             | 0.413   |
| 10 Year Freedom from Acute Cellular Rejection    | 100.0%        | 90.0%             | 0.119   |
| 10 Year Freedom from Antibody-Mediated Rejection | 91.8%         | 91.9%             | 0.996   |
| Baseline Creatinine, Mean $\pm$ SD               | 3.5 $\pm$ 2.0 | 1.3 $\pm$ 0.6     | <0.001  |
| 5 Year Creatinine, Mean $\pm$ SD                 | 1.4 $\pm$ 0.2 | 1.6 $\pm$ 1.0     | 0.300   |
| 10 Year Creatinine, Mean $\pm$ SD                | 2.4 $\pm$ 1.6 | 2.0 $\pm$ 1.6     | 0.206   |

**Methods used** Between 1999 and 2008 we assessed 27 HKTx recipients. A control group that received only heart transplants (HTx) was included ( $n=496$ ). Endpoints of this study included renal function in terms of serum creatinine at baseline, 5 years, and 10 years post-transplant, 10 year survival, 10 year freedom from cardiac allograft vasculopathy (CAV, as defined by  $\geq 30\%$  stenosis via angiography), 10 year freedom from non-fatal major adverse cardiac events (NF-MACE: myocardial infarction, new congestive heart failure, percutaneous coronary intervention, implantable cardioverter defibrillator/pacemaker implant, stroke), and 10 year freedom from rejection.

**Summary of results** There was no significant difference in 10 year survival, freedom from CAV, NF-MACE, or rejection between the two groups. HKTx recipients had a significantly increased baseline creatinine as expected (see table 1). By 5 and 10 years post-transplant, however, there is no difference in creatinine between HKTx patients and HTx alone patients. Of note, HKTx patients improve creatinine immediately due to the kidney being transplanted, but by 10 years post-transplant, renal function begins to decline. The control population also demonstrates a steady increase in creatinine long-term due to calcineurin inhibitor immunosuppression.

**Conclusions** HKTx patients have good outcome 10 years after transplant. Renal function tends to decline long-term in both HKTx and HTx alone patients. Larger numbers are needed to confirm these findings.

### 237 IS THERE A BENEFIT OF METFORMIN AFTER HEART TRANSPLANTATION?

T Hage, S Dimbil, R Levine, E Passano, M Hamilton, J Kobashigawa. *Cedars-Sinai Medical Center, Los Angeles, CA*

10.1136/jim-2018-000939.236

**Purpose of study** Diabetes (DM2) occurs in about 30% of heart transplant (HTx) recipients, likely in part due to steroid use. Metformin, an oral anti-hypoglycemic agent, may have immunomodulatory effects and may prevent rejection and cardiac allograft vasculopathy (CAV). We assessed the impact of metformin on outcomes in HTx recipients.

**Methods used** We assessed 229 HTx patients with DM2 between 2010 and 2017. Patients were divided into groups: metformin pre-HTx ( $n=21$ ), post-HTx ( $n=22$ ), pre and post-HTx ( $n=10$ ), and not on metformin ( $n=176$ ). Metformin was

Abstract 237 Table 1

| Endpoints   | Group A:<br>DM2 on<br>Metformin<br>pre-HTx<br>(n=21) | Group B:<br>DM2 on<br>Metformin<br>post-HTx<br>(n=22) | Group C:<br>DM2 on<br>Metformin<br>pre-HTx<br>and post-<br>HTx (n=10) | Group D:<br>Control<br>Group w/o<br>Metformin<br>Use<br>(n=176) | P-Value |
|---|--|---|---|---|---------|
| 1 Year Survival                                       | 76.2%  | 95.5%   | 100.0%  | 92.0%   | 0.076*  |
| 1 Year Freedom from<br>CAV                            | 95.2%  | 90.9%   | 90.0%   | 95.5%   | 0.779   |
| 1 Year Freedom from<br>NF-MACE                        | 85.7%  | 72.7%   | 90.0%   | 83.0%   | 0.647   |
| 1 Year Freedom from<br>Any-Treated Rejection          | 76.2%  | 86.4%   | 90.0%   | 88.6%   | 0.442   |
| 1 Year Freedom from<br>Acute Cellular<br>Rejection    | 90.5%  | 100.0%  | 100.0%  | 96.0%   | 0.391   |
| 1 Year Freedom from<br>Antibody-Mediated<br>Rejection | 90.5%  | 100.0%  | 90.0%   | 93.2%   | 0.562   |

\*Pairwise analysis between Group A and Group D, p=0.038

continued for at least one-year post-HTx. Endpoints assessed: 1 year survival, 1 year freedom from CAV (>30% stenosis), 1 year freedom from non-fatal major adverse cardiac events (NF-MACE: myocardial infarction, heart failure, coronary intervention, defibrillator/pacemaker, stroke), and 1 year freedom from any-treated rejection (ATR), acute cellular rejection (ACR), and antibody-mediated rejection (AMR).

**Summary of results** There was a trend towards reduced 1 year survival in DM2 patients on metformin pre-HTx with a significant decrease in 1 year survival in the metformin pre-HTx group versus the no metformin group (see table 1). There was no significant difference in 1 year freedom from CAV, NF-MACE or rejection.

**Conclusions** The use of metformin is not associated with improved outcomes post HTx, and when given pre-HTx, may be associated with decreased survival. Further study is necessary to determine if this relationship is causal or simply association related to the risk of pre-transplant diabetes.

## Case Reports I

### Concurrent Session

8:00 AM

Friday, January 25, 2019

#### 238 EPIDEMIC DROPSY: RAPID DETERIORATION FOLLOWING RARE EXPOSURE

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10.1136/jim-2018-000939.237

**Case report** Epidemic dropsy is a life threatening condition that results from intoxication with oil or seeds contaminated with *Argemone Mexicana* (Mexican prickly poppy), which

contains sanguinarine and dehydrosanguinarine. These toxic alkaloids cause widespread capillary dilatation and increased permeability that can lead to multi-organ failure. Although Argemon-related dropsy is most commonly seen in India, this highlights a rare case in the United States.

An 8-month-old Indian male infant with a history of URI symptoms presented to the ED with a rash and bilateral lower extremity swelling. He had received two different antimicrobials for the URI and was given an herbal treatment of 'poppy seeds' sent by relatives in India. These seeds were crushed and mixed in with his food intermittently prior to admission. Vital signs on admission were only notable for tachycardia and hypertension. His physical exam showed delayed capillary refill, a diffuse, reticular blanching rash, and bilateral lower extremity edema. CBC was notable for leukocytosis, anemia, and thrombocytopenia. Additional labs showed a high reticulocyte count, a uric acid of 8.3 mg/dL and LDH of 536 U/L. Otherwise, electrolytes, liver function tests, ESR, CRP, urinalysis, INR, Coombs test, and blood cultures were all unremarkable. Respiratory viral panel resulted positive for human metapneumovirus. His abdominal ultrasound was notable for hepatomegaly. Patient was later transferred to the PICU for refractory hypertension and clinical decompensation. His echocardiogram then showed mild pulmonary artery hypertension, small bilateral pleural effusions, and ascites. He developed respiratory and cardiac failure with metabolic lactic acidosis and died on day four of hospital admission. The family provided a sample of the 'poppy seeds' which tested positive for the aforementioned toxic alkaloids.

Epidemic dropsy is extremely rare with no recent published cases in the United States. Literature from India highlights clinical findings consistent with this patient's presentation and disease progression. This tragic case presentation demonstrates that epidemic dropsy is a rare but potentially lethal condition not well known in the United States, and also stresses the importance of a thorough investigation of all home remedies or herbal supplements given to pediatric patients.

#### 239 CONGENITAL ERYTHROPOIETIC PORPHYRIA: NOVEL GENETIC MUTATION OF A RARE DISEASE

IG Rentería. UCSF Fresno, Clovis, CA

10.1136/jim-2018-000939.238

**Case report** Background: Congenital erythropoietic porphyria (CEP) is a rare autosomal recessive disease that presents in infancy. Only approximately 200 cases have been reported in the literature. It is caused by a deficiency in uroporphyrinogen III synthase (UROS) within the heme biosynthesis pathway due to a mutation in UROS gene. The predominant findings are photosensitivity and hemolytic anemia. Clinical presentations can also include red urine, photomutilation, hypertrichosis, hepatomegaly, and thrombocytopenia. Congenital erythropoietic porphyria can be confirmed by presence of excess porphyrins in erythrocytes, plasma and urine. The only known cure for CEP is bone marrow transplant reserved for children with severe cutaneous and hematologic involvement. The only effective management is prevention of skin and eye complications by avoidance of sunlight and certain indoor lighting. Current molecular genetic analysis claims to



detect >97% of previously reported mutations as well as novel mutations.

**Case presentation** HR is an ex-38 week now 2 month old female that presents to the ED for fussiness, decreased oral intake and pink urine. Patient had dark-colored urine since birth that parents described as ‘watered down coca-cola.’ Urinalysis done while she was in the NICU for phototherapy was unremarkable. Two days prior to presentation patient’s urine changed color to a bright pink. UA was again unremarkable. Further laboratory work up showed hemoglobin of 7.7 (g/dl), and a slightly elevated bilirubin of 2.8 (mg/dL). Given presentation of pink urine and anemia there was concern for CEP. Slit lamp analysis of urine showed fluorescence, which can be seen in CEP. Patient was found to have elevated urine porphyrins. Genetic testing confirmed diagnosis of CEP via a novel genetic mutation.

**Conclusion** CEP is a rare disease, yet the patient followed the natural course in her clinical presentation. However, her genetic testing showed that she is a compound heterozygote meaning two different variants in the autosomal recessive gene. Genetic testing targeted analysis of UROS gene confirmed diagnosis of CEP with compound heterozygous mutations in the UROS gene (c.<sub>26-196A</sub>>G/c.<sub>63=2T</sub>>c). Both alleles identified in her UROS gene are previously unreported.

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#### A CASE OF PARAQUAT-INDUCED RHABDOMYOLYSIS AND HEPATIC INJURY PRESENTING WITH TAKOTSUBO CARDIOMYOPATHY

S Jaka, J McFarland, E Gunz, L Moosavi, C D’Assumpcao, T Parker, F Joolhar, A Heidari, T Win. *Kern Medical-UCLA, Bakersfield, CA*

10.1136/jim-2018-000939.239

**Case report** 45 year old Hispanic female with DM, HTN, and DLD presented to the hospital with progressive upper and lower extremity weakness for 1 month. She was found to have troponins of 2.57 and worked up for NSTEMI. Coronary angiogram showed no obstructive disease and transthoracic echo (TTE) showed a left ventricular ejection fraction (LVEF) of 20%–25% with akinetic mid and distal segments and apical ballooning highly suggestive of TM. Patient was then started on guideline-directed medical therapy for non-ischemic cardiomyopathy. Critical lab values on presentation were: CK 14848, LDH 1414, ALT 748, and AST 651. An extensive infectious and rheumatologic workup returned within normal limits. EMG studies showed active myopathy, MRI brain was unremarkable, and MRI pelvis showed diffuse muscular edema bilaterally through proximal thighs. Further history from the patient elucidated that her muscle weakness began around the time she started working in a new grape field where paraquat had been sprayed one month prior. TTE repeated 6 days after admission showed recovery of LVEF to 50%–55% and no regional wall motion abnormalities coinciding with the patient regaining upper and lower extremity muscle strength, resolving CK and transaminitis. Patient was followed in clinic one week after discharge where she demonstrated complete resolution of muscle weakness.

**Discussion** Takotsubo cardiomyopathy (TM) is a syndrome of reversible left ventricular (LV) systolic dysfunction typified by

LV apical ballooning and mid and apical segment akinesis but without obstructive coronary artery disease. We presented the case of reversible TM in a patient with rhabdomyolysis and transaminitis secondary to paraquat exposure. Paraquat is a non-selective contact herbicide which can lead to severe systemic toxicity. Obtaining a detailed history including occupational and toxic exposures plays a critical role in rapid diagnosis for a reversible cause of a fatal disease. Recognition of this rare presentation is crucial as disease progression can lead to severe multi-organ failure and early discontinuation of paraquat exposure can lead to an excellent outcome, as in this case.

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#### ANTICOAGULATION CONUNDRUM: MECHANICAL MITRAL VALVE THROMBOSIS IN PREGNANT PATIENT ON ENOXAPARIN

A Sandhu, F Joolhar, K Doyle, K Tangonan, R Sidhu. *Kern Medical, Bakersfield, CA*

10.1136/jim-2018-000939.240

**Case report** Mechanical prosthetic valves for many decades have bestowed upon patient’s around the world a second chance after their native valves have been ravaged by disease or rendered non-functional by congenital anomalies. However, these miraculous interventions have their own hidden costs in the form of increased risk of thrombosis, which to a great extent is dependent as much as on the type of the valve but also its position. Furthermore, the patient’s own propensity towards thrombus formation, be it a hereditary predilection or being in an increased hypercoagulable physiological state such as pregnancy, makes the presence of these prosthetic valves an issue of even greater concern. We present here a case of a 33-year-old gravid female with a mechanical prosthetic valve at the mitral position who had been on anticoagulation with Warfarin until finding out about her pregnancy and had then abruptly stopped this medication. Subsequently patient was found to have thrombus formation on her mechanical mitral valve on transthoracic echo after presenting to the emergency department with left upper quadrant pain and elevated troponin. Patient was initiated on therapeutic dose of Enoxaparin and levels of Xa monitored every 4–6 hours to ensure therapeutic targets, after patient refused to restart Warfarin due to concerns of the risks it posed to her pregnancy. Patient was transferred to higher level of care due to being a high-risk OB pregnancy with plans to continue monitoring thrombus progression with serial transthoracic echoes. Multiple recommendations exist regarding the management of thrombus formation in patients with prosthetic valves be it bio prosthetic or mechanical, however, there are no clear cut dictum available in the literature regarding the approach to this issue, and therefore, this case serves to highlight the importance of tailoring the treatment plan in accordance with the priorities of the patient, as well as ensuring clear communication and detailed discussion regarding the risk, benefits and alternatives.

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**SEQUELAE OF RAMSAY HUNT SYNDROME: CASE REPORT AND REVIEW OF LITERATURE**

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10.1136/jim-2018-000939.241

**Introduction** Ramsay Hunt syndrome is characterized by a reactivation of *Varicella zoster virus* (VZV) resulting in damage to cranial nerves V, VII, IX, and X. Its infrequency, contagious nature, ability to mimic more benign diagnoses, and potential long-term sequelae make rapid and accurate diagnosis challenging but essential.

**Case description** Our patient is a 65-year-old, immunocompromised gentleman with COPD, MGUS, chronic anemia, and lupus nephritis who woke up 9 days prior to admission with pruritic 'bug bites' on his right ear and periauricular burning. He was evaluated by his PCP, diagnosed with bacterial otitis externa, and treated accordingly. Over the ensuing days his pain increased and included a sore throat with dysphagia.

On the day of admission he awoke to find right hemifacial paralysis. Upon admission he reported right ear pain with motor and sensation loss to his ipsilateral face. He also noted right eye pain, tinnitus, nausea, vomiting, new onset snoring, and cough. On exam there were multiple small vesicles on a background of erythema around his right ear and the right side of his scalp and face. There was erythema with white exudate of the right posterior pharynx with clear midline demarcation. He was diagnosed with Ramsay Hunt syndrome, placed on airborne precautions, and treated with antivirals and steroids. His hospital course was complicated by dysphagia, aspiration, and new onset of nocturnal oxygen desaturations.

At 3 month follow-up, he reported unimproved right hemifacial paralysis, hearing loss in the right ear, vertigo with falls, nausea, vomiting, right ear pain, right facial pain, and right eye exposure keratitis.

**Discussion** This case illustrates important teaching points regarding Ramsay Hunt syndrome. Complications from Ramsay Hunt span multiple cranial nerves and vary in severity – including hemifacial paralysis, postherpetic neuralgia, exposure keratitis, vertigo, hearing loss, obstructive sleep apnea, dysgeusia, and aspiration. Studies have shown that early diagnosis and treatment is important to avoid long term sequelae.

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**LEPTOMENINGEAL MYELOMA**

H Saab. Kern Medical, Bakersfield, CA

10.1136/jim-2018-000939.242

**Case report** Patient is a 41-year-old Hispanic female who initially presented to the ED complaining of a 1 month history of fatigue and diffuse body pain. Laboratory studies revealed anemia, hypercalcemia (13.7), and paraprotein gap. XR bone survey revealed diffuse small, punched-out lesions clinically consistent with multiple myeloma. Bone marrow biopsy performed for definitive diagnosis showed plasma cell myeloma and VDR chemotherapy was subsequently initiated.

Approximately 10 weeks later patient presented to the ED complaining of rapidly expanding 'masses' over her left eye. Physical exam was notable for additional masses in her parotid regions bilaterally, arms, and bilateral elbows consistent with plasmacytomas. Brain MRI revealed scattered enhancing lesions in the skull vault as well as nodular dural enhancing lesions likely secondary to myeloma. IV Decadron and Cytoxan were started with resolution of plasmacytomas. Patient was discharged to home however re-presented due to intractable nausea/vomiting and severe headache. Lumbar puncture revealed elevated opening pressure, lymphocytosis, and elevated CSF protein. Subsequent brain MRI revealed nonspecific, deep white matter bilateral scattered increased FLAIR and T2 signals. About 24 hours post-admission patient developed swelling, diplopia, and decreased vision in the right eye. Physical exam was significant for decreased lateral right eye movement. The diagnosis of meningeal carcinomatosis secondary to multiple myeloma was then made. Intrathecal chemotherapy with Methotrexate was initiated with significant improvement.

Although patient proved to respond to treatment temporarily, successful long-term treatment was unable to be achieved. Her neurological symptoms secondary to stage IV multiple myeloma proved to be both debilitating and progressive despite aggressive chemotherapy and ultimately resulted in death.

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**A CASE OF PRIMARY AORTIC MURAL THROMBUS IN THE SETTING OF HETEROZYGOUS PROTHROMBIN GENE MUTATION**

H Younis, R Sidhu, J Beier, E Cobos, T Win. Kern Medical – UCLA, Bakersfield, CA

10.1136/jim-2018-000939.243

**Background** Primary aortic mural thrombosis (PAMT) is a very rare presentation of prothrombin G20210A-mutation (PTGM). Presented is a case of a patient who is heterozygous for PTGM and was found to have PAMT.

**Case presentation** A 59-year-old Caucasian male with history of uncontrolled hypertension, Chronic obstructive pulmonary disease, and obstructive sleep apnea presented to the hospital with abdominal pain. He was found to have an incarcerated ventral hernia and small bowel obstruction requiring an exploratory laparotomy. His post-operative course was complicated by *Clostridium difficile* pseudomembranous colitis. He underwent colectomy with an ileostomy due to toxic megacolon. On hospital day 20, an abdominal CT-scan was done for surgical planning which incidentally showed a PAMT in the descending aorta. A transesophageal echocardiogram (TEE) confirmed a thrombus measuring 1.6 × 1.5 × 8 cm in descending aorta but did not show any intracardiac thromboembolic sources. Hypercoagulability workup was positive for heterozygous PTGM but all other hypercoagulability labs were normal. He was treated with anticoagulation using heparin bridged with warfarin. Surgical/endovascular treatment options were not considered due to the patient's complicated post-operative course. Repeat TEE after 15 days showed a persistent thrombus with slight interval reduction in size. No clinical events of thromboembolism were observed within 30 days after the diagnosis.

**Conclusion** No previous studies showed an association between PTGM and PAMT. Our case suggests that in patients with PAMT prothrombin gene mutations should be considered as a differential. It is still unclear whether systemic anticoagulation or surgical intervention is the treatment of choice in this clinical setting.

## Endocrinology and Metabolism II

### Concurrent Session

8:00 AM

Friday, January 25, 2019

#### 245 EFFECTS OF OBESITY ON INSULIN SENSITIVITY AND CARDIOMETABOLIC RISK IN ADOLESCENTS WITH TYPE 1 DIABETES

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10.1136/jim-2018-000939.244

**Purpose of study** Type 1 Diabetes (T1D) is associated with increased cardiovascular disease (CVD) risk, despite current improvements in glycemic lowering therapies. Youth with T1D have not escaped the global obesity epidemic, with nearly 40% of US children with T1D considered overweight/obese. Obesity is a major contributor to insulin resistance and CVD risk in the general population. Accordingly, we hypothesized that increased BMI would have a negative impact on insulin sensitivity and metabolic parameters associated with CVD in T1D adolescents.

**Methods used** We performed cross-sectional studies in 136 youth (mean  $\pm$ SD, ages:  $16 \pm 2.2$  years, Tanner stage:  $4.6 \pm 0.8$ ) with T1D and stratified them according to BMI%tiles: lean T1D (<85% ile) (n=82), overweight T1D (5%–85% ile) (n=28), and obese T1D (>85%ile) (n=26), and had a comparator group of obese youth with type 2 diabetes (T2D) (n=59). CVD risk factors including blood pressure, fasting lipid panel, c-reactive protein and transaminases were measured. Insulin sensitivity was assessed by glucose infusion rate (GIR) from a hyperinsulinemic-euglycemic clamp adjusted for fat-free mass (FFM) by DXA. Data between groups were compared with ANOVA.

**Summary of results** All groups had similar Tanner stage and HbA1c, and BMI between the T1D and T2D obese groups were matched. As BMI increased, GIR decreased ( $12.1 \pm 4.1$  mg/kg FFM/min in lean T1D vs.  $8.3 \pm 3.3$  in obese T1D,  $p < 0.001$ ). The GIR of the obese T1D group was similar to the T2D group ( $p = 0.475$ ). The systolic ( $124 \pm 7$  mmHg vs.  $114 \pm 12$ ,  $p < 0.001$ ) and diastolic blood pressures ( $73 \pm 4$  mmHg vs.  $67 \pm 7$ ,  $p < 0.002$ ) and c-reactive protein ( $2.3 [0.9, 3.7]$  units/Lvs.  $0.3 [0.2, 0.5]$ ,  $p = 0.002$ ) were significantly higher in the obese vs. lean T1D group, but there were no significant differences in triglycerides, ALT, AST, or HDL cholesterol.

**Conclusions** Obesity was associated with insulin resistance, elevated blood pressure and inflammation in T1D youth, emphasizing the importance of weight management to prevent CVD in T1D. Of note, and contrary to our hypothesis and in

contrast to T2D youth, not all components of the metabolic syndrome worsened as BMI increased in T1D, arguing for more research on the unique mechanism(s) of insulin resistance and cardiometabolic risk in T1D.

#### 246 RECURRENT DIABETIC KETOACIDOSIS PREDICTS MAJOR ADVERSE CARDIOVASCULAR EVENTS IN TYPE 1 DIABETES

I Fallahi, F Qeadan, MR Burge. *University of New Mexico Health Sciences Center, Albuquerque, NM*

10.1136/jim-2018-000939.245

**Purpose of study** Patients with Type 1 Diabetes (T1D) have a 2–4 fold increase in death from cardiovascular disease and are also at risk for premature death from diabetic ketoacidosis (DKA). We hypothesize that patients with more than one episode of DKA will have higher odds of a subsequent Major Adverse Cardiac Event (MACE) as compared to those with only a single episode of DKA.

**Methods used** Using a large, consolidated, relational database of Electronic Health Records, adult T1D patients with at least one episode of DKA were identified between the years 2005–2010 using ICD-9 codes. Primary outcome was the occurrence of a MACE using ICD-9/10 codes from the date of the first DKA episode through 2017, encompassing 7–12 years of follow up. Multivariable logistic regression was used to determine the odds of MACE occurrence for those with Recurrent DKA while adjusting for major covariates.

**Summary of results** Of the 6,547 T1D patients with at least one episode of DKA, 1372 had more than one episode of DKA, and 923 patients experienced a subsequent MACE. Patients experiencing Solitary DKA were older ( $42 \pm 17$  years) as compared to those with Recurrent DKA ( $35 \pm 14$  years,  $p < 0.001$ ), and a one year increase in age conferred a 6.4% higher odds of experiencing MACE (95% CI 1.06–1.07). As shown in the Data table 1, subjects with Recurrent DKA were significantly more likely to experience MACE after adjusting for age, gender, race/ethnicity, and marital status. Patients with elevated serum creatinine were more likely to experience MACE as compared to those with normal serum creatinine. Adjusting for total serum cholesterol inflated the odds of MACE among patients with Recurrent DKA (OR=2.72; 95% CI 1.74–4.24).

**Conclusions** In this study, Recurrent DKA conferred an increased risk of MACE after adjusting for age, gender, race and ethnicity, marital status, A1c, creatinine, and total cholesterol. Patients with elevated serum creatinine were more likely to experience MACE.

Abstract 246 Table 1

|                                      | OR for MACE | 95% C.I.  |
|--------------------------------------|-------------|-----------|
| Recurrent DKA vs. Solitary DKA       | 1.84        | 1.53–2.22 |
| Male vs. Female Sex                  | 1.14        | 0.98–1.33 |
| Married vs. Single                   | 1.08        | 0.88–1.32 |
| A1c $\geq$ 6.5% vs. A1c<6.5%         | 1.26        | 0.50–3.20 |
| Non-Caucasian vs. Caucasian          | 0.65        | 0.41–1.04 |
| Elevated vs. Normal Serum Creatinine | 1.47        | 1.18–1.82 |

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### SERUM COPEPTIN AND NT-PROBNP ARE ASSOCIATED WITH CENTRAL AORTIC STIFFNESS AND FLOW HEMODYNAMICS IN ADOLESCENTS WITH TYPE 1 DIABETES

IL Melena, P Bjornstad, M Schafer, U Truong, A Baumgartner, L Chung, P Wiromrat, H Kim, JE Reusch, KJ Nadeau. *University of Colorado Anschutz Medical Campus, Aurora, CO*

10.1136/jim-2018-000939.246

**Purpose of study** Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in type 1 diabetes (T1D). In recent years, N-terminal pro-brain natriuretic peptide (NT-proBNP) and highly-sensitive C-reactive protein (hsCRP) have been linked with measures of CVD. Copeptin, a stable precursor of arginine vasopressin, is increasingly recognized as an important risk factor for CVD and cardiovascular mortality in adults with T1D. While we have previously demonstrated that adolescents with T1D have impaired vascular function, little is known about the relationships between NT-proBNP, hsCRP, copeptin and impaired vascular health in youth with T1D. Accordingly, we examined the associations between NT-proBNP, hsCRP and copeptin, with MRI derived vascular stiffness and shear hemodynamics in adolescents with T1D.

**Methods used** Forty-nine pubertal adolescents with T1D (age  $17 \pm 2$  years, Tanner Stage:  $4.6 \pm 0.8$ ), from the previous EMERALD study, were assessed for copeptin, NT-proBNP and hsCRP, and aortic hemodynamics from MRI. Ultrasensitive copeptin was measured on KRYPTOR Compact Plus analyzers using the commercial sandwich immunoluminometric assays (Thermo Fisher Scientific, Waltham, MA). The ultrasensitive copeptin assay has a lower limit of detection of 0.9 pmol/L and a functional assay sensitivity of  $< 2$  pmol/L. Spearman correlations and adjusted (for Tanner Stage and HbA1c) generalized linear regressions were applied to examine the relationships.

**Summary of results** Copeptin inversely associated with both ascending aortic ( $\beta \pm SE$ :  $-4.48 \pm 1.97$ ,  $p=0.03$ ) and descending aortic relative area change ( $\beta \pm SE$ :  $-3.18 \pm 1.39$ ,  $p=0.03$ ). NT-proBNP was positively associated with descending aorta time-averaged wall shear stress ( $\beta \pm SE$ :  $0.94 \pm 0.27$ ,  $p=0.002$ ). In contrast, hsCRP did not correlate with any measure.

**Conclusions** In conclusion, serum copeptin and NT-proBNP correlated with vascular stiffness and shear hemodynamics in youth with T1D, potentially offering a non-invasive way to identify and monitor the development of CVD in the at-risk T1D population. More research is now needed on the potential causality of these biomarkers in the development and progression of CVD in T1D.

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### IMPACT OF OBESITY ON CARDIOVASCULAR FUNCTION IN ADOLESCENTS WITH TYPE 1 DIABETES

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10.1136/jim-2018-000939.247

**Purpose of study** Cardiovascular disease (CVD) is the leading cause of mortality in type 1 diabetes (T1D) and cardiovascular (CV) abnormalities are already present in normal-weight youths with T1D. Obesity is increasing in T1D, likely exacerbating CVD risk. We hypothesized that markers of CV health would worsen with increasing body mass index (BMI), and

that obese T1D adolescents would approach the CVD profile of T2D adolescents.

**Methods used** Participants of varying BMIs were taken from the RESISTANT, EMERALD, AIRS cohorts and stratified according to BMI%tiles: lean T1D ( $< 85\%$  ile,  $n=82$ ), overweight T1D ( $85\% - 95\%$  ile,  $n=28$ ), and obese T1D ( $> 95\%$  ile,  $n=26$ ), in addition to a comparator group of youths with type 2 diabetes (T2D,  $n=59$ ) of similar BMI as the obese T1D group. All participants had fasting serum cystatin C and creatinine measured to estimate glomerular filtration rate (eGFR), heart rate, systolic (SBP) and diastolic blood pressure (DBP), brachial artery distensibility (BAD) by Dynapulse and echocardiography. Participants from EMERALD also had  $VO_{2peak}$  measurements during bicycle ergometry to analyze cardiovascular fitness.

**Summary of results** Compared to the lean T1D group, the obese T1D group had significantly higher resting heart rate ( $p<0.05$ ), SBP ( $p<0.001$ ), DBP ( $p=0.003$ ), mean arterial pressure ( $p<0.001$ ) and prevalence of hypertension ( $p<0.001$ ); the obese T1D group had significantly lower  $VO_{2peak}$  ( $p<0.001$ ) and BAD ( $p=0.01$ ). The obese T1D group did not differ significantly from the T2D group; in fact, mean arterial pressure ( $p=0.047$ ) and prevalence of hypertension ( $p=0.001$ ) were higher in obese T1D, although those with T2D had a higher eGFR ( $p=0.01$ ).

**Conclusions** Obesity further worsens CV health of adolescents with T1D, creating a CV phenotype similar to youths with T2D. Therefore, in addition to glycemic control, emphasis must be placed on lifestyle counseling and weight management in the treatment of T1D.

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### NON-PHYSIOLOGICAL USE OF INSULIN IS ASSOCIATED WITH A1C INERTIA IN TYPE 2 DIABETES

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10.1136/jim-2018-000939.248

**Purpose of study** Insulin treatment of type 2 diabetes (DM) often does not achieve A1C goals. Though guidelines exist for initiating and titrating insulin, there is little to guide management with physiological insulin replacement (PIR) as a concomitant quantitative goal. We therefore examined the prevalence of non-PIR (NPIR) in primary care, and tested for possible impact on glycemic control compared with patients on predominantly-PIR (PPIR).

**Methods used** Pharmacy records were obtained for 891 insulin-using DM patients over 9 months in 2 primary care clinics. NPIR was defined as use of (a) long-acting insulin alone, dose  $> 0.5$  units/Kg.day; (b) NPH/Regular insulin in equal ( $\pm 10\%$ ) doses in the AM and PM; or (c) basal/prandial insulin in a ratio  $> 55\%:45\%$ . PPIR was insulin use that did not meet NPIR criteria. Exclusion criteria were missing data, co-management in a DM program, type 1 DM, use of U500 insulin ( $n=420$  excluded). Of the remaining 471 patients, 270 (57.5%) were potentially under-dosed (insulin dose  $< 0.5$  units/Kg/day +  $A1C > 7.5\%$ ). Since impact on A1C of NPIR could not be separated from under-dosing, this group was also excluded from further analysis. This left 113 patients with NPIR (24%) and 88 (18.7%) PPIR.

**Summary of results** At baseline, both groups were similar in age, sex, ethnicity, BMI, no. of comorbidities (all  $p > 0.18$ ). Mean ( $\pm$ SEM) duration of follow-up was  $25.5 \pm 0.7$  and  $25.6 \pm 0.83$  weeks for NPIR and PPIR, respectively (NS). Insulin dose was  $0.93 \pm 0.04$  and  $0.95 \pm 0.03$  units/Kg/day for NPIR and PPIR (NS), and no. of insulin adjustments was  $0.81 \pm 0.09$  and  $1.07 \pm 0.12$  ( $p = 0.07$ ). The primary outcome, A1C, was unchanged in NPIR,  $9.1 \pm 0.18\%$  vs.  $9.0 \pm 0.18\%$ . Baseline A1C in PPIR was  $9.4\% \pm 0.17\%$ , and  $8.7\% \pm 0.15\%$  at follow-up ( $p = 0.0001$ ). A greater decrement in A1C was seen in the PPIR group,  $0.62 \pm 0.15\%$  vs.  $0.10 \pm 0.13\%$  in NPIR ( $p = 0.009$ ).

**Conclusions** Use of NPIR was common in type 2 DM patients studied. Over 50% appeared under-dosed despite elevated A1C, and 24% were on NPIR. Improvement in A1C over 25 weeks in PPIR, but not NPIR, was clinically and statistically significant. We conclude that adhering to physiological principles of insulin replacement can counter A1C inertia and achieve better glycemic control for similar insulin dosing. We suggest that including concepts of PIR may improve management in insulin-treated type 2 DM.

### 250 THYROID STORM PRECIPITATED BY DIABETIC KETOACIDOSIS AND ALCOHOL WITHDRAWAL

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10.1136/jim-2018-000939.249

**Introduction** We report a case of thyroid storm masked by diabetic ketoacidosis (DKA) in the setting of alcohol withdrawal. The patient's clinical symptoms did not improve despite correction of his DKA and alcohol withdrawal, leading to a belated diagnosis of thyroid storm.

**Case report** A 33 year-old male with history of poorly controlled type 1 diabetes mellitus A1c 13.4% (Ref 4.4%–5.6%), chronic alcohol use disorder, and essential hypertension was found to have DKA with a blood glucose of 402 mg/dl, an anion gap of 32 (Ref 8–16), arterial pH of 7.15 (Ref 7.32–7.43), serum bicarbonate 7 mmol/L (Ref 20–30 mmol/L), positive urinary ketones, temperature  $38.5^\circ\text{C}$ , heart rate 160 bpm, and blood pressure 90/70 mmHg. Blood Ethanol Level was negative, but a urine drug screen was positive for cannabinoids. He was confused but could provide details about his condition and his home medications, and he asserted that he had been compliant with his insulin therapy. He reported drinking one pint of hard liquor daily. He had no prior history of admission for alcohol withdrawal or seizures, or of thyroid disease.

DKA protocol was initiated with a rapid improvement in blood pressure, but heart rate remained elevated in the 140 s, and he became more confused, so he was started on intravenous lorazepam for alcohol withdrawal without improvement in his heart rate or mental status. TSH was subsequently found to be less than 0.007 mIU/ml (Ref 0.36–3.74 mIU/ml), and Free T4 was elevated 3.6 ng/dl (Ref 0.7–1.6 ng/dl). The patient's Burch-Wartofsky score was 45, which is strongly suggestive of thyroid storm. Propylthiouracil, propranolol, and stress-dose glucocorticoid therapy was initiated, and the patient rapidly improved.

**Discussion and conclusions** Untreated Thyroid Storm is associated with mortality rates as high as 25%, while DKA carries a

mortality risk of approximately 5%–10%. The risk of dying when these conditions are co-morbid is not certain. Both Thyroid Storm and DKA are conditions that can be precipitated by underlying illness or stress, and while the exact sequence of events remains uncertain in this case, it seems likely that Thyroid Storm was precipitated by DKA and possible ethanol withdrawal. This case reinforces the notion that the search for an underlying cause in DKA must be exhaustive and relentless.

### 251 DEVELOPMENT OF A GESTATIONAL DIABETES EDUCATION AND AWARENESS PROGRAM: DHULIKHEL, NEPAL

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10.1136/jim-2018-000939.250

**Purpose of study** One in seven births worldwide is affected by Gestational Diabetes Mellitus (GDM) and it is becoming increasingly detrimental in developing countries. Recent epidemiological studies in Nepal indicate that the national prevalence of GDM was 6.6%, and 4.68% in patients seen at Dhulikhel Hospital (DH), both of which are steadily rising. Currently, no focused GDM education exists for patients at DH and care providers are not confident in patient understanding of the disease. As GDM is associated with adverse effects on both mother and child, it is necessary to design and implement curriculum which will improve understanding and promote adoption of effective management strategies.

**Methods used** This intervention fostered multi-departmental collaboration to create curriculum for weekly GDM education sessions at DH, a diet infographic, and a patient-specific brochure detailing GDM mechanism, recommended diet and exercise habits, and medication regimen. Initially, a community assessment was conducted to identify local strengths, specific needs, and best practices for information dissemination. Using this knowledge, educational materials were drafted, edited, then translated into Nepali. The inaugural education session was conducted in the OB/GYN department of DH, facilitated by representatives from each department involved in material creation. Patient understanding was assessed before and after the session using surveys, measured by verbal response and hand raising.

**Summary of results** Eight participants, six physiotherapy students, and representatives from the Nutrition, Community Programs, OB/GYN, Pharmacy, and Physiotherapy Departments attended the first session. In subsequent evaluation of patient comprehension, understanding of the danger of high blood sugar during pregnancy improved by 60.7% and 100% of participants recognized medication is unnecessary to control GDM. Moreover, 2/3 care providers surveyed stated they were 100% likely to use the printed materials and refer their patients to attend future sessions.

**Conclusions** The education methods augmented existing diabetes education efforts at DH. Post-session evaluations of care providers and patients revealed the course was necessary and appreciated. Future directions include training OB/GYN nurses and outreach center staff to conduct the sessions and distribution of printed materials at outreach centers.

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**METFORMIN ASSOCIATED SEVERE LACTIC ACIDOSIS WITHOUT PRE-EXISTING RENAL DISEASE**<sup>1,2</sup>K Abad, <sup>3</sup>C Kien. <sup>1</sup>University of New Mexico, Albuquerque, NM; <sup>2</sup>NMVAHCS, Albuquerque, NM; <sup>3</sup>Arizona State University, Tempe, AZ

10.1136/jim-2018-000939.251

**Case report** Metabolic acidosis is a common disorder in those admitted to the ICU. Identifying the cause of acidosis is critical for management. We present a case of acute renal failure with lactic acidosis in a patient without a history of renal disease taking metformin. A 69 year old man with type 2 DM, coronary artery disease and hypertension was admitted with a history of decreased urine output after two weeks of intermittent nausea and vomiting. During this time the patient continued to take in limited fluids and medication, including lisinopril 10 mg a day and metformin 850 mg three times a day. On initial examination, he was afebrile, hypertensive and in no distress. Bowel sounds were present with minimal abdominal tenderness. Lab tests revealed a WBC of  $10.9 \times 10^3$  per  $\text{mm}^3$  with 83% neutrophils, a serum creatinine (Cr) of 12.2 mg/dl, carbon dioxide of 8 mmol/L, potassium of 6.2 mmol/L and an anion gap of 25 mmol/L. Arterial blood gases showed a pH of 7.13,  $\text{pO}_2$  of 78 mm Hg and a  $\text{pCO}_2$  of 21 mm Hg. Abdominal/pelvic CT was unremarkable. The patient had normal renal function (Cr 0.97 mmol/L) three weeks prior. Broad spectrum antibiotics and sodium bicarbonate were administered. A 4 hour hemodialysis was performed. Five hours post dialysis arterial pH was 7.14 and serum lactic acid 18.9 mmol/L. An 8 hour hemodialysis was initiated resulting in 12 hours of dialysis during the first hospital day. Post second dialysis, serum lactic acid was 2.2 mmol/L and continued to decrease. After the prolonged dialysis, the patient improved significantly. Blood cultures were negative. He was discharged on hospital day 12 with the diagnosis of metformin associated lactic acidosis in the setting of acute tubular necrosis from gastrointestinal fluid loss. Two months later the Cr was 1.13 mmol/L. Severe lactic acidosis from metformin is rare. Metformin has a large volume of distribution and accumulates in erythrocytes and intestinal cells resulting in less efficient removal with dialysis and rebound lactic acidosis. Prolonged dialysis may be necessary for metformin lactic acidosis to improve outcome. Patients receiving metformin should be counseled to stop metformin and seek medical care in the setting of illnesses causing volume depletion

## Gastroenterology

## Concurrent Session

8:00 AM

Friday, January 25, 2019

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**USE OF NON-INVASIVE MARKERS AND FIBROSCAN® TO DETERMINE SEVERITY OF LIVER DISEASE IN PATIENTS WITH CHRONIC HEPATITIS B**

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10.1136/jim-2018-000939.252

**Purpose of study** Guidelines for surveillance and treatment of chronic hepatitis B (CHB) are based on a four-phase

classification system with the aim of preventing end-stage liver disease. However, providers lack guidelines for patients not included in the predefined phases (referred to as 'indeterminate' in this study) which results in unnecessary liver biopsies. FibroScan® (FS) is a novel way to measure the amount of liver fibrosis with high sensitivity (Sn) and specificity (Sp) for lack of significant scarring. This study examines the correlation between noninvasive serologic markers for fibrosis with FS, establishes a FS cutoff score below which significant fibrosis is unlikely and proposes a clinical algorithm to assess patients in the indeterminate phase.

**Methods used** Data from the Alaska Native Tribal Health Consortium CHB cohort were used for this study. Inclusion criteria: 1) patients with CHB in the indeterminate phase, 2) with FS data, 3) not currently being treated for CHB. Variables include FIB4, APRI, NAFLD fibrosis score, ultrasound (U/S), FS, and liver biopsy. The Sn, Sp, positive predictive value (PPV), negative predictive value (NPV) and misclassification (Mis) were calculated comparing multiple cutoffs of FS and established cutoffs of FIB4, APRI, NAFLD, and U/S. Those comparisons with Sp >80%, NPV or PPV >80% and Mis <20% were considered good approximations of one another. These results were used to create a clinical algorithm.

**Summary of results** Eighty-eight patients met the inclusion criteria, 9 had liver biopsy results (considered the gold standard measurement of fibrosis), all with no or mild fibrosis. A cutoff FS of >8 kPa most closely approximated the other non-invasive measures of fibrosis and this value was used as the cut-off in comparisons. Sixty-three (72%) patients had both FIB4 and FS with Sp of 91%, PPV of 50%, NPV of 81% and Mis of 16%. Fifty-eight (66%) had both FIB4 and U/S with Sp of 100%, PPV of 100%, NPV of 25% and Mis of 64%. Twenty-nine (30%) had both a NAFLD score and FS with Sp 96%, PPV of 75%, NPV of 92% and Mis of 10%. Using the clinical algorithm, the fibrosis level can be estimated in 22 patients, avoiding liver biopsy.

**Conclusions** A combination of non-invasive tests can be used to evaluate liver fibrosis in patients in the indeterminate phase and limit the need for liver biopsy.

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**PERIAORTIC FAT: A POTENTIAL BIOMARKER FOR METABOLIC DISEASE IN OVERWEIGHT CHILDREN**<sup>1</sup>S Santos, <sup>2</sup>T Armstrong, <sup>2</sup>S Ghahremani, <sup>3</sup>KV Ly, <sup>2</sup>HH Wu, <sup>4</sup>KL Calkins. <sup>1</sup>David Geffen School of Medicine, Los Angeles, CA; <sup>2</sup>UCLA, Los Angeles, CA; <sup>3</sup>Midwestern University, Glendale, AZ; <sup>4</sup>UCLA, Los Angeles, CA

10.1136/jim-2018-000939.253

**Purpose of study** The function of adipose tissue is determined by its location and type (white vs. brown fat). In adults, periaortic fat and white fat promote metabolic disease. However, little is known about periaortic fat in children. Using a novel research tool, free-breathing magnetic resonance imaging (MRI), this study aimed to: 1. measure periaortic fat volume and content and 2. investigate correlations between periaortic fat, hepatic fat, and clinical characteristics in children.

**Methods used** Healthy and overweight (body mass index  $\geq 85^{\text{th}}$  percentile) children with non-alcoholic fatty liver disease (NAFLD) were eligible. Periaortic adipose tissue volume and proton-density fat fraction (PDFF), a biomarker for adiposity

content, were measured near the abdominal aorta, along with hepatic PDFF, a biomarker for hepatic steatosis, using free-breathing MRI.

**Summary of results** Healthy children (n=9, median age 10.9 [IQR 9.7–13.0]) and overweight children (n=9, age 15.2 [12.7–16.0]) completed the study (p=0.03). In the overweight group, 56% had insulin resistance and their median [IQR] body mass index was greater than the healthy group (33.2 kg/m<sup>2</sup> [29.0–36.1] vs. 17.6 kg/m<sup>2</sup> [16.1–18.4], p<0.0005). In comparison to healthy children, periaortic adipose tissue volume was greater in overweight children (5.3 cm<sup>3</sup> [4.8–6.9] vs. 3.2 cm<sup>3</sup> [2.9–3.7], p<0.0003). Likewise, periaortic adipose tissue PDFF (53% [50–55] vs. 31% [29–32], p<0.0001) and hepatic PDFF (18.1% [13.7–26.0] vs. 2.4% [2.2–2.6], p<0.0005) were significantly greater in overweight vs. healthy children. Adipose tissue volume and PDFF correlated with body mass index z-score (r=0.84 and r=0.89, p<0.001 each) and hepatic PDFF (r=0.69 and r=0.62, p<0.01 each). In contrast, periaortic adipose tissue volume was negatively correlated with serum high density lipoprotein (r=-0.83, p<0.01). **Conclusions** In this study, overweight children with NAFLD had increased periaortic fat volume and PDFF and hepatic PDFF compared to their healthy counterparts. A higher fat content in the periaortic region (*i.e.*, PDFF) may indicate increased susceptibility to metabolic diseases, including dyslipidemia and NAFLD.

#### 255 SHORT & LONG TERM SURGICAL AND BOWEL OUTCOMES OF ANTEGRADE CONTINENCE ENEMAS: SINGLE CENTER EXPERIENCE

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10.1136/jim-2018-000939.254

**Purpose of study** Fecal incontinence has a significant impact on quality of life of children with defecation disorders. Treatment ranges from medications that modify stool consistency/transit to antegrade continence enema (ACE) that facilitates rectosigmoid emptying. Surgical creation of ACE via catheterizable channel or cecostomy tube allow for predictable bowel movements, social continence, and independence. Despite advances, surgical and bowel outcomes vary between centers. We aim to characterize short and long term surgical and bowel management outcomes of children with defecation disorders who had surgical creation of ACE at Seattle Children's Hospital (SCH). **Methods used** Retrospective analysis of 171 children treated with ACE at SCH between 1997–2017. Short (≤90 days) and long (>90 days) term surgical complications and bowel management outcomes were noted. Bowel outcomes were assessed based on frequency of fecal incontinence, predictability of stool, and compliance.

**Summary of results** 171 children (47% female, 3–21 years) underwent an ACE with mean follow up of 70 months [range, 1–178]. Diagnoses include myelodysplasia (59%), anorectal malformation (19%), functional intractable constipation/fecal incontinence (14%), sacral agenesis (4%), and other (4%). Short term surgical complications were seen in 45% (infection, leaking, stoma closure), 17% of which had re-operation. Long term surgical complications (stenosis, leaking, granulation) were seen in 56%, 20% of which had surgical revision. Successful bowel management

at short term was seen in 75% and 12% of those with unsuccessful outcomes were non-compliant. At last follow up, 62% had successful bowel management and 30% were non-compliant.

**Conclusions** ACE offers successful bowel management in 75% at short and 62% at long term follow up. Non-compliance accounted for 50% (short-term) and 80% (long-term) of ACE failure. Diligent follow up and patient education should be implemented to improve compliance. Surgical complications were seen in 45% at short and 56% at long term follow up, majority requiring surgical intervention. Multidisciplinary surgical and medical care models are critical in the care of children with an ACE.

#### 256 OUTCOME OF GASTROSTOMY TUBE IN NEONATES AND INFANTS: CAN GASTROSTOMY TUBE BE AVOIDED? A PILOT STUDY

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10.1136/jim-2018-000939.255

**Purpose of study** Premature babies often have morbidities requiring feedings via nasogastric (NG) or gastrostomy (G) tube. NG tube is preferred for short-term and gastrostomy tube (GT) for long-term feeding assistance. However, it is not always possible to predict how long a feeding tube may be needed. We reviewed charts of NICU patients with GT placement regarding duration of GT use to identify patients who could have been discharged with NG tube and avoided surgery.

**Methods used** Retrospective chart review of patients with GT in NICU over 2 years and follow up until GT removal or for >1 year regarding GT use. Clinical parameters were compared between patients requiring GT for <2 months vs. >2 months. ANOVA linear regression statistical analysis was used to identify parameters that can predict short-term GT need.

**Summary of results** Of 66 patients, 4 were excluded (lost to follow up/death). GT was used for <2 months in 18 patients and for >2 months in 44 patients (see table 1). Three models were used in ANOVA linear regression statistical analysis. Model 1 factored in effects of birth weight, percent PO intake at time of GT placement, gestational age, and sex. Birth weight, percent PO intake, and gestational age were significant (p<0.05) for differences between patients with GT use <2 months vs. >2 months. Model 2 added age at GT placement. Model 3 added the effect of comorbidities. Using Models 2 and 3 yielded a significant difference only in birth weight.

**Conclusions** Gestational age, birth weight, and percent PO intake at GT placement were significantly higher in patients

Abstract 256 Table 1

|                             | GT (n=18) | GT>2 months (n=44) | ANOVA (p<0.05) |
|-----------------------------|-----------|--------------------|----------------|
| Gestational age (weeks)     | 34        | 33                 | significant    |
| Male (%)                    | 9 (50%)   | 23 (52%)           | ns             |
| Birth weight (g)            | 2337      | 2101               | significant    |
| Age at GT placement (days)  | 68        | 81                 | ns             |
| % PO intake at GT placement | 26.6      | 22.5               | significant    |

using GT for <2 months vs. >2 months. We are continuing this study to determine which clinical parameters may be important in deciding NG vs. G tube placement in NICU babies to minimize risks and optimize outcomes.

[Additional data collection in progress.]

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#### SIMETHICONE PRETREATMENT WITH GATORADE-POLYETHYLENE GLYCOL 3350-BISACODYL IN AN EFFORT TO IMPROVE BOWEL WALL VISUALIZATION

M Rishi, N Manasewitsch, M Svendsen, J Kaur, M Ulanja, E Osgaard. *University of Nevada Reno School of Medicine, Reno, NV*

10.1136/jim-2018-000939.256

**Purpose of study** To compare the efficacy of adding simethicone to Gatorade-Polyethylene Glycol (PEG) 3350-Bisacodyl bowel prep against standard bowel prep in an effort to reduce intraluminal bubbles and foam during standard colonoscopy. Current colonoscopy preparation includes the use of a nonabsorbable electrolyte solution. However, significant intraluminal foam and bubbles are often noted during procedures which can lead to missing small lesions or polyps and requires the use of simethicone infused saline lavage. Prior studies have examined the use of simethicone in conjunction with ascorbic acid with Golytely and simethicone with PEG solution and fleet enema.

**Methods used** A randomized, double-blind, controlled, clinical trial was performed. 250 participants meeting standard colonoscopy inclusion criteria were enrolled and randomized into a placebo treatment or treatment with 200 mL liquid simethicone added to the bowel prep. The Boston Bowel Prep scale was completed at the time of procedure, number of intraluminal bubbles polyps and masses detected, and procedure time and patient reported side effects were noted. Intraluminal bubbles were graded on a I-IV scale. Grade I was >90% of the mucosa able to be seen, and no irrigation was required. Grade IV was when <50% of the mucosa was free of foam bubbles, and irrigation was required.

**Summary of results** 168 participants completed the study where 84 were assigned to the simethicone group and 84 to the placebo group. There was a significant improvement of Bubbles grade in the simethicone treatment arm compared to placebo ( $p < 0.001$ ).  $1.51 \pm 0.26$  polyps per colonoscopy were noted for the simethicone group while  $1.15 \pm 0.15$  polyps per colonoscopy were noted for the control group; however, this was not significant ( $p = 0.2438$ ).

**Conclusions** Simethicone pretreatment with Gatorade-PEG 3350-bisacodyl bowel prep significantly reduced the number of bubbles and had a better intraluminal bubbles score when compared to the control group. However, there was no significant difference in the number of polyps recorded. This may indicate that better bubbles scores do not necessarily impede the detection of intraluminal polyps during standard colonoscopy.

## Genetics I

### Concurrent Session

8:00 AM

Friday, January 25, 2019

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#### DEVELOPING A MOUSE MODEL FOR HYPERTRIGLYCERIDEMIA ASSOCIATED WITH LMF-1 DEFICIENCY

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10.1136/jim-2018-000939.257

**Purpose of study** Cardiovascular disease (CV) is the leading cause of death worldwide. Elevated triglycerides (TG) levels are a risk factor for CV. TG levels in the blood are regulated by vascular lipases such as lipoprotein lipase (LPL) that hydrolyzes TG. LPL deficiency leads to increased levels of TG in the blood stream referred to as Hypertriglyceridemia (HTG). Lipase Maturation Factor 1 (*LMF1*) is an ER chaperone involved with proper folding and activation of lipases such as LPL. In absence of functional *LMF1*, lipases remain inactive resulting in HTG in humans with mutations in *LMF1*. While *LMF1* deficiency is not lethal in humans, *LMF1* deficient mice offspring die 1–2 days after birth likely due to HTG and circulatory problems by ingestion of high fat in the mother's milk. The purpose of this study is to develop a conditional *LMF1*-deficient mouse model to circumvent the lethality associated with constitutive *LMF1* deficiency. Successful generation of a viable *LMF1*-deficient mouse model will allow the development of gene therapy approaches in future studies.

**Methods used** We utilized the lox/cre system to generate mice with conditional *LMF1* deficiency. Mice with loxP sites flanking exon 1 of the *LMF1* gene (floxed) were crossed with transgenic mice carrying a tamoxifen-inducible Cre transgene driven by ubiquitously expressed ubiquitin C promoter (UBC-Cre). Homozygous floxed/floxed; UBC-Cre mice (*LMF1*-KO) were injected with tamoxifen after weaning and *LMF1* expression in metabolic organs was analyzed by quantitative RT-PCR. Mice were metabolically characterized through measurements of body weight, adiposity and plasma lipid levels.

**Summary of results** Activation of Cre recombinase in *LMF1*-KO mice resulted in >90% reduction in *LMF1* expression. *LMF1*-KO mice were viable and exhibited normal gross morphology, but markedly elevated plasma TG and cholesterol levels.

**Conclusions** *LMF1*-KO mice generated in our study recapitulates the hyperlipidemia phenotype associated with *LMF1* deficiency in human subjects. Characterization of these mice will allow us to investigate the metabolic role of *LMF1* in different tissues. Furthermore, *LMF1*-KO mice will facilitate the development of *LMF1* replacement gene therapy approaches in HTG associated with *LMF1* deficiency.



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**BROOKE-SPIEGLER SYNDROME AND MOLECULAR HITS IN CYLD TUMORS**AR Aycinena, DT Belefond, J Van Ziffle, J Shieh. *UCSF, San Francisco, CA*

10.1136/jim-2018-000939.258

**Purpose of study** BSS or CYLD cutaneous syndrome (CCS) is characterized by cylindromas, trichoepitheliomas, and spiradenomas that form typically in the head/neck region. Tumors can be disfiguring, with up to 1 in 4 individuals requiring complete surgical removal of the scalp. There is a risk for parotid basal cell adenomas as well as malignancy. It is unclear what fuels tumor growth (e.g. UV exposure) and why tumors are limited to specific body areas. We hypothesize that tumor growth, which is associated with second hits in *CYLD*, may also be accompanied by additional changes in tumor suppressors or oncogenes. There are no current management guidelines for patients. Here we describe a new case of CCS with a novel mutation and a review of all reported CCS cases. We discuss potential management strategies and monitoring for malignancy.

**Methods used** Capture-based NGS was performed on 510 cancer-related genes, total sequence footprint of 2.8 Mb from blood/excised tumor. We performed a review of all published *CYLD* mutations and molecular results. Mass locations were characterized and variants were classified by function.

**Summary of results** We found 89 different pathogenic variants in the literature. These suggest LoF as a mechanism. We describe a Hispanic woman with characteristic facial masses, a family history of lesions, and two children at risk for CCS. We identified a novel frameshift variant, *CYLD* c.1759dupA p. M587fs (in 49% of 874 reads). Tumor cells showed 95% mutation, implicating tumor LOH. Interestingly, of the 500 additional cancer genes tested, no significant variants were detected in tumor. We did find rare reports of tumor in areas that are not sun exposed, e.g. lungs.

**Conclusions** We noted a majority of families with CCS in the literature are European. We report a novel *CYLD* variant that may not have previously been described due to under-ascertainment of Hispanic individuals. We verify that LOH is an important mechanism of tumorigenesis in CCS (in 65%). We did not find somatic alterations in common cancer genes, suggesting sequencing may be needed on parotid/malignant tumors. A broader or epigenetic assessment may also be important. A clinical trial with a kinase inhibitor is in progress for CCS. Clinical management should include monitoring for transformation. It is unclear if ultrasound of the parotid glands should be considered.

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**22Q11.2 DELETION SYNDROME- A LOOK AT THE FINDINGS IN CONFIRMED CASES FROM A DIVERSE GROUP OF CHILDREN**B Gangaram, A Slavotinek, O Klein, A Wiita. *UCSF, San Francisco, CA*

10.1136/jim-2018-000939.259

**Purpose of study** Analyze the records of children with new 22q11.2 deletion syndrome diagnosis for:

- Phenotypic differences in children of underrepresented minority groups
- Genotype-phenotype correlations
- Factors contributing to early diagnosis

- Clinical utility of a current evaluation strategy after diagnosis.

**Methods used** All patients with a chromosome 22q11.2 deletion diagnosed by Microarray at the UCSF Cytogenetics between Oct. 2014 and Dec. 2017 were identified. Their medical records were reviewed. Exclusion criteria were age greater than 18 years and previous 22q11 del diagnosis. 26 children met criteria and were included.

**Summary of results** There was an equal male: female distribution among our patients and 65% were from Hispanic or other minority ethnic groups. A bimodal peak in age distribution was noted: early diagnosis (below 2 months; 46%) and school age diagnosis (4–12 years; 34%). Of those in the first category, an abnormal newborn screen for severe combined immunodeficiency (SCID) was present in most (58%); Microarray testing for these cases led to the diagnosis. In the second category, only 1/3 had classically described facial dysmorphisms. Speech delay (expressive) was present in all; short stature (88%) and hyper nasal speech (75%) were found in most. None of these had hypocalcemia or major cardiac defects. Renal ultrasound was abnormal in only one child and brain ultrasounds were all normal. Most patients had typical deletions but 15% had small deletions. All of the latter were found in children from minority background. Very few parents of probands underwent testing.

**Conclusions** Increased recognition that a positive SCID screen can be a surrogate marker for lymphocytopenia in newborns with 22q11.2 deletions followed by chromosomal microarray testing could increase early diagnosis rate. Previous studies showed that classically described facial features may not be present in children of non-European ethnicities. This study suggests that the combination of short stature, hypernasal speech and expressive speech delay should increase clinical suspicion for 22q11.2 deletion syndrome in children of minority background, even when facial features are absent. Renal and head ultrasound as part of the workup of newly diagnosed patients with 22q11.2 appear to have a low yield in our patients and may not be cost effective.

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**SOLVING THE PUZZLE OF LOW PENETRANCE IN A FAMILY WITH A PROXIMAL 15Q11.2 (BP1-BP2) MICRODELETION**S Ramanathan, RD Clark. *Loma Linda University School of Medicine, Loma Linda, CA*

10.1136/jim-2018-000939.260

**Case report** A proximal microdeletion of 15q11.2, affecting the non-imprinted region between breakpoints 1 and 2 (BP1, BP2) in the Prader-Willi/Angelman region, is found in about 1% of genetics patients who undergo microarray for cognitive, psychiatric or behavior problems. The deletion is often inherited from a normal or mildly affected parent. The estimated penetrance is 10%. Our patient, a 9 year old female had a 512 kilobase deletion at 15q11.2 (del15q11.2), between BP1 and BP2, that included 4 genes: *NIPA1*, *NIPA2*, *CYFIP1* and *TUBGCP5*. She had speech delay, attention deficient hyperactivity disorder (ADHD) and intellectual disability. She did not meet criteria for autism spectrum disorder (ASD) although she had repetitive speech, lack of imaginative play and gaze avoidance. Parental testing was recommended. At age 13, she was referred to Genetics again for absence seizures. At that time, FISH confirmed that the deletion was maternally inherited. Sequencing *NIPA1*, *NIPA2*, *CYFIP1* and *TUBGCP5* detected a

'homozygous' frameshift variant in *NIPA2*, c.525\_528del (p. Asn177Phefs\*5), which was also detected in her father as a heterozygous change. The family history was negative for seizures although the mother had mild learning problems. Two neurotypical brothers have not been tested. The del15q11.2 (BP1-BP2), which varies between 253 kb and 1.5 Mb, has been reported as a susceptibility factor for a range of developmental and neurological findings, including developmental and speech delay, behavior problems, ADHD, ASD and intellectual disability. Additional modifiers that influence the clinical presentation such as other CNVs acting in an additive fashion or in an epistatic manner as part of the same pathway or gene network may also explain the variable phenotype associated with this deletion. *NIPA2* encodes a ubiquitously expressed Mg<sup>2+</sup> transporter. Heterozygous *NIPA2* variants have been implicated in childhood absence epilepsy in the Han Chinese. We propose that two hits, a microdeletion and a frameshift variant, that both affected *NIPA2* in our patient, caused her clinical features. Familial studies are pending in her unaffected siblings. We recommend the strategy of sequencing the second copy of deleted alleles to refine their pathogenicity and recurrence risks.

#### 262 TWO LARGE MULTI-GENERATIONAL FAMILIES WITH *SMAD3*-RELATED LOEYS-DIETZ SYNDROME

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**Case report** Loeyes-Dietz (LDS) is a well-known syndrome with an increased risk for arterial tortuosity, aortic aneurysm and other multisystem findings. Pathogenic variants in six loci cause LDS, include *TGFBR1*, *TGFBR2*, and *SMAD3*. *SMAD3*-related disease is called the 'aneurysms-osteoarthritis' subtype due to the prominent joint phenotype seen in the initial families. We report two large multi-generational families that expand our understanding of *SMAD3* disease.

Family 1 is a 6 generation Sicilian/Italian family ascertained by the University of Washington in a male with aortic dissection at age 40. In 2013 a variant in *SMAD3* [c.269G>A (p. Arg90His)] was identified and subsequently found in his 50 year old brother following a fatal dissection and in 4 additional affected family members. Aortic aneurysm has been reported in at least 7 family members and dissection with death occurred in one with an aortic root diameter of 3.14 cm. Not all affected individuals have had osteoarthritis while hypertelorism was noted in most examined individuals carrying this variant.

Family 2 is a 5 generation Japanese family ascertained following aortic dissection in a 22 year old male, who had a first cousin diagnosed with an aortic aneurysm at age 38. A variant in *SMAD3* [c.990dupC (p.Val331Argfs\*31)] has been identified in at least 6 family members with aortic aneurysm/dissection, with another 6 obligate affected or mutation-positive individuals without known cardiovascular concerns, including a great aunt who passed away at age 95. Osteoarthritis has not been reported in any of these individuals, while all of the family members evaluated in our clinic had hypertelorism.

Recent literature suggests that LDS caused by *SMAD3* may be as common as that caused by *TGFBR1* and *TGFBR2*. Osteoarthritis may not always be a distinguishing feature of the *SMAD3* subtype of LDS and additional clinical features overlap those of other LDS syndromes. Identification of families with *SMAD3* pathogenic variants should prompt early imaging, and our experience suggests that pharmacologic and surgical intervention may be indicated at an earlier age than in any of the other aortopathies.

#### 263 CLINPHEN EXTRACTS AND PRIORITIZES PHENOTYPES FROM MEDICAL RECORDS TO ACCELERATE GENOMIC DIAGNOSIS

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**Purpose of study** Genetic diseases affect an estimated 7 million births per year worldwide. Diagnosis often requires curation of hundreds of genetic variants per case. Gene-ranking tools shorten this process by matching variant-containing genes to disease phenotypes. These tools require patient phenotypes be manually encoded from clinical documents, a slow and imprecise process. With surging demand for clinical sequencing and periodic reanalysis of unsolved cases, a fast alternative to manual phenotype coding is needed.

**Methods used** We developed ClinPhen, an efficient and highly accurate tool that extracts and prioritizes HPO terms from health records. ClinPhen was tested against existing phenotype prioritization tools (cTAKES and MetaMap) and against term extraction by experienced practitioners, using records from four institutions. The effect of automated HPO term extraction on gene-ranking was also measured with diagnosed cases. **Summary of results** ClinPhen showed a 20x speedup over existing tools, with a higher precision and sensitivity. Its prioritization algorithm improved the performance of a gene-ranking tool (Phrank), bringing the causative gene to within the top 15 ranked genes, comparable to performance with manually-extracted terms. This was further improved by phenotype filtering.

**Conclusions** Compared to manual phenotype coding, ClinPhen potentially saves hours per case in diagnosis. ClinPhen can substantially contribute to greater efficiency of the molecular diagnostic pipeline. We foresee that ClinPhen may also prove useful in monitoring patient records for new findings relevant to their diagnosis.

#### 264 NEONATAL GENOMIC SEQUENCING HIGHLIGHTS UNCOMMON PRESENTATIONS OF COMMON PATTERNS OF MALFORMATION PRIOR TO CLINICAL RECOGNITION

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**Case report** In some patterns of malformation the cardinal features evolve over time making diagnosis in infancy problematic. Applying broad genomic testing in infants has the potential to diagnose patterns of malformation before the cardinal features manifest. We report 2 infants who were diagnosed with common syndromes by rapid whole genome sequencing (rWGS). This report highlights uncommon neonatal presentations of the pattern of malformation which had not yet manifest clinically.

Neonates with unexplained disease were referred by Rady Children's Hospital neonatologists to the IRB-approved RCI GM Biorepository Protocol for rWGS. Variants were classified by ACMG guidelines with supporting evidence from available literature. Pathogenic variants or likely pathogenic variants were confirmed by orthogonal testing.

A term male presented with hyperinsulinemic hypoglycemia. Trio rWGS identified a known pathogenic *de novo* heterozygous variant in *NSD1* (c.5431C>T, p.Arg1811Ter). He had normal growth and no other physical features to suggest Sotos syndrome (MIM #117550). Neonatal hyperinsulinemic hypoglycemia has been previously described as an under-recognized feature of Sotos syndrome.

A term female presented at 8 days of life with seizures. Trio rWGS identified the recurrent heterozygous variant in *FGFR3* (c.749C>G, p.Pro250Arg) that causes Muenke syndrome (MIM #602849). The variant was inherited from a mother who had craniosynostosis that was previously thought to be isolated. Neonatal seizures were reported in children who were later diagnosed with Muenke syndrome after they developed craniosynostosis. As a result of early diagnosis by rWGS, surveillance for craniosynostosis and hearing loss was initiated.

In both cases gene panel testing based on presenting features would have missed the diagnosis. Longitudinal follow-up will provide insight into the penetrance of cardinal features and inform the early natural history of these common patterns of malformation. A Medi-Cal project implementing rWGS in other tertiary neonatal intensive care units is underway and may result in early ascertainment of other common patterns of malformation.

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#### CLINICAL WHOLE GENOME SEQUENCING: THE SALVATION FOR DIAGNOSTIC ODYSSEYS?

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10.1136/jim-2018-000939.264

**Purpose of study** We sought to evaluate clinical utility of Whole Genome Sequencing in ending 'Diagnostic Odysseys'. As cost of whole genome sequencing (WGS) is decreasing rapidly, a number of genetic testing CLIA/CAP certified laboratories are offering WGS on a clinical basis at reduced costs and turnaround times. We report our initial experience and results of clinical whole genome sequencing performed through our precision genomics clinic at UC Davis.

**Methods used** 18 Individuals with no definitive genetic diagnosis, with their clinical presentation ranging from global developmental delay, non-verbal autism spectrum disorders, multisystem involvement including vision and hearing loss and neurological manifestations, were evaluated at the 'Precision Genomics Clinic' and recruited for this study. All individuals had previous extensive work up including chromosomal microarrays, biochemical

tests and targeted gene or Next generation sequencing tests that were negative.

Buccal swabs were collected for DNA extraction and sent for Whole Genome Sequencing (WGS) to Perkin Elmer Laboratory.

**Summary of results** 10 individuals received results: definitive positive test in two individuals, likely pathogenic in two siblings, Variants of uncertain significance (VUS) in three individuals, and, negative test results in three individuals. Positive test results include mosaic splice site variants, missense variant, a 3' UTR frame shift and exon deletions.

**Conclusions** Overall, our experience with WGS has been encouraging and yielded answers in 40% individuals. Families that were going through 'diagnostic odysseys' were relieved to have a diagnosis and were eager to pursue treatment options. In summary, our first ten WGS have yielded positive test result in 40% of tested individuals and is higher than average positive chromosome microarray (10%–15%) and whole exome sequencing (25%–30%) test results. The potential of WGS in identifying underlying genetic etiology is higher with better coverage of coding regions, promoter and other untranslated regions. This makes it an ideal first test when combined with proper counseling, deep phenotyping and correct pricing. Although, these are early days, we postulate that WGS is poised to be the first-tier, one, genetic test in the future.

## Neonatology General III

### Concurrent Session

8:00 AM

Friday, January 25, 2019

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#### NEWBORN CARE AFTER DELIVERY: A SITUATION ANALYSIS IN RURAL RWANDA

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**Purpose of study** In Rwanda, the NMR is reported at 16.5 deaths per 1000 live births. 59% of neonatal deaths occur in the first 48 hours of life and 90% during the first week of life. Focus on adequate care delivery in the first week of life is necessary to achieve a reduction of neonatal mortality to the national goal of less than 7/1000 by 2035.

The purpose of this study is to analyze data regarding deliveries and neonatal outcomes at Kabutare District Hospital (KDH), located in Huye District, Rwanda and perform a gap analysis of the current structure of neonatal care delivery in the health system.

**Methods used** The study took place in KDH between July 2017 to June 2018 involved review of delivery and neonatal outcomes data collected by the hospital, including births that occurred at the hospital and in the ambulance en route. A team of international and local professionals formed a neonatal steering group to determine gaps in care delivery and identify opportunities for improvement. Focus group sessions as well as direct observation of care were used to determine gaps in care delivery.

Abstract 267 Table 1 SASSIE

| Dose (mg/kg) | #  | Male | Gestational Age mean (wk) | Birth Weight mean (g) | Death | Respiratory Severity Score at 28 d (Mean±SD) | Survive w/o BPD 36 wk (%) | Survive w/o BPD 40 wk (%) |
|--------------|----|------|---------------------------|-----------------------|-------|--|---------------------------|---------------------------|
| 0.025        | 8  | 6    | 25.3                      | 885                   | 0     | 4.5±3.7                                      | 38                        | 63                        |
| 0.05         | 8  | 2    | 25.3                      | 704                   | 0     | 5.4±3.7                                      | 0                         | 13                        |
| 0.10         | 9  | 4    | 24.4                      | 651                   | 3     | 3.5±2.4                                      | 13                        | 13                        |
| All          | 25 | 12   | 25.0                      | 743                   | 3     |  | 17                        | 29                        |
| 0-TOLSURF    | 48 | 24   | 25.1                      | 742                   | 2     | 4.4±2.9                                      | 31                        | 60                        |

**Summary of results** In the study period, 2768 deliveries were reported at KDH, with a monthly average of 231 deliveries. Neonatal mortality averages 10.7% (range: 1.7% to 19.4%). The highest percentage of mortalities occurred in the 15 hours between 17:01–08:01. The most common cause of neonatal mortality at KDH is birth asphyxia (at 74% of deaths), followed by prematurity (at 16%), and respiratory disease and sepsis (5% each). 73.6% of neonatal deaths occur in the hospital setting while 26.3% occur en route to the hospital in an ambulance. The main gaps in delivery of care occurred due to a lack of skills and knowledge in proper resuscitation techniques, as well as a shortage of skilled providers and equipment available at deliveries.

**Conclusions** Birth asphyxia carries the largest burden of neonatal mortality at KDH. Interventions to improve the health care capacity through well applied evidence-based strategies are urgently needed.

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#### PILOT DOSE ESCALATION TRIAL OF BUDESONIDE IN SURFACTANT IN VENTILATED EXTREMELY LOW GESTATIONAL AGE NEWBORNS

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**Purpose of study** Yeh demonstrated a decrease in bronchopulmonary dysplasia (BPD) in preterm infants <1500 grams treated with budesonide in surfactant (BIS) (2008, 2016). The dose used (0.25 mg/kg) may be too high.

**Methods used** 24 extremely low gestational age newborns (ELGAN) intubated between 3–14 days of age at 4 centers were treated with up to 5 daily doses of BIS at 3 sequential dosing levels (0.025, 0.5, 0.1 mg/kg). Infants were excluded if treated with steroids or for PDA. DSMB reviewed response and AEs at each level before proceeding. Clinical outcomes at 28 d, 36 and 40 wk, along with blood budesonide and tracheal aspirate cytokine levels were determined to assess budesonide pharmacokinetics and anti-inflammatory effects (data pending). Infants were matched with surfactant-treated infants from Trial Of Late SURfactant (TOLSURF).

**Summary of results** Only 25 of 272 (9%) ELGAN screened were enrolled at the 3 dosing levels over 12 months. 1 infant was withdrawn. Table 1 All 21 surviving infants required respiratory support at 28d. 17% survived w/o BPD at 36 wk and 29% at 40 wk. None of the 4 deaths or serious AEs were judged to be treatment related. Budesonide blood levels at each dose were proportional to those reported by Yeh.

**Conclusions** With current clinical management, only very low GA, fragile infants are currently intubated at 3–14 days of age and many receive treatment for PDA, which limits candidates for BIS therapy. There was no apparent improvement in clinical outcome for high risk infants treated with all doses BIS compared to surfactant alone. Response to intratracheal BIS may be limited in infants <26 wk due to immaturity and multifactorial disease.

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#### PERCEPTIONS OF QUALITY OF LIFE

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10.1136/jim-2018-000939.267

**Purpose of study** The purpose of this project is to assess differences in perceptions of suffering and quality of life between various providers working in the neonatal intensive care unit when presented with different disease and disability states.

**Methods used** We assessed perceptions of suffering and quality of life by administering a REDCap survey via email to providers working in the neonatal intensive care unit, including nurse practitioners, fellow physicians, attending physicians, and nursing staff. The survey comprised six hypothetical patients/disease states described using the Mark 2 version of the health utilities index, adapted from the studies completed previously by S. Saigal. Respondents were asked to evaluate these hypothetical disease states, and assessed degree of suffering and overall quality of life using a 6 point Likert scale. Demographic information was also collected including age, gender, marital status, whether they have children, religious preferences, and personal experience with disabilities. Baseline demographics were summarized and compared using two-sample t-tests and Fisher's exact tests. Responses to each case were compared between providers and nurses using Fisher's exact tests and chi-square tests. Logistic regression was used to determine the independent association between survey response (binary) and provider type (provider vs. nurse), after adjusting for age, having children and religion based on bivariate results. Significance was set at 0.05 unless otherwise noted.

**Summary of results** Our cohort included 123 respondents comprised of 45 providers (attending providers, fellows, and neonatal nurse practitioners) and 78 nurses. In the adjusted model, compared to providers, nurses were more likely report greater suffering for one case scenario (AOR 4.23; 95% CI 1.26–19.49).

**Conclusions** When compared to physicians and neonatal nurse practitioners, nursing staff are more likely to perceive suffering in a case of a child with disabilities. Additional research is needed to understand whether differences in perceptions of

Abstract 269 Table 1

| Variable  | Epoch 1 (2013–2015) | Epoch 2 (2017)   | p value |
|---|---------------------|------------------|---------|
| Total number of births at participating institutions  | 10,97,799           | 3,60,423         |         |
| Incidence of MAS requiring NICU admission among total live births at participating institutions | 1379 (0.126%)       | 402 (0.112%)     | <0.0001 |
| Incidence of MAS among all NICU admissions ≥36 weeks gestation                                  | 7.45%               | 5.86%            | <0.0001 |
| Delivery room intubations   | 499/1378* (36.2%)   | 109/400* (27.3%) | 0.0009  |
| Post DR – any type of intubated respiratory support   | 375/1379 (27.2%)    | 111/402 (27.6%)  | 0.87    |
| Post DR- High frequency ventilation   | 384/1377* (27.9%)   | 101/402 (25.1%)  | 0.27    |
| Use of Inhaled Nitric oxide   | 299/1379 (21.8%)    | 97/402 (24.1%)   | 0.32    |
| ECMO  | 34/1379 (2.5%)      | 5/402 (1.2%)     | 0.18    |
| Pneumothorax  | 162/1379 (11.8%)    | 50/402 (12.4%)   | 0.7     |
| Moderate/Severe HIE   | 138/1362* (10.1%)   | 46/400* (11.5%)  | 0.43    |

\*values missing in some subjects

suffering and quality of life among neonatal physicians and nurses impacts our interactions with parents of medically complex children.

**269** MECONIUM ASPIRATION SYNDROME: IMPACT OF 2016 NRP 'NO-SUCTION' GUIDELINES IN CALIFORNIA

<sup>1</sup>VK Kalra, <sup>2</sup>H Lee, <sup>2</sup>L Sie, <sup>1</sup>M Underwood, <sup>1</sup>S Lakshminrusimha. <sup>1</sup>UC Davis Children's Hospital, Sacramento, CA; <sup>2</sup>Stanford University School of Medicine, Stanford, CA

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**Purpose of study** The guidelines for peripartum management of meconium stained amniotic fluid (MSAF) have changed over the last 2 decades. In 2016, the Neonatal Resuscitation Program (NRP) recommended that initial resuscitation of non-vigorous infants with MSAF follow the same principles as for those with clear fluid. This change was based on lack of evidence for benefit and on randomized controlled trials performed in India. The effect of these guidelines on the incidence of meconium aspiration syndrome (MAS) in US is unknown. Purpose of this study was to evaluate the effect of implementation of revised NRP guidelines on the incidence and severity of MAS in California.

**Methods used** California Perinatal Quality Care Collaborative (CPQCC) database was queried for the years 2013–2017 to describe the incidence, therapeutic modalities and outcome characteristics of infants who developed MAS. Results were analysed based on pre and post guideline epoch (2013–15 vs 2017).

**Summary of results** There was a significant decrease in the incidence of MAS, intubations in delivery room without any change in invasive mechanical ventilation, high frequency ventilation (HFOV), inhaled nitric oxide (iNO) or ECMO following implementation of the new NRP guidelines. Associated conditions such as pneumothorax and moderate/severe HIE did not change between the two epochs.

**Conclusions** Overall incidence of MAS decreased in 2017 compared to 2013–15 without any increase in pneumothorax, moderate/severe HIE, invasive ventilation, HFOV, iNO and ECMO among infants with MAS. These findings support current NRP guidelines recommendations against routine tracheal suctioning for infants born through MSAF.

**270** CAN POINT OF CARE ULTRASOUND BE USEFUL IN ASSESSMENT OF BRONCHOPULMONARY DYSPLASIA?

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10.1136/jim-2018-000939.269

**Purpose of study** Our study aims to evaluate the utility of point of care lung ultrasound (POCLU) to assess severity of BPD in premature infants.

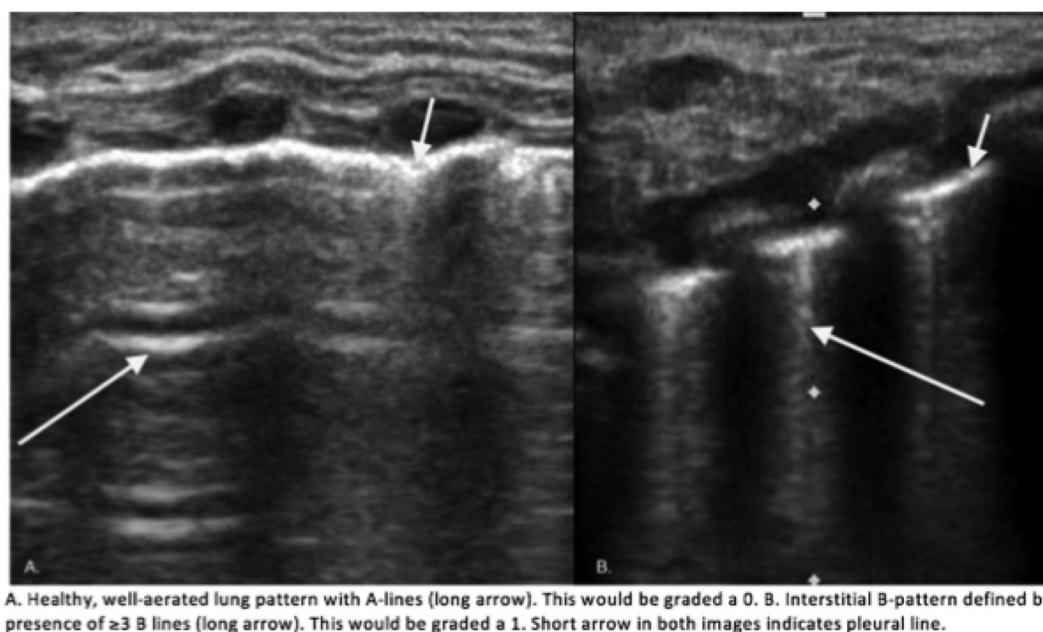
**Methods used** Infants <34 weeks with NIH criteria for BPD were enrolled at 36–37 weeks CGA. POCLU was performed by a single investigator. Multiple views of bilateral upper and lower anterior and lateral lung fields were obtained using a linear 10–12 Hz transducer. 2 blinded co-investigators scored each view using a scoring system adapted by De Luca et al from an adult ICU index, for a total of 0–18 points (higher score for worse disease). Scores were averaged between the two raters and interrater reliability was calculated.

**Summary of results** 4 subjects (mean GA 25+2 mean BW 711 g) have been enrolled in this ongoing study, 3 with moderate BPD and 1 with severe BPD. Moderate BPD subjects scored 0.5–4, while the severe BPD subject scored 3.5. Moderate interrater reliability (k=0.417).

**Conclusions** Our study is the first to examine POCLU in assessment of BPD severity in NICU. As we include additional subjects, we aim to determine if modifications to the scoring system are necessary to optimize the ability of POCLU to characterize BPD severity.

Abstract 270 Table 1 Lung ultrasound scores

| Patient | BPD clinical severity | Score #1 | Score #2 | Average Score |
|---------|-----------------------|----------|----------|---------------|
| BPD 1   | Severe                | 4.0      | 3.0      | 3.5           |
| BPD 2   | Moderate              | 0.0      | 1.0      | 0.5           |
| BPD 3   | Moderate              | 2.0      | 3.0      | 2.5           |
| BPD 4   | Moderate              | 3.0      | 5.0      | 4.0           |



Abstract 270 Figure 1 Lung ultrasound patterns

## 271 TARGETING EPITHELIAL MEMBRANE PROTEIN 2 (EMP2) IN RETINOPATHY OF PREMATURITY

A Chu, M Sun, M Wadehra, L Gordon. *UCLA, Los Angeles, CA*

10.1136/jim-2018-000939.270

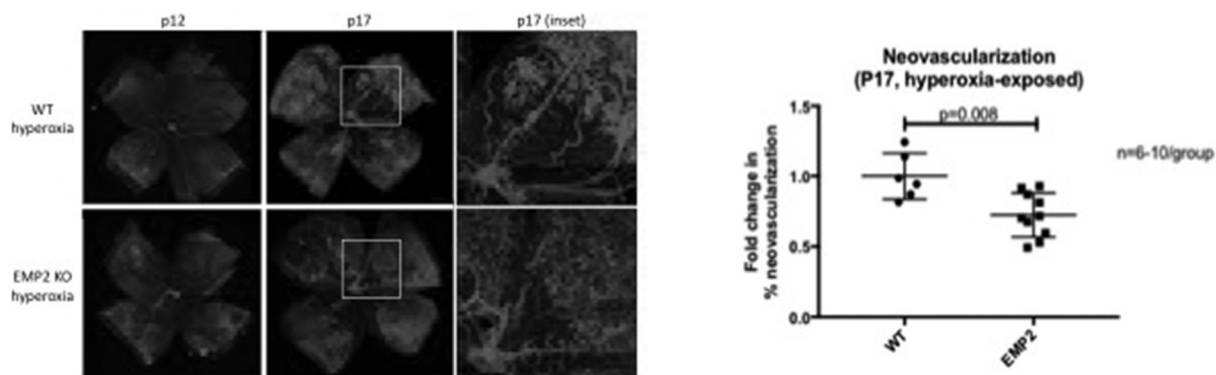
**Purpose of study** Retinopathy of prematurity (ROP) is a devastating disease that affects neonates born prematurely, when exposure to relative hyperoxia then hypoxia leads to disordered retinal neovascularization mediated by vascular endothelial growth factor (VEGF) and hypoxia-inducible factor 1 alpha (Hif1 $\alpha$ ) signaling. Epithelial membrane protein-2 (EMP2) is a protein that has been described in cancer, placental diseases, and ophthalmologic disease, to mediate angiogenesis via HIF1 $\alpha$  and VEGF. Therefore, the purpose of our study was to evaluate the role of EMP2 in ROP. Our hypothesis is that knock-down of EMP2 will ameliorate progression of aberrant neovascularization in ROP via RPE-dependent Hif1 $\alpha$  and VEGF signaling.

**Methods used** We utilized a well-established mouse model of hyperoxia (75% oxygen levels) exposure from P7 to P12 to induce retinopathy in our WT C57Bl6 and EMP2 genetic

knock-out (KO) mice (on a C57BL6 background). We assessed peak vaso-obliteration at P12 and peak neovascularization at P17 using whole mount imaging (figure 1, left panel).

**Summary of results** EMP2 KO attenuates the neovascularization phase in hyperoxia-induced retinopathy: We found no difference in vasoobliteration (WT:  $1 \pm 0.143$  fold change,  $n=10$ ; EMP2 KO:  $1.058 \pm 0.078$  FC,  $n=10$ ;  $p=0.277$  by Student's t-test with Welch's correction) between WT and EMP2 KO mice exposed to hyperoxia from P7 to P12. However, there was an  $\sim 28\%$  reduction in neovascularization in our EMP2 KO mice (WT:  $1 \pm 0.164$  FC,  $n=6$ ; EMP2 KO:  $0.724 \pm 0.156$  FC,  $n=10$ ;  $p=0.008$  by Student's t-test with Welch's correction) (figure. 1, right panel) compared to WT.

**Conclusions** Our findings suggest that EMP2 modulation plays a role in the neovascularization seen in a mouse model of retinopathy of prematurity. Ongoing studies to identify mechanisms involved in disease modulation after EMP2 KO are underway. These findings establish a foundation for novel basic biological processes and potentially a novel therapeutic target in ROP.



Abstract 271 Figure 1

## Neonatology – Perinatal Biology I

## Concurrent Session

8:00 AM

Friday, January 25, 2019

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**VASODILATION OF FETAL AND ADULT SHEEP PULMONARY ARTERIES BY NITROSOGLUTATHIONE**<sup>1</sup>A Chadha, <sup>1</sup>T Liu, <sup>1,2</sup>A Blood. <sup>1</sup>Div of Neonatology, Loma Linda University, CA; <sup>2</sup>Longo Center for Perinatal Biology, Loma Linda University, CA

10.1136/jim-2018-000939.271

**Purpose of study** Nitric oxide (NO) is a potent endogenous and therapeutic pulmonary vasodilator. S-nitrosothiols (SNOs), molecules containing NO bound to a sulfur group, are products of NO metabolism. Like NO, SNOs vasodilate by activation of guanylate cyclase (GC). Unlike the short-lived NO, SNOs are stable enough to circulate systemically and are proposed to augment the vasodilatory effects of both endogenous and inhaled NO (iNO). Nitrosoglutathione (GSNO), a small, membrane impermeable SNO, vasodilates mesenteric vasculature more effectively than femoral vasculature, suggesting the effects of SNOs vary by organ. In the mesenteric artery, GSNO's vasodilatory potency is similar to NO itself. This has not been studied in pulmonary arteries. We hypothesized that GSNO vasodilates fetal and adult sheep pulmonary arteries with a potency similar to NO itself.

**Methods used** Arteries from adult and near-term fetal sheep lungs were isolated for wire myography. After precontraction with serotonin (5-HT, 1  $\mu$ M) relaxation responses to increasing concentrations of GSNO or NO were recorded. Responses were normalized to time-controls that received only 5-HT. Responses were quantified as the EC<sub>50</sub> (log<sub>10</sub> molar concentration at which 50% of maximal vasodilation was achieved) and E<sub>max</sub> (maximal vasodilation response as a percent of tension achieved with 5-HT).

**Summary of results** GSNO resulted in similar vasodilation of fetal (EC<sub>50</sub> = -6.6  $\pm$  0.53, E<sub>max</sub> = 88%  $\pm$  20%, n=6) and adult (EC<sub>50</sub> = -7.3  $\pm$  1.4, E<sub>max</sub> = 62%  $\pm$  23%, n=11) arteries, suggesting GSNO is equally potent in both vessel types. These results are similar to prior work in fetal mesenteric arteries, suggesting the vasodilatory effects of GSNO are similar in both vascular beds. In adult pulmonary arteries, NO resulted in vasodilation comparable to GSNO (EC<sub>50</sub> = -6.4  $\pm$  0.34, E<sub>max</sub> = 52%  $\pm$  7%, n=8). Preliminary experiments with fetal pulmonary arteries suggest that fetal pulmonary arteries also respond similarly to NO.

**Conclusions** GSNO, a SNO produced endogenously and in response to iNO therapy, dilates isolated sheep mesenteric and pulmonary arteries, with sensitivity and potency comparable to that of NO itself. Given that GSNO is membrane impermeable and does not release NO, it is unclear how GSNO and NO are both able to activate intracellular GC at comparable concentrations.

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**PROLONGED IGF-1 INFUSION INCREASES MYOBLAST PROLIFERATION IN LATE GESTATION FETAL SHEEP**<sup>1</sup>S Heard, <sup>1</sup>S Shaw, <sup>1</sup>E Chang, <sup>1</sup>P Rozance, <sup>2</sup>S Jonker, <sup>1</sup>L Brown. <sup>1</sup>University of Colorado School of Medicine, Biddeford, ME; <sup>2</sup>Oregon Health and Science University, Portland, OR

10.1136/jim-2018-000939.272

**Purpose of study** Insulin like growth factor-1 (IGF-1) is an important fetal growth factor that regulates both somatic and skeletal muscle growth. It binds IGF-1 and insulin receptors to trigger downstream signaling pathways to stimulate cell proliferation and size. We hypothesized that prolonged IGF-1 infusion would increase myoblast proliferation and activate signaling proteins that regulate growth within hindlimb skeletal muscle in late gestation fetal sheep.

**Methods used** Fetal catheters were surgically placed in mixed Western breed pregnant sheep at 120 days gestation (dGA, term 147 dGA). After 6 days of recovery, fetuses were randomized to receive chronic infusion of human recombinant IGF-1 LR3 (6.6  $\mu$ g/kg/hr; n=7) or saline (n=5) for 7 days. Tibialis anterior (TA) and flexor digitorum superficialis (FDS) muscles were collected, weighed, and frozen at the end of the study. Immunohistochemical quantification of myoblasts (anti-Pax7), replicating myoblasts (anti-Ki67), myofibers (anti-laminin), and nuclei (DAPI) was performed. Protein expression of total and phosphorylated Akt (Ser473), Erk (Thr202/Tyr204), and p70S6 kinase (Thr389) was measured by Western blot analysis. Group (IGF-1, saline) and muscle type (TA, FDS) main effects were analyzed using two-way ANOVA.

**Summary of results** Fetal weight, TA, and FDS muscle weights were similar between groups. The ratio of Pax7 +nuclei per myofiber was 18% higher (p<0.05) and the ratio of Pax7 +myoblasts that also were Ki67 +was 27% higher (p<0.05) in the IGF-1 group compared to saline. Contrary to our hypothesis, the ratio of phosphorylated to total Erk was lower in the IGF-1 group (p<0.05); Akt and p70S6 kinase were similar between groups.

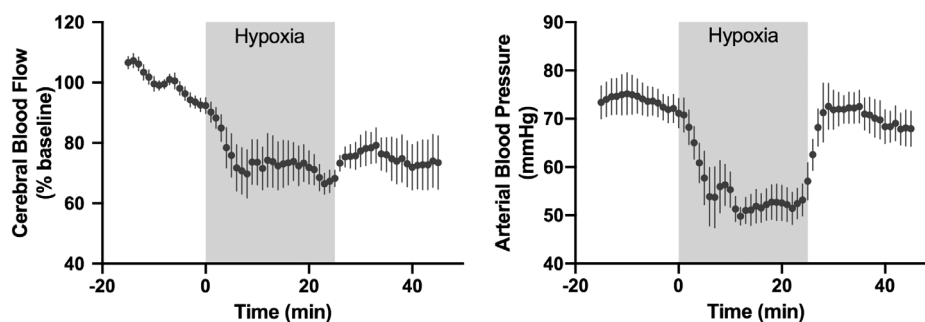
**Conclusions** Fetal infusion of IGF-1 for one week in late gestation increased the pool of Pax7 +myoblasts and the percent of myoblasts actively proliferating in skeletal muscle. We speculate that reduced activated Erk is either the result of negative feedback, or that IGF-1 regulates fetal myoblast proliferation via alternate pathways. These results are important for understanding how fetal IGF-1 concentrations regulate skeletal muscle growth, as maintenance of lean mass in adulthood depends on a normal endowment of skeletal muscle early in development.

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**CEREBRAL VASCULAR RESPONSE TO HYPOXIA IN NEWBORN LAMBS**<sup>1</sup>P Agrawal, <sup>1,2</sup>A Blood, <sup>1,2</sup>G Power. <sup>1</sup>LLUMC, Loma Linda, CA; <sup>2</sup>Longo Center for Perinatal Biology, Loma Linda, CA

10.1136/jim-2018-000939.273

**Purpose of study** Brain blood flow is regulated by a balance of vasodilating and vasoconstricting factors in the cerebral



Abstract #274 Figure 1

vasculature. In response to hypoxic stress, the fetus redistributes blood flow from the periphery to critical organs such as the brain by increasing arterial pressure with unchanged or perhaps decreased cerebral vascular resistance. This response helps maintain cerebral oxygen delivery at the expense of other organs. Birth is associated with a catecholamine surge and vasoconstriction of the cerebral vasculature, which may alter the cerebral blood flow response to hypoxia. The ability of the neonate to redistribute blood flow to the brain has not been fully studied. We hypothesized that hypoxia would lead to increased cerebral blood flow in newborn lambs.

**Methods used** Fetal sheep were instrumented at gestational age 139 to 142 days (term 145 days). An arterial catheter was inserted for measurement of blood pressure and gases. A composite laser doppler flow and tissue  $PO_2$  probe was inserted into the cerebral cortex for continuous monitoring of brain blood flow and oxygenation. Lambs were delivered via C-section, sedated, and mechanically ventilated. About 30 min after birth, hypoxia was induced by decreasing  $FiO_2$  to 10%–12% for a period of 30 min. Data are shown as mean  $\pm$  SEM.

**Summary of results** 7 near-term newborn lambs weighing  $3.4 \pm 0.3$  kg were studied at  $140 \pm 0.3$  days gestation. Hypoxia resulted in a fall in brain tissue  $PO_2$  from  $34 \pm 4.3$  Torr to  $10.4 \pm 1.4$  ( $p < 0.01$ ) and an arterial  $PO_2$  of  $22 \pm 4.45$  Torr. In response to hypoxia, arterial blood pressure decreased from  $73 \pm 3$  mmHg to a nadir of  $34 \pm 3.6$  mmHg ( $p < 0.01$ , 1-way ANOVA) and cerebral blood flow decreased by  $23.8\% \pm 5.5\%$  ( $p < 0.001$ ). Heart rate remained unchanged.

**Conclusions** In contrast to the fetus, newborn lambs respond to hypoxia with a decrease in cerebral blood flow and arterial pressure. Postnatal cerebral vasoconstriction and an inability of the newborn lamb to elevate arterial blood pressure could explain the reduction in cerebral blood flow.

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#### PROLONGED AMINO ACID INFUSION INTO INTRAUTERINE GROWTH RESTRICTED (IUGR) FETAL SHEEP DOES NOT INCREASE MYOFIBER AREA

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10.1136/jim-2018-000939.274

**Purpose of study** Prolonged (10 day) amino acid infusion into late gestation IUGR fetal sheep increased leucine oxidation rates but had limited effects on protein accretion. However, in postnatal animal models, amino acids have been shown to increase skeletal muscle-specific protein accretion rates, which

would lead to increased muscle size. We hypothesized that a prolonged amino acid infusion into IUGR fetal sheep would increase muscle weight and sectional area.

**Methods used** Intravenous catheters were surgically placed into IUGR and control (CON) fetal sheep during late gestation. IUGR fetuses were randomly assigned to receive TrophAmine® (IUGR-AA;  $n=9$ ) or saline (IUGR-Sal;  $n=8$ ) for  $\sim 10$  days. CON fetuses received saline ( $n=8$ ). At the end of infusion, tibialis anterior (TA) and biceps femoris (BF) muscles were weighed. TA was sectioned ( $10 \mu m$ ) and incubated with anti-myosin heavy chain (MHC) type I, anti-MHC type IIa, and anti-laminin to determine fiber type-specific cross sectional area. RNA was isolated from BF and genes that regulate amino acid transport and metabolism, the tricarboxylic acid cycle, and mitochondrial biogenesis were measured using qPCR.

**Summary of results** BF ( $p < 0.05$ ) and TA weights ( $p = 0.07$ ) were lower in IUGR compared to CON but were not different between IUGR-AA and IUGR-Sal groups. Similarly, type I and IIa myofiber areas were smaller in IUGR compared to CON ( $p < 0.05$ ), but were not different between IUGR groups. Expression of neutral amino acid transporter B(0) (SLC1A5) and branched-chain aminotransferases (BCAT 1, 2) were lower in IUGR compared to CON ( $p < 0.05$ ), but not different between IUGR groups. Finally, genes that regulate energy metabolism PGC1 $\alpha$  ( $p = 0.1$ ) and nuclear respiratory factors (NRF 1, 2;  $p < 0.05$ ) were upregulated in IUGR-AA compared to IUGR-Sal.

**Conclusions** Prolonged amino acid infusion into IUGR sheep did not increase muscle weight or myofiber area. Reduced B(0) transporter and BCAT expression suggest reduced amino acid entry into IUGR muscle, even in the presence of increased amino acid supply. Instead, genes that promote mitochondrial biogenesis were upregulated in IUGR-AA, which might serve to facilitate increased leucine oxidation. Increasing fetal amino acid supply in established IUGR does not overcome restricted skeletal muscle growth.

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#### MATERNAL/FETAL TOTAL LIPID CONCENTRATIONS IN GROWTH RESTRICTED BABOON

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10.1136/jim-2018-000939.275

**Purpose of study** Fatty acids (FA) are critical for fetal brain development. In humans, maternal lipids markedly increase by term. Little is known about placental FA transport in intrauterine growth restriction (IUGR), associated with



neurodevelopmental impairment. We recently demonstrated increased placental FA binding and transport proteins in a baboon model of IUGR due to maternal nutrient restriction (MNR). Here we analyzed maternal (M) and fetal (F) plasma lipid concentrations across the final trimester. We hypothesized that M lipid concentrations increase by term, and F/M concentration ratios are lower in the MNR fetus.

**Methods used** Pregnant baboons were fed control (C, ad lib) or MNR diet (70% of control calories) from gestation day (GD) 30 (term is ~GD184). Plasma samples (M uterine vein; F umbilical vein) were collected at GD-120 (C n=8/MNR n=9), -140 (C n=6/MNR n=7), and -170 (C n=6/MNR n=6). Brain weight was obtained at necropsy. Targeted lipidomic analysis was performed by GC-MS after extraction of plasma FA in total lipids (TL). Differences and correlations were assessed by student's *t* test and Pearson's coefficient.

**Summary of results** Weights were similar between groups until GD170 when MNR fetal and placental weights trended smaller by 7% and 6% respectively. Advancing gestational age correlated with increased maternal TL concentrations in control ( $R^2=0.32$ ;  $p=0.009$ ) and MNR ( $R^2=0.19$ ;  $p=0.045$ ) and decreased fetal TL concentrations in control ( $R^2=0.35$ ;  $p=0.006$ ) and MNR ( $R^2=0.28$ ;  $p=0.01$ ). F/M TL ratios in both control ( $R^2=0.46$ ;  $p=0.001$ ) and MNR ( $R^2=0.42$ ;  $p=0.001$ ) decreased across gestation. At GD170 F/M ratio in MNR was greater than control ( $p=0.047$ ). Fetal brain weights did not differ between groups.

**Conclusions** We established a longitudinal lipid profile in baboon maternal and fetal plasma. MNR did not alter TL F/M ratios until 3rd trimester. Maternal TL concentrations increase with gestation in both groups, even with decreased dietary FA availability. The decrease in fetal TL across gestation in MNR fetuses that maintain their brain growth is consistent with preferential lipid uptake by the brain. Maintained lipid delivery to support normal brain growth may be due to the increased placental FA transport capacity.

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#### MATERNAL TOBACCO SMOKE EXPOSURE ALTERS PLACENTAL SETD8 AND PHOSPHOLIPID PROFILES

J Whitham, E Barrett, R Kaddu, C Weinheimer, L Joss-Moore, H Wang. *University of Utah, Salt Lake City, UT*

10.1136/jim-2018-000939.276

**Purpose of study** Maternal tobacco smoke (MTS) exposure sex-specifically programs adult-onset disease in human and rat models, often with altered offspring fatty acids (FA). The placenta regulates fetal FA acquisition by sequestering fatty acids in placental phospholipids or by transporting FA to the fetal circulation. The expression of genes responsible for placental storage and transport are regulated by epigenetic modifications, including methylation of histones by Setd8. We recently demonstrated that MTS decreases transport of the critical FA docosahexaenoic acid (DHA) and arachidonic acid (AA) to the male fetus, but not the female fetus, in a rat model. However, the effects of MTS on placental Setd8 expression and placental phospholipid FA profiles is unknown. We hypothesize that MTS causes sex-divergent changes in Setd8 protein abundance in association with altered phospholipid profiles in the rat placenta.

**Methods used** Pregnant rats were exposed to tobacco smoke (MTS) or room air (Control) from E11 to term (E21).

Placenta were collected at term. Western blot was used to measure Setd8 protein abundance, and GC/MS was used to quantify levels of each phospholipid class.

**Summary of results** In male placenta, MTS increased Setd8 protein abundance compared to control ( $223\pm43\%$ ,  $p<0.05$ ). In female placenta, MTS did not alter Setd8 protein abundance. The predominate phospholipid species detected were phosphatidylethanolamine (PE), phosphatidylcholine (PC) and sphingomyelin (SM). MTS did not affect the total amount of any phospholipid fraction. MTS did result in sex-divergent changes in the composition of FA chains within each class. The primary difference was in the female MTS placenta where PE and PC species containing long chain fatty acids (DHA, AA) were reduced. Similar changes were not detected in male placenta.

**Conclusions** We conclude that MTS causes sex-divergent changes in Setd8 protein abundance in association with altered phospholipid profiles in the rat placenta. Given our previous observation of less DHA and AA transport to male pups in MTS, we speculate that placental genes governing fatty acid storage may be upregulated in male rat pups. Ongoing work is evaluating histone methylation by Setd8 on these genes.

### Surgery III

#### Concurrent Session

8:00 AM

Friday, January 25, 2019

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#### ASSESSING TECHNICAL COMPETENCE: DEVELOPING A TECHNICAL SKILLS EXAM FOR GENERAL SURGERY TRAINEES PERFORMING ROBOTIC CHOLECYSTECTOMIES

CA Aziz, JC Quispe, K Medani, E Yung. *Loma Linda University School of Medicine, Irvine, CA*

10.1136/jim-2018-000939.277

**Purpose of study** The level of technological advancement in surgery has dramatically shifted, especially in the field of robotic surgery. As the practice of surgery advances, it is essential that training programs match the rigor of innovation. The purpose of this project is to create an objective standardized method to assess the capabilities of surgical trainees performing robotic cholecystectomies.

**Methods used** Seven surgical trainees ranging from post-graduate year (PGY) 3 to 6 were evaluated for 12 consecutive weeks using an evaluation form. This form is a compilation of three validated assessment tools: Global Evaluative Assessment of Robotic Skill (GEARS), Observational Teamwork Assessment for Surgery (OTAS), and Objective Standardized Assessment of Technical Skill (OSATS). Attending surgeons completed the form after the trainees participated in a robotic cholecystectomy. Data was analyzed using SAS [Version 9.4].

**Summary of results** The primary outcome variables were OSATS, GEARS and OTAS. The predictor variables were PGY level and the number of cholecystectomies performed. Linear regression showed that PGY level is a significant predictor for OTAS ( $p\text{-value}=0.002$ ), but not for OSATS and GEARS ( $p\text{-value}=0.21$  and  $0.18$  respectively). However, a trend suggests possible correlation between PGY level and OSATS and

**Abstract 278 Table 1** OSATS, GEARS, and OTAS mean scores by PGY level

| PGY Level | Average OSATS<br>(scored out of 80) | Average GEARS<br>(scored out of 30) | Average OTAS<br>(scored out of 36) |
|-----------|-------------------------------------|-------------------------------------|------------------------------------|
| 3         | 58                                  | 21.5                                | 19                                 |
| 4         | 10                                  | 23                                  | 26                                 |
| 5         | 58                                  | 24                                  | 28                                 |
| 6         | 72                                  | 26                                  | 32                                 |

GEARS. The number of cholecystectomies is a useful predictor for the procedure OR time ( $p=0.02$ ), shown by the strong negative correlation ( $R=-0.87$ ). PGY level is not a significant predictor for the OR time ( $p=0.13$ ).

**Conclusions** The evaluation tool created in this study suggests a difference in skills between various trainee levels. Due to the short length of the study and limited participants, the outcomes were restricted. We believe that this instrument may be an objective way to assess technical skills of trainee surgeons and should further be explored via a long-term study and larger cohort. If validated, this can be extrapolated to other procedures to assess robotic skills.

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#### USE OF A NOVEL NON-INVASIVE SKIN CLOSURE DEVICE FOR PREVENTION OF WOUND DEHISCENCE IN TRUNK-BASED SURGERY

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10.1136/jim-2018-000939.278

**Purpose of study** Wound dehiscence is a cause of morbidity in patients with abdominal incisions. In procedures such as abdominoplasty, the incision is under significant tension during the healing process. Even so, the wound is constantly stressed and at significant risk of dehiscence. Literature review shows dehiscence rates ranging as high as 33%. However, a novel wound closure device known as ZipLine has recently been implemented with great success in preventing wound breakdown in Orthopedic and Cardiothoracic surgery. Zipline is a non-invasive, adhesive device that can be used in place of or supplemental to sutures for skin closure. It has been shown to be stronger, less ischemic, and more resistant to shearing forces than sutures and staples. Use of this device has not been reported in Plastic Surgery, so we aim to demonstrate the benefit of the Zipline in preventing wound dehiscence after abdominoplasty.

**Methods used** A retrospective analysis of 5 patients who underwent surgical closure with a non-invasive zipper system was conducted from March to September 2018. Information regarding the patient's age, gender, body mass index (BMI), smoking history, and steroid use was collected and surgical procedure notes were reviewed.

**Summary of results** Table 1 displays the surgical outcomes of each patient. Patients ranged from 33 to 73 years old, with BMI ranging from 23.5 to 34.2. Three patients were smokers with over 20 pack-years and two patients were steroid users for medical conditions. These are known risk factors for poor healing post-operatively. For each patient the wound was

**Abstract 279 Table 1**

| Patient | Age/<br>Gender | BMI  | Total<br>Pack-<br>Years | Steroid<br>Use | Hx of<br>Bariatric<br>Surgery | Use of<br>Liposuction | Wound<br>Complications* |
|---------|----------------|------|-------------------------|----------------|-------------------------------|-----------------------|-------------------------|
| A       | 33F            | 23.6 | 0                       | N              | N                             | N                     | NONE                    |
| B       | 33F            | 31.6 | 0                       | N              | N                             | Y                     | NONE                    |
| C       | 63F            | 34.2 | 40                      | N              | Y                             | N                     | NONE                    |
| D       | 73F            | 29.4 | 57                      | Y              | N                             | N                     | NONE                    |
| E       | 60F            | 31.7 | 20                      | Y              | N                             | N                     | NONE                    |

\*Wound complications are dehiscence, erythema, or drainage.

found to be intact with no incidence of dehiscence, erythema, or drainage for up to 6 months.

**Conclusions** Zipline has reduced common wound complications of dehiscence and delayed healing. Results from these patients presents a worthwhile option that is easy to use and beneficial for post-operative patient care. A larger trial is underway with expanded indications across the trunk.

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#### METHAMPHETAMINE-POSITIVE PATIENTS: THE SAME BUT DIFFERENT FROM OTHER BURN-INJURED PATIENTS

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10.1136/jim-2018-000939.279

**Purpose of study** Previous studies suggest that burn patients testing positive for methamphetamines (MA+) have worse outcomes and longer hospital lengths of stay (LOS). We compared outcomes for MA+patients to all burn patients admitted to our center. We then matched and compared MA+with methamphetamine-negative patients (MA-). We hypothesized that MA+patients would have worse outcomes.

**Methods used** Following IRB approval we reviewed all burn admissions within a four-year period (January 2014 – December 2017). We did two comparisons – total patients vs MA+; and matched MA- vs MA+. Of 1535 total patients, 273 (17.8%) were MA +on toxicology screen. Of these, 194 MA +patients were matched with 194 MA- patients based on age, TBSA, and inhalation injury. Data collected included burn etiology, length of stay, number of operating room (OR) visits, discharge disposition, and more. Census data (2011) was used as an economic marker for patients based on zip code.

**Summary of results** Compared to the total population, MA +patients had larger burns, longer LOS, shorter LOS/

**Abstract 280 Table 1** Burn outcomes for total population of MA + and MA- patients using t-test

| Outcome  | MA+            | MA-            | p-value |
|--|----------------|----------------|---------|
| TBSA [%]   | 15.7 (SD=17.3) | 12.2 (SD=16.5) | 0.0004  |
| LOS [days]   | 17.7 (SD=25.3) | 14.1 (SD=21.2) | 0.033   |
| LOS/TBSA [%/days]                                      | 2.0 (SD=3.3)   | 2.8 (SD=8.0)   | 0.022   |
| OR visits/LOS [visits/days]                            | 0.04 (SD=0.1)  | 0.05 (SD=0.1)  | 0.031   |
| Discharged home with no services [% of total patients] | 82.2           | 75.5           | 0.01    |

TBSA, fewer OR visits/LOS, and were more likely to be discharged home without services (table 1). But when MA +patients were matched with MA- patients based on burn size, age, and inhalation injury, we found no significant differences. MA +patients in both comparison groups were from lower SES backgrounds, with significant difference in all measures of education, income, and poverty level ( $p<0.05$ ).

**Conclusions** MA+patients have lower SES, larger burns, and longer LOS when compared to the typical burn population. Once TBSA, age, and inhalation injury are controlled for, MA +status does not affect measures of patient outcomes. With burn severity controlled for, methamphetamine use, by itself, does not alter outcomes. The main burden of MA is that its use leads to larger burns in a population with fewer resources than the general population.

### 281 REGENERATIVE MEDICINE AND ACUTE WOUND CARE: CURRENT METHODS AND THE PROMISE OF THE FUTURE

DD Gordon, EY Choi, CP De Guzman, S Gupta. *Loma Linda University School of Medicine, Loma Linda, CA*

10.1136/jim-2018-000939.280

**Purpose of study** Each year, millions of emergency departments visits are for traumatic injuries. Many of these injuries result in acute wounds such as abrasions and lacerations with soft tissue loss. If these wounds are not properly treated, infections, hypertrophic scarring, and other complications may arise. To reduce these types of complications, regenerative medicine methods are currently being developed and tested. Regenerative medicine can be defined as the use of therapeutic techniques to help restore natural tissue function. This demarcates a clear distinction between tissue repair, which culminates in a nonfunctional scar, and regeneration, which results in tissue that is comparable with the original in form and function. The aim of this study was to evaluate the current state of regenerative medicine technologies in the context of acute wound care while reviewing their individual challenges and opportunities.

**Methods used** A comprehensive review of the literature along with case examples was used for this review to highlight advantages, risks, and future possibilities of various types of regenerative medicine techniques.

**Summary of results** 50 articles were identified and reviewed. Multipotent stem cells, tissue engineering, composite epithelial autografts, and combined gene delivery with stem cell therapy approaches all showed promise, but more conclusive data is needed before they should be widely accepted. Alongside these developments, the use of 3D scaffolds or matrices, peptides, small molecules, and RNA inhibitors are nascent methods with potential to aid in the acute wound healing process. When the evidence was evaluated, there was no clear frontrunner for a new standard of care in the treatment of acute wounds.

**Conclusions** The use of these broad facets of regenerative technologies have shown promising results. However, in addition to the scientific questions that remain unanswered, some methods also pose financial and ethical challenges. Ultimately, the goal of regenerative medicine is to promote the regenerative pathway while avoiding fibrotic tissue formation and

infection. As science progresses into the future, we anticipate that regenerative methods will be included in the standard of care.

### 282 EFFECT OF ALVIMOPAN ON RECOVERY AFTER BOWEL SURGERY IN THE ABSENCE OF ENHANCED RECOVERY PROTOCOL

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10.1136/jim-2018-000939.281

**Purpose of study** Alvimopan is a peripherally acting  $\mu$ -opioid receptor antagonist that is FDA approved to accelerate bowel recovery following bowel surgery. Prior studies have shown shortened length of hospital stay (LOS) and hastened return of bowel function (ROBF) for colorectal surgery patients administered alvimopan. However, some studies have noted that alvimopan may be associated with enhanced recovery protocols (ERPs), which could be responsible for some of its reported effects in clinical practice. This retrospective cohort study examined the effect of alvimopan on ROBF and LOS for patients undergoing bowel surgery for Crohn's disease in the absence of ERP.

**Methods used** Cases were selected from a dataset of patients who underwent bowel surgery for Crohn's Disease, excluding those managed on ERP. ROBF was defined as passage of first stool or ostomy output. Unadjusted analyses of both dependent variables were performed using Mann-Whitney U tests. Adjusted analysis for ROBF was performed using multivariate logistic regression with forward selection (entry  $p<0.05$ ) to compare odds of accelerated ROBF while controlling for demographic and procedure variables and perioperative medical treatment. Accelerated ROBF was defined as  $<50$ th percentile across all patients.

**Summary of results** There were 53 patients included in the analysis, 25 administered alvimopan in the study cohort and 28 not administered alvimopan as the control. Unadjusted analysis showed the study cohort had a significantly shortened time to ROBF (median=2.0 vs. 3.0 days,  $p=0.02$ ). Adjusted analysis demonstrated that the study cohort was more likely to have accelerated ROBF when controlling for surgical approach (OR=6.7, 95% CI=1.7–35.1,  $p=0.01$ ). The median LOS was five days for both cohorts, but Mann-Whitney test showed a non-significant trend towards shortened LOS for the study cohort, ( $p=0.06$ ).

**Conclusions** Patients administered alvimopan for bowel surgery related to Crohn's Disease had a significantly decreased time to ROBF when not managed on an ERP. Although not statistically significant, there was also a trend towards shortened LOS. Further study will be required to determine if these results are generalizable to other colorectal surgery patients, and to characterize the activity of alvimopan when used in the setting of ERP.

### 283 AN INTERDISCIPLINARY APPROACH TO ORGANIZE METHODS OF BIOFILM TREATMENT AND PREVENTION

CP De Guzman, EY Choi, DD Gordon, S Gupta. *Loma Linda University, Loma Linda, CA*

10.1136/jim-2018-000939.282

**Purpose of study** Preventing the development of bacterial biofilms and removing established biofilms is a challenging clinical issue. Literature suggests that biofilm-mediated infections are a major cause of many serious postoperative complications like capsular contracture and joint infection. Currently there is no reliable method to prevent development of or treat already established biofilms and in many situations, removal of an infected foreign object is often the only viable method of treatment. Though the widespread interest in biofilms has caused numerous advancements in biofilm prevention and treatment, much of the research and information is spread across a wide array of diverse fields and specialties. Very little has been done to unify these approaches.

**Methods used** In this study, we aimed to develop a streamlined method to organize the different approaches used to tackle the issue of biofilms. After reviewing the literature, each approach was subdivided into if the approach focused on biofilm treatment or biofilm prevention. The groups were then further organized by underlying mode of action, noting the clinical field that the approach was evaluated in, continually subdividing groups until an extensive organization scheme was developed.

**Summary of results** Research on biofilms may be grouped into a handful of different categories. Research either focused on killing the bacteria, inhibiting the bacterial development of biofilm, making the surrounding environment a place where biofilms lose their adhesive properties, and for the case of treatment, the dissolution of established biofilms. The treatment used to achieve these effects also followed a pattern of being a type of antibiotic, surfactant, small molecule that altered the biofilms proteins or polysaccharides, disinfecting agent, metallic nanoparticle, or one of a handful of other groups identified in the study.

**Conclusions** This organization method of the biofilm literature creates an easy way to understand the major approaches used to treat and prevent biofilms and may be a helpful tool to navigate the current literature and create more efficient and productive research efforts in the future.

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#### SEVERITY OF LIVER PATHOLOGY PREDICTS IMPROVEMENT IN TRANSAMINASE LEVELS IN PATIENTS WHO UNDERWENT SLEEVE GASTRECTOMY PROCEDURE: A RETROSPECTIVE ANALYSIS

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10.1136/jim-2018-000939.283

**Purpose of study** Hepatic steatosis is a disease process in which the liver becomes congested with fat. Circulating hepatic transaminase elevation and ultrasound change are hallmarks of the condition. In a minority of cases, hepatic dysfunction ensues and progression to cirrhosis may occur. It is not known if body weight, body mass index (BMI), age, glycated-hemoglobin (HbA1C), liver enzyme levels (AST, ALT, ALP) and ultrasound findings are accurate predictors of pathologic severity of hepatic steatosis, and it is also not known if hepatic steatosis influences the degree of successful weight loss or glucose regulation after bariatric surgery.

**Methods used** This study retrospectively evaluated 100 patients who underwent a sleeve gastrectomy procedure, concurrent liver biopsy and lab-work at baseline and 6 months post-op.

**Summary of results** The best predictor of improved AST and ALT was the pathology score of severity of hepatic steatosis on H and E staining of liver biopsies obtained at the time of sleeve gastrectomy. Preoperative ultrasound scores did predict the variance in liver biopsy pathology scores, but did not predict the variance in AST and ALT improvement. Future directions of this study could take into account a greater number of subjects.

**Conclusions** It is anticipated that a greater understanding may emerge of the effects of these variables on the outcomes of future body weight and glucose control in bariatric patients. In addition, these findings may point to opportunities to identify individuals at greater risk for progression to cirrhosis and hepatic failure, possibly enabling earlier and more targeted therapies.

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#### A NEW MULTI-MODALITY PROTOCOL FOR KELOID MANAGEMENT USING ADVANCED TECHNOLOGIES

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10.1136/jim-2018-000939.284

**Purpose of study** Keloids are well known to be challenging sequelae to trauma and surgical procedures. They are produced in response to aberrant wound healing with overactive fibroblasts driving the proliferation of the keloidal tissue outside the initial boundary of trauma. Keloids are difficult to treat with no consistent and successful protocol for management. However, multiple-modality treatment methods combining surgical excision and immediate post-operative radiation have shown reduced recurrence rate. The purpose of this report is to demonstrate one such protocol showing success in treating multiple keloids on the same patient along with a subset of others. The patient is an African American male with a history of painful keloids over the torso, neck, and face with a surgical history of multiple resections and laser treatments over the last 8 years without significant reduction of keloidal burden.

**Methods used** Treatment protocol consists of: Topical Imiquimod for 6 weeks pre-resection, Triamcinolone 40 mg/ml injected into the planned excision margin 10–14 days pre-excision (dosage: 1 mg/kg body weight), surgical excision with no tension applied to closure using Integra artificial dermis, immediate post-op radiation (within 6 hours of resection), followed by steroid injection as listed above at 6 weeks and 10 weeks post-op.

**Summary of results** A right abdominal wall keloid was surgically excised following the above protocol to the subcutaneous tissue with design of advancement flaps to close most of the 72 cm<sup>2</sup> defect. Meshed Integra was used to close the remainder and the patient received adjuvant radiotherapy within 6 hours post-op. A single fraction 10 Gy electron beam radiation was used. Wound was completely epithelialized after 4 months with no recurrent keloids after 23 months. A left back shoulder keloid was excised similarly with complete wound healing at 5 months and no recurrent keloids at 19 months. Bilateral facial keloids were similarly excised with complete wound healing at 4 months and no recurrent keloids as of 11 months. Five other

patients have had single keloids excised following this protocol without recurrence with follow-up periods up to 14 months.

**Conclusions** Treatment of keloids with this multi-modality protocol is a promising step towards a consistent and successful form of management.

## Behavior and Development I

### Concurrent Session

10:15 AM

Friday, January 25, 2019

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#### SOCIOECONOMIC FACTORS IMPACT THE INFLUENCE OF ADVERSE CHILDHOOD EXPERIENCES ON HEALTH OUTCOMES

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10.1136/jim-2018-000939.285

**Purpose of study** Adverse childhood experiences (ACEs) are associated with chronic diseases in adulthood (such as cardiovascular disease, depression, and obesity) and health problems in childhood (such as behavior problems and early substance use). ACEs include physical, sexual, and emotional abuse; domestic violence; parental separation; and household substance abuse, mental illness, and incarceration. However, not all children exposed to ACEs develop poor outcomes. This brief review aims to collect published results on whether socioeconomic factors mediate or moderate the relationship between ACEs and health outcomes.

**Methods used** A PubMed search was conducted to find papers meeting four criteria: 1) measured exposure to ACEs; 2) measured socioeconomic factors (poverty/income, education, race/ethnicity); 3) conducted analyses for mediation or moderation; and 4) used a longitudinal or cohort study design. Filters restricted results to human studies published in English in the last 10 years.

**Summary of results** Screening by title and abstract of the 527 PubMed search results yielded 19 papers examining a relationship of interest; 4 more papers were included from paper references or personal libraries. There was support for moderation of the relationship between ACEs and child behavior problems by family poverty (3/3 studies) and child IQ (3/3). There was support for mediation of the relationship between ACEs and child risky behaviors by child IQ (2/2). There was support for mediation by adult poverty of the relationship between ACEs and adult physical health (3/3) and adult mental health (4/5). There was support for mediation by adult educational achievement of the relationship between ACEs and adult mental health (4/4).

**Conclusions** Current literature suggests that low-income children may benefit most from interventions reducing the impact of ACEs on behavior problems, and that interventions reducing adult poverty may be most effective for reducing the impact of ACEs on adult health outcomes. Interventions supporting educational achievement may positively impact outcomes for children and adults. More research is needed on

the influence of socioeconomic status on child physical health and on the potential influence of race/ethnicity.

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#### 'GRANDPA SPEAKS, NOBODY LISTENS.' GEROTRASCENDENCE, A CHANGE IN MINDSET OF ALASKA NATIVE ELDERS

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10.1136/jim-2018-000939.286

**Purpose of study** Meeting the needs of Alaska Native (AN) Elders in remote, indigenous communities is critical to supporting healthy aging and community sustainability. This study allows AN Elders from the Aleutian and Pribilof Island (API) region to share their experiences to better understand indigenous perspectives on successful aging. Local context and grounded perspective are needed to develop community specific health programs that help Elders cope with aging-related changes.

**Methods used** This study employed a community based participatory approach to interview 19 Elders from two API communities. Using a 20-item questionnaire based on Kleinman's explanatory model, researchers facilitated a discussion on aging and their experiences of being an Elder. Researchers conducted qualitative thematic analysis by identifying characteristics and activities of Elders responding to aging-related changes.

**Summary of results** This study identified 5 core elements of successful aging, 4 of which formed Lewis's AN model of successful aging (2011): *Mental and Emotional Wellbeing*, *Spirituality*, *Purposefulness*, *Physical Health and Mobility*, and *Gerotranscendence*. Perseverance, sharing with others, and family are important themes in *mental and emotional wellbeing*. Involvement with the Church and a strong connection to place are core components of *spirituality*. Elders describe generativity and a sense of *purpose* in engaging with their community. Acknowledging personal limitations and adapting to physical changes are key concepts of *physical health and mobility*. The unique finding of this study is the change in mindset Elders experience as they self-reflect, described by Tornstam (2005) as *gerotranscendence*. Elders describe being more intentional in their relationships and a realizing stronger connection to traditional cultural and spiritual activities.

**Conclusions** This exploratory study is a framework to help understand the experiences of AN Elders and what enables them to age well. This study has limitations and is not a comprehensive or exclusive list of activities and characteristics that ensure one will age successfully. Findings will inform health-care providers about Elders values and improve patient centered care. Community organizations can engage Elders in meaningful activities that promote well-being through self-reflection and purposeful teaching.

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#### PILOT TEST OF AN ONLINE BIAS REDUCTION CURRICULUM FOR MEDICAL STUDENTS

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10.1136/jim-2018-000939.287

**Purpose of study** Research indicates that unconscious biases on the part of health professionals impact patient-provider

interactions and health outcomes, particularly for racial/ethnic minority patients. Although training in unconscious bias is widely accepted by the medical community, the effectiveness of these educational efforts is not well documented, especially in the case of medical students. The current study aims to assess the effectiveness of a curriculum exposing medical students to the role of bias in healthcare and evidence-based strategies for reducing its impact on patient-provider relations.

**Methods used** As part of an online applied Preventative Medicine course, 168 third-year students from a medical school in Southern California learned about the role of bias in healthcare, took an implicit association test, and were introduced to evidence-based strategies for overcoming bias. Students' written reflection assignments concerning the implementation of a bias reduction strategy with a patient were qualitatively analyzed. Changes in pre and post tests were examined regarding knowledge and attitudes about the role of bias in healthcare and confidence using the evidence-based bias reduction strategies.

**Summary of results** Results from the written reflection assignments revealed that perspective-taking (n=51) and seeking individuating information (n=30) were the most frequently addressed bias reduction strategies. The most frequently reported biases were associated with patient's weight (n=58) and ethnicity/race (n=36). Pre and post test scores revealed significant improvements in knowledge (p=0.00) and awareness (p=0.00) about the role of bias. Students' self-confidence in their ability to recognize their own biases (p=0.00) and employ bias reduction strategies (p=0.00) also improved based on an examination of pre and post test scores.

**Conclusions** An online module including active learning strategies significantly improved medical students' knowledge about the role of bias in health care, bias awareness, and confidence employing evidence-based bias reduction strategies with patients. Future research should examine whether such a brief online bias reduction curriculum has long-term implications for addressing medical student bias and its direct impact on patient-provider interactions.

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#### MATERNAL-FETAL LEAD TOXICITY FROM AN OLD SLUG: THE POISONED INFANT AT 21

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10.1136/jim-2018-000939.288

**Case report** Our prior report described a female delivered at term by caesarean section to a 31 year old cashier who had been shot at age 16, the bullet lodging in the body of her fourth lumbar vertebra. The mother's blood lead (Pb/B) had risen from 31 mcg/dl in her second trimester to 75 and 85 mcg/dl two months post-partum (normal Pb/B, 5 mcg/dl). The infant's birth defects were many. They included tracheo-broncho-malacia with compression of the left main bronchus by a large patent ductus arteriosus, dysplasia of the aortic valve with a tortuous aorta, and a large patent foramen ovale. Surgery corrected the cardiovascular abnormalities, but magnetic resonance imaging of the brain was done for developmental delay. Partial septo-optic dysplasia was found with hypoplasia of the septum pellucidum, thinning of the corpus

callosum, and dilated cerebral ventricles. Bilateral hearing deficits at 13 weeks exceeded 55 decibels in each ear. She went home with nasal oxygen and hearing aids. Her Pb/B was 37 mcg/dl at 19 weeks, falling to 20 mcg/dl after 4 cycles of dimercaptosuccinic acid chelation. It stabilized at 4 mcg/dl at 30 months, and was undetectable at age 16. Her oxygen need resolved at age 12 months. She had recurrent left lower lobe pneumonia 4 times, but not after age 10. Recent pulmonary follow-up noted rare use of albuterol for asthma. Spirometry was normal. Cardiac ultrasound showed stable, 4 cm dilation of the ascending aorta. Her cardiologist concluded 'She is doing very well.' Routine follow-up at age 22 is planned.

**Conclusion** It is unclear if chelations at weeks 18–24 played a role in the infant's development in the face of her serious birth defects, many of which were successfully treated by early surgery. Such chelations of lead-exposed children at 12–40 months had no benefit in 2 large series. All that can be said is that this chelation during infancy appeared well tolerated and may have been helpful. A recent report raised the possibility that chelation of the mother prior to her pregnancy might have avoided the serious fetal toxicity which occurred. It seems unlikely that many toxicologists would have done so in this case, since the mother's Pb/B was only 31 mcg/dl. Orthopedists who saw her during her 20 s recommended no treatment.

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#### IMPACT OF MATERNAL VERBAL SCAFFOLDING ON LANGUAGE AND COGNITIVE DEVELOPMENT IN TODDLERS WITH PRENATAL POLYSUBSTANCE EXPOSURE

<sup>1</sup>J Lowe, <sup>1</sup>A Qamruddin, <sup>2</sup>C Murray-Krezan, <sup>2</sup>J Stephen, <sup>1</sup>R Rieger, <sup>1</sup>S Cano, <sup>1</sup>L Bakhireva. <sup>1</sup>University of New Mexico, Albuquerque, NM; <sup>2</sup>MIND Institute, Albuquerque, NM

10.1136/jim-2018-000939.289

**Purpose of study** Prenatal polysubstance exposure (PPE) can result in a variety of developmental sequelae. This study examines maternal scaffolding on the development of toddlers with PPE.

**Methods used** Fifty-one maternal-infant pairs (25 PPE and 26 controls) were identified from the ENRICH study. Maternal-infant pairs were seen at: birth, 6 months, and 20 months. At 20 months, verbal scaffolding was coded during a 5 min video of mother and child play. A diagnostician administered the Bayley Scales of Infant Development (BSID-III). Scaffolding scores between PPE and control subjects were compared. Association between maternal scaffolding and infant BSID-III language and cognitive scores were assessed by correlation and multiple linear regression. The scaffolding-by-maternal education and scaffolding-by-study group interactions were examined.

**Summary of results** The sample included 63% Hispanic/Latina mothers; 43% of mothers had high school or lower education; 51% of infants were female; and the average age of child at assessment [CMMK1] was 20.2±1.2 months. There were no significant differences in the total scaffolding scores between the study groups (p=0.6). There was a significant association between total scaffolding and BSID-III language (r=0.4; p=0.003), and also between complex scaffolding and language (r=0.4; p=0.005). In multivariable analysis, maternal education (p=0.001) and

total scaffolding ( $p=0.01$ ) were significant predictors of infants' language development. Maternal education ( $p=0.0007$ ) but not scaffolding ( $p=0.6$ ) was a significant predictor of BSID-III cognitive development. Neither study group nor the interaction between study group and total scaffolding were significantly associated with language or cognitive development. The interaction between total scaffolding and maternal education was not significant for either outcome.

[CMMK1]As the statistician, I request this remains. It is important to explicitly state what is being reported.

**Conclusions** These preliminary results demonstrate that maternal education and scaffolding, but not PPE, have a strong association with infant language development.

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#### PARENTAL PERCEPTION OF CHILDREN'S BODY WEIGHT AND CHILDREN'S BMI

J Sawada, Y Lozano, A Carnduff, E Williams, S Harris, C Irani, E Medina, M Baum. *Loma Linda University, Loma Linda, CA*

10.1136/jim-2018-000939.290

**Purpose of study** The adult obesity rate in San Bernardino is 27%, as this has been an increasingly concerning issue especially regarding those within the low-income population, with limited access to health choices of food and environments to exercise. Parental perception of whether their child is of healthy ( $BMI < 85\%$ ) or unhealthy weight ( $BMI > 85\%$ ) might further add complexity of obesity in children of low income families. This study examines whether or not parents' perception of their children's body weight is correlated to their children's actual BMI.

**Methods used** Children in San Bernardino County, from ages 9–15 years, were referred by a pediatric clinic to participate in Operation Fit, a camp designed to teach kids about exercise and nutrition to live healthier lifestyles. This camp was aimed at children at an unhealthy BMI. At the week long day camp, a parental survey included a question assessing their impression of their children's weight. Their answers were compared to their children's BMI.

**Summary of results** Logistical analysis was used with a sample size of  $n=705$ , which evaluated the difference between the frequencies of parents perceiving their children as 'too skinny, too fat, or just right' and their children having a healthy weight compared to an unhealthy weight ( $BMI > 85$  percentile). Based on the frequencies alone, 69.57% of parents who perceived their children as 'just right' had children with an unhealthy weight, while 66.17% of parents who perceived their children as 'too fat' had children with an unhealthy weight. A follow up chi-squared test was done but showed no statistical significance ( $p=0.15$ ).

**Conclusions** The results showed no statistically significant association between parents' perception of their children's weight and their children having an unhealthy weight.

Parental perception of their children's weight is based on variable subjective criteria which may contribute to predictive factors outside of the scope of this study, as further studies can be done to better understand this relationship.

## Global Health II

### Concurrent Session

10:15 AM

Friday, January 25, 2019

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#### COMMUNITY DELIVERY AND UPTAKE OF CONTRACEPTION AND GENDER-BASED, POST-VIOLENCE CARE AMONG YOUNG WOMEN IN SEME SUB-COUNTY, KENYA

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10.1136/jim-2018-000939.291

**Purpose of study** Kenyan women aged 15–24 experience higher mistimed and unwanted pregnancies than in other age groups, and 58%–90% report not using any contraceptives. Additionally, HIV infections are highest in this age category and young women in sub-Saharan Africa are twice as likely to be infected as young men. This exploratory mixed-methods study was conducted in partnership with Pamoja, a community-based organization in the Seme sub-county, in rural western Kenya. Low uptake for contraceptives and gender-based post-violence care (GBPVC) for women in the DREAMS (Determined, Resilient, Empowered, AIDS-Free, Mentored, Safe) Initiative were identified by Pamoja. DREAMS is a US government funded program that aims to reduce HIV rates among women aged 10–24. This study aimed to provide insight into the challenges surrounding delivery of contraception and GBPVC as HIV prevention strategies among a vulnerable population in rural Kenya.

**Methods used** Five focus group discussions (FGDs) ( $n=40$ ) were conducted with women aged 18–24 who were enrolled in DREAMS. FGDs were held in different areas of Seme in order to obtain a representative sample. A discussion guide was developed with questions regarding knowledge, attitudes, and availability/access of contraceptives and GBPVC; questions were designed to explore how women thought about and made decisions regarding these topics. FGDs were led by a team of students from the University of British Columbia, Canada, with a Pamoja staff member fluent in Luo translating during the interviews. Key Informant Interviews ( $n=10$ ) were also conducted with health service providers and Pamoja staff members. All discussions were recorded for transcription and translation purposes.

**Summary of results** Qualitative data analysis using NVivo is in progress and results are pending. Preliminary analysis has shown significant misconceptions, myths, and stigma persisting around contraception and GBPVC, signifying a need for continued community education.

**Conclusions** This exploratory study helped to identify knowledge gaps and operational considerations that can be addressed and modified in community programs such as DREAMS to increase uptake of contraceptives and GBPVC among AGWY and ultimately to reduce HIV transmission.

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### IMPACT OF FOOD SECURITY, DIET, DIABETES, AND HYPERTENSION ON ISCHEMIC HEART DISEASE IN THE DOMINICAN REPUBLIC

A Maret, M Fotoohi, R Rauber. *University of Nevada, Reno School of Medicine, Reno, NV*

10.1136/jim-2018-000939.292

**Purpose of study** The leading cause of death worldwide is ischemic heart disease (IHD), accounting for 11.2% of all deaths. In the Dominican Republic, IHD and cardiovascular disease (CVD) are the foremost causes of premature, preventable death with mortality rates twice that of other Central American countries. Over the past decade, IHD/CVD morbidity and mortality in the Dominican Republic have failed to improve despite aggressive prevention and treatment programs. Similar trends were observed throughout Central America. The severe, persistent health impact of IHD on communities in this region necessitates continued research to understand how local circumstances contribute to its prevalence and mortality.

**Methods used** Hypothesized local IHD risk factors include rising rates of diabetes and food insecurity (having limited/unreliable sources of safe, nutritional food), minimal healthcare access, and dietary guideline ignorance. Relationships between IHD and health metrics were also examined (including blood glucose, BMI, blood pressure, and chronic diseases). Data was collected from 70 participants in rural areas of the Dominican Republic using surveys, glucometers, and sphygmomanometers. Subjects were grouped based on the above metrics, and group rates of reported chest pain and pre-test coronary artery disease scores were compared.

**Summary of results** Patients experiencing typical chest pain had significantly increased blood pressures (mean of 150 versus 137,  $p=0.044$ ) and were more likely to meet diagnostic criteria for hypertension ( $p=0.065$ ). Approximately 21% of the population had elevated blood sugar, of which only 20% were receiving treatment. Nearly 80% of the population had a low or very low degree of food security (55% and 23%, respectively). Of the eleven measured dietary guidelines, 58% of individuals were meeting them only 'somewhat well' (meeting five to six goals) and 20% were meeting them 'not well at all' (four or fewer).

**Conclusions** These results demonstrate the prevalence of examined risk factors and suggest a correlation between these measures and IHD/CVD in the region. Suggested interventions are included that specifically target local deficiencies in healthcare and individual behaviors, emphasizing accessibility and feasibility in both at risk populations and global health settings.

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### SICKLE CELL DISEASE IN THE INDIGENOUS THARU POPULATION OF NEPAL: A SUSTAINABLE APPROACH TO IMPROVING AWARENESS IN THE COMMUNITY THROUGH THE TRAINING OF COMMUNITY HEALTH WORKERS

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10.1136/jim-2018-000939.293

**Purpose of study** Among the indigenous Tharu population of Nepal, there is a high prevalence of sickle cell disease; an estimated 9.3% of the population screens positive for the HbS allele. Since 2015, our research team has worked to establish screening and diagnosis for sickle cell disease (SCD) in the

rural district of Dang, Nepal. A needs assessment indicated that, although many are affected by the disease, the population has a poor understanding of SCD and screening rates would likely improve following education and knowledge dissemination within the community.

**Methods used** In partnership with Creating Possibilities Nepal, an educational module on SCD was developed for the community. Topics included: physiology, causes/inheritance, signs/symptoms, diagnosis, and treatment of SCD. Community health workers (CHWs) were invited from the local health posts to attend a 6 hour training day. During the session, CHWs furthered their understanding of SCD through interactive learning and facilitated discussion. A questionnaire was used to assess knowledge of SCD before and after the session. **Summary of results** Forty-two CHWs were trained to deliver the SCD module, ranging from 27 to 62 years old (mean=43 YO); their experience working as a CHW ranged from 2 months to 37 years (mean=17 years). Ninety-five percent of participants had previous experience leading health information sessions, but none on the topic of SCD. Knowledge of sickle cell disease improved after the training day by 43% (mean baseline score 3.76/8 (SD 3.31) v 7.21/8 (SD 0.81),  $p<0.0001$ ).

**Conclusions** The SCD training session was successful in educating the CHWs; they have gone on to share information by leading SCD information sessions at their local health posts and mothers group meetings. This approach has resulted in a sustainable model for improving screening rates and knowledge of SCD in Dang. Periodic knowledge reinforcement sessions will be held for CHWs. Future efforts should focus on establishing record keeping at local health posts, improving infrastructure for rural SCD medication delivery, and overall access to care.

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### DEPRESSION AND SUICIDALITY IN NAIVASHA, KENYA; INVESTIGATING THE INTENTIONALITY OF POISON INGESTION AND PROVIDING CLINICAL TOOLS FOR THOSE CARING FOR SUICIDAL PATIENTS

S Lawson. *University of Washington, Anchorage, AK*

10.1136/jim-2018-000939.294

**Purpose of Study** Kenya is a low to middle income country with a high prevalence of depression and suicide via poison ingestion. I aimed to assess the etiology of poisonings in Naivasha, to provide training on suicide screening and safety planning for community health workers, and to provide hospital staff with education and tools to intervene with patients that attempt suicide.

**Methods used** Records from the Naivasha District Hospital were reviewed from December 2017 to June 2018. Data abstraction from 76 charts internally coded for poisoning focused on demographics, intentionality, type of poisoning, and treatment. I designed continuing medical education that included a literature review on depression, suicidality, organophosphate poison (OPP) and other pesticide poisonings as well as a 'pocket card' on commonly ingested toxins. I provided training to several clinics on PHQ-9 and CESD-10 depression screening tools that have been validated in Kenya as well as safety planning guidelines for clinicians managing patients expressing suicidality. Evaluation of the educational resources was done via self-assessment surveys.



**Summary of results** 97% of poisonings in the Naivasha district hospital over 7 months were intentional, compared with 60%–80% of poisonings in similar communities worldwide. Men aged 21–30 were most likely to die of intentional poisoning (7%). The most common reason for suicidality was a quarrel with a loved one or family member. Only 8% of poisonings were with OPP, however, nearly 85% of poisonings were given an OPP treatment, atropine. Generally, clinicians felt positively and wanted to implement the clinical tools, however, a subset felt the tools would fail patients without adequate systemic mental health care.

**Conclusions** The relatively high proportion of intentional poisonings at the Naivasha hospital suggest that suicidality is a significant problem in the community. There have been several recent studies demonstrating high rates of suicidality and easy access to agricultural toxins in Kenya. Taken together, these findings suggest that Naivasha faces a serious problem of suicidality and poisoning. Possible methods to address that concern include: increased staffing of psychiatric clinicians, regulation of pesticide sales, and implementing educational public health campaigns.

#### 296 QUALITY IMPROVEMENT OF INTRODUCTORY FEMALE REPRODUCTIVE HEALTH EDUCATION IN RURAL NEPAL

Z Zhou. *University of Washington, Bozeman, MT*

10.1136/jim-2018-000939.295

**Purpose of study** Reproductive health topics are social taboos in Nepal. Cultural beliefs that isolate and stigmatize menstruating women are prevalent. In addition, due to enduring tradition and poverty, arranged marriages for young girls are common and result in teen pregnancies. Lack of reproductive-health knowledge makes teenage girls vulnerable to long-term health and socioeconomic consequences. The Department of Community Programs (DCP) at Dhulikhel Hospital (DH) provides reproductive health education in rural communities; but the only teaching material DCP had was powerpoint presentations. This project aimed to assist DCP in improving the quality and measuring the effectiveness of introductory teaching materials on female reproductive health for 7th- to 10th-grade students in rural communities served by DH.

**Methods used** Background research identified several sources, including the Nepal Demographic and Health Survey 2016, the Health Ministry's Annual Report, and several primary studies and review articles about reproductive health in Nepal. Informal conversations with local residents provided cultural and social insights for the project. Interviews with community partners, physicians at DH and educators at DCP, helped establish project aims and identify educational topics for quality improvement.

**Summary of results** A curriculum was written to cover three sequential lessons: 1) Female Reproductive System and Puberty, 2) Menstruation and Menstrual Cycle, and 3) How Pregnancy Occurs, Teen Pregnancy and Family Planning. For each lesson, a powerpoint presentation, lesson plan and assessment quiz were created. Four DCP educators who reviewed the new curriculum at a workshop found the materials simple to use and appropriate for the target audience. Twenty-six female 7th-grade students participated in a trial lesson on menstrual cycle at a local private high school. Mean quiz scores improved from 56% before to 88% after the lesson.

**Conclusions** The project provided a concrete and concise basis for educators at DCP to prepare for and teach lessons in the new curriculum, which could be a building block for related materials in the future. Next, DCP partners will translate the new teaching materials into Nepali and begin teaching the lessons in their target audience. Collaborative efforts to revise and improve products from this project will be ongoing.

#### 297 HYPERTENSION EDUCATION IN A COMMUNITY BASED SETTING FOR SOMALI IMMIGRANTS

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10.1136/jim-2018-000939.296

**Purpose of study** Purpose/background: Auburn, WA is home to many rapidly growing groups of immigrants and refugees including Somali, Iraqi, and Marshallese. Traditional service providers in this area have lacked educational programming that has been vetted by and developed for these communities.

**Methods used** Methods: Interviews were conducted with community members at the Auburn YMCA, Auburn Food Bank, Refugee Women's Health Alliance, and the Somali Health Board about the strengths and challenges they saw in these communities. Common concerns were increasing rates of chronic disease such as hypertension, diabetes, and obesity. The Somali community was identified as a population of interest given its long history of strong community health promotion in northern King County and the recent immigration of many Somali families to the Auburn area.

**Summary of results** Results: To target this area of concern, a literature review was produced on the topic of disease and disease prevention in immigrant communities and the effectiveness of various modalities of hypertension education. Additionally, a pilot interactive education seminar on hypertension was provided to the Auburn YMCA and Somali Community Health Board with the first session scheduled for autumn 2018 in south Seattle. A second session is still being explored which would take place at the Auburn YMCA.

**Conclusions** Conclusions: Immigrant communities face unique health challenges and are often underserved by traditional service providers. Auburn, WA, given its growing number of immigrant and refugee residents, is particularly well positioned for a health intervention designed for these communities. Next steps would include implementation of the hypertension education pilot program in Auburn WA.

#### 298 EXAMINING THE FACTORS AFFECTING IMMUNIZATION FOR UGANDAN CHILDREN

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10.1136/jim-2018-000939.297

**Purpose of study** The purpose of this study is to understand, from the perspectives of caregivers and local health care professionals, what factors affect immunization for Ugandan children.

**Methods used** Questionnaires were administered from July 16th to August 4th, 2018, in the form of interviews, to caregivers and local health care professionals at Soroti Regional

Referral Hospital, in Soroti, Uganda. Caregivers of children aged 9 to 23 months and health care professionals who were involved in pediatric care and/or administration of vaccines were invited to participate in the study. The collected data was analyzed with SPSS statistical analysis software and thematic analyses were done.

**Summary of results** Most caregivers (98%) felt that vaccines were beneficial for their child and 74% of caregivers responded that vaccines were beneficial because they prevented diseases. Moreover, 74% of caregivers accurately reported that child immunization begins at birth, but only 10% accurately reported that child immunization ends at nine months. The main factors that affect immunization for Ugandan children were identified to be miscommunication between caregivers and the health care professionals administering vaccines and inconsistent immunization schedules found on the Child Health Cards. Inaccuracy in recording the dates of immunizations and miscommunication of the vaccines given or not given are categorized under 'miscommunication'. Furthermore, as suggested by the participating caregivers, the emerging themes for why other caregivers may not vaccinate their children are lack of information and misconceptions rooted in fear and mistrust of vaccines.

**Conclusions** This study has identified a need for immunization education outreach, especially for caregivers who live in remote villages far from health facilities. Most caregivers had a positive attitude towards child immunization but lacked information about the benefits of vaccines. Furthermore, this study identified two factors that affect immunization for Ugandan children: miscommunication between caregivers and health care professionals and inconsistency in the immunization schedule found on the child health cards.

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### IMPLEMENTING A MOBILE APP FOR FIELD GLOBAL HEALTH RESEARCH: SUCCESSES, CHALLENGES, AND FUTURE DIRECTIONS

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10.1136/jim-2018-000939.298

**Purpose of study** To simplify the data collection process for an established project aimed at maternal-neonatal quality improvement in the rural Nepal Himalaya.

**Methods used** In May 2017, data collection was transferred from a paper-based system to EpiCollect5 (Imperial College London), a not-for-profit integrated data collection software that allows for offline data collection and later upload to a secure server. Implementation required training Nepali health workers on the app, addressing technical issues, adapting current databases, and integrating datasets from before and after the method switch. Visiting physicians and medical students also required ongoing training.

**Summary of results** In the 15 months since implementation, 395 surveys have been administered. Principal Investigator Dave Levy, MD states 'It has become our preferred method for collecting data as seen by our field team making the change from pen/pencil and paper to EpiCollect without any input from us on whether to do it/not do it.'. Ang Jangmu Sherpa, Program Manager, remarks 'It is easy to use. Don't have to carry paper. Save time and energy as well as good

for environment if we don't have to use [a lot] of paper.' The app also allows for collection of GPS coordinates for each survey. All members of the field team owned an compatible Android or iOS device prior to implementation. Challenges included the initial training period, lack of electricity in remote villages to charge devices, and the necessity to sustainably train permanent and visiting staff.

**Conclusions** Mobile data collection has the potential to streamline research projects in developing countries. It allows for standardized data collection and enables new measurements. This cloud-based system has allowed for faster data sharing between Nepal and the US, and may allow for potential new projects including tracking neonatal outcomes over time using GPS coordinates. EpiCollect5 has been adopted by Nepali team members for its efficiency and ease-of-use, and they have thus far been able to sustainably continue the use of the app with little outside assistance.

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### BARRIERS TO CONTRACEPTIVE CARE AMONG RESETTLED SYRIAN REFUGEE WOMEN

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10.1136/jim-2018-000939.299

**Purpose of study** Amidst efforts to address the unique health needs of resettled refugees in the United States, barriers to reproductive healthcare among refugee women remain understudied and poorly understood. As the national political climate becomes increasingly hostile to both refugee and women's health, a qualitative study of this underserved, vulnerable population's experience of reproductive healthcare is urgently needed to address disparities in access to high-quality, respectful contraceptive care. This study identifies factors that contribute to disparities in access to contraceptive care while exploring resettled refugees' lived experiences of family planning services and interactions with reproductive healthcare providers more broadly.

**Methods used** The study employs the ethnographic methods of participant observation and person-centered interviewing (Levy and Hollan 1998), through which participants' life narratives, future aspirations, and deepest struggles are elicited to gain a holistic understanding of the individual's experience.

**Summary of results** In addition to the typical obstacles individuals of low socioeconomic status face when seeking healthcare, unique cultural, religious, and language barriers exist between refugee populations and healthcare providers. Such barriers become particularly salient in the field of family planning, in which patients' religious beliefs and cultural background may have an especially strong impact on their interactions with providers and even on the decision to seek care at all. Personal histories of war trauma and sexual violence add an additional layer of complexity to refugees' experiences of reproductive healthcare.

**Conclusions** Barriers to contraceptive care for resettled refugee women exist at the individual, community, and system-wide level. There is an urgent need for further exploratory research on barriers within specific communities to inform provider trainings and develop strategies for integrating culturally-sensitive, non-judgmental contraceptive counseling into routine care.

## Health Care Research II

## Concurrent Session

10:15 AM

Friday, January 25, 2019

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**THE USE OF ARTIFICIAL INTELLIGENCE IN TEACHING HUMAN HISTOLOGY**

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10.1136/jim-2018-000939.300

**Purpose of study** Learning the normal histologic characteristics of human tissue can be challenging for medical students, as the histologic details that distinguish one type of tissue from another can be quite subtle. Assistance from an artificial intelligence (AI) system trained in identifying these slight variations can save time and enhance long-term retention for students. Our application is designed to help in teaching normal histology by providing the learner with a differential diagnosis list of tissue types that have visual features similar to those in a given image. This will assist the learner in recognizing the differences between similar specimens while allowing the learner to actively be engaged in learning the topic through use of multiple complimentary resources.

**Methods used** In order to design the most accurate AI/machine learning (ML) model, multiple algorithms (Alexnet, Squeezenet and Resnet50) were employed and then compared to build models through a transfer learning approach. A fixed number of images per histology tissue type was employed to train these deep neural network algorithms. The algorithm that produced the model with the best performance across all histology types was then incorporated into the iOS and android app. The app allows learners to take a photo of a microscopic image using their mobile device, or upload a photo from another source, for which the machine gives a differential identification of the source image.

**Summary of results** Not surprisingly, our preliminary results show that the predictive capability of our histology ML models is directly tied to the respective deep neural network employed in building these models. In general, the models built with the Resnet50 neural network outperformed those that used Alexnet and Squeezenet.

**Conclusions** The goal is to ultimately build an accurate AI/ML model that is deployed on an iOS and android mobile device as a standalone app independent of cellular data and internet, with a very user friendly interface.

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**EVALUATION OF A CLINICAL PATHWAY FOR ROCURONIUM BLOCK AND NEOSTIGMINE OR SUGAMMADEX REVERSAL**

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10.1136/jim-2018-000939.301

**Purpose of study** Postoperative residual neuromuscular blockade (PRNB) is a frequent complication in patients receiving

rocuronium, observed in 41% of cases in our prior data and 34%–57% in the literature. A new reversal agent, sugammadex, may be more effective in reducing PRNB, however, its acquisition cost is \$89 versus \$19 for the alternative, neostigmine with glycopyrrolate. The aim of this study was to evaluate a protocol for management of rocuronium and reversal, with choice of reversal agent based on depth of block.

**Methods used** We developed a protocol for the management of rocuronium and reversal to reduce known PRNB risk factors: 1. Adjust rocuronium dose for patient age, gender, and BMI; 2. Reverse rocuronium blockade with neostigmine only if 4 twitches without fade are present, or with sugammadex for deeper blocks. Acceleromyography was used to measure train-of-four ratio (TOFR) in the PACU. Patients ages 18–80 years undergoing abdominal or orthopedic surgery at Harborview or University of Washington Medical Centers and requiring rocuronium reversal between May 21 and Sept 21, 2018 were included. The primary endpoint was the incidence of PRNB on arrival to the PACU, defined as normalized TOFR <0.9. We calculated actual pharmacy costs and estimated the cost if sugammadex were to be used for all cases.

**Summary of results** We enrolled 125 patients; complete data were available for 112. Mean age was 47 years (SD 16), mean BMI 28 kg/m<sup>2</sup> (SD 6), 50 (45%) were women. 68 (61%) patients were reversed with neostigmine. The overall incidence of PRNB was 4.5% (95% CI: 1.4, 10.1%). The total acquisition cost for all reversal drugs was \$5208. The cost would have been \$9968 with unselected sugammadex use.

**Conclusions** A protocolized management of rocuronium and neostigmine or sugammadex reversal was associated with a low incidence of PRNB. Assuming 30 million patients in the US undergo pharmacological reversal after perioperative paralysis annually, adoption of this protocol in appropriately selected patients could save more than \$1 billion compared to universal use of sugammadex. A RCT could compare this protocol to the use of sugammadex in all cases, in terms of both the incidence of PRNB and cost.

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**THE EFFECT OF A TWO-WAY RADIO SYSTEM UPON CLINICAL COMMUNICATION**

JR Brown, Z Campwala, A Li, H You, AS Amasyali, M Alsyof, M Shah, M Hajiha, D Baldwin, S Abourbih, D Baldwin. *Loma Linda University, Loma Linda, CA*

10.1136/jim-2018-000939.302

**Purpose of study** Improving communication between doctors and nurses in a clinic setting may improve efficiency and patient satisfaction while decreasing costs. The purpose of this study is to evaluate the impact of two-way radio communication in the urology outpatient clinic and its effect on efficiency and patient satisfaction.

**Methods used** Members of the urologic clinic including an attending physician, endourology fellow, clinic nurse and clinic MA wore two-way radio headsets during typical clinics. In half of the visits the nurses radios were not on (controls), in the other half all radios were on (experimental setting). Patients and reviewers were blinded to radio function. Blinded, independent reviewers measured efficiency during 8 clinic days over an 8 week period. Primary endpoints included the time from physician completing

discharge documents to patient receiving discharge paperwork, and time from physician completing discharge documents to patient discharge. Secondary outcomes included a questionnaire for patient and staff regarding the satisfaction with the radio system. Statistical analysis were performed using a Mann-Whitney U test, with  $p < 0.05$  considered significant.

**Summary of results** Times for 110 visits during 8 different clinics were compared including 55 with the two-radios on, and 55 visits with radios off. Use of the radio decreased the time between the printing of discharge documents and the patients receiving the documents by 66% (2.3 vs 6.75 mins respectively;  $p < 0.001$ ). In addition, radio use resulted in a 58% decrease in total discharge time (3.3 vs 7.8 mins respectively;  $p < 0.001$ ). 92% of patients felt the doctor's radio use did not impact communication. During the period of radio use, the physicians overall satisfaction ranking rose from 13/15 to 5/15 compared to other physicians in the group. 83% of staff agreed or strongly agreed that two-way radio use improved efficiency.

**Conclusions** Implementation of radio communication in a clinic setting showed a significant decrease in patient wait times and total discharge time. Improved clinic efficiency improved patient and staff satisfaction and may improve quality and reduce costs.

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#### DYSPHAGIA IN HEALTHY ELDERLY ADULTS: HOW IMPORTANT IS GLOTTIC INSUFFICIENCY?

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10.1136/jim-2018-000939.303

**Purpose of study** Dysphagia is a major cause of morbidity in elderly patients. Though often studied, the process and true prevalence of dysphagia in this population remain unknown. In this study, we enrolled healthy elderly persons to determine which voice and aerodynamic parameters are associated with dysphagia. Our hypothesis was that glottic insufficiency would be a contributor to dysphagia in elderly patients.

**Methods used** A prospective study was established with enrollment of consecutive consenting adults over 65 with dysphagia but no major laryngeal, neurologic, or oncologic pathology presenting to a tertiary center. Patient questionnaires included VHI-10, RSI, CSI, DSI, SVHI-10, EAT-10, and PILL-5. Acoustic and aerodynamic measures and a full ENT exam including stroboscopic imaging and FEES were obtained. The data was divided into two groups based on whether the patient endorsed he/she had dysphagia or not when asked.

**Summary of results** There were no significant differences in Maximum Phonation Time [Nondysphagic (ND): 15.63 s  $\pm$  8.78; Dysphagic Patients (D): 15.19 s  $\pm$  6.85], Noise-to-Harmonics Ratio (ND: 0.22  $\pm$  0.10; D: 0.27  $\pm$  0.15), Mean Airflow During Voicing (ND: 137.90 L/sec  $\pm$  93.96; D: 110.00 L/sec  $\pm$  74.58), or Mean Peak Air Pressure (ND: 6.99 cm H<sub>2</sub>O  $\pm$  2.60; D: 6.10 cm H<sub>2</sub>O  $\pm$  1.90) between the dysphagic and nondysphagic groups. Questionnaire data showed EAT-10 (ND: 2.00  $\pm$  2.89; D: 10.29  $\pm$  6.98) and PILL-5 (ND: 1.11  $\pm$  1.63; D: 5.11  $\pm$  4.42) scores were

significantly higher in the dysphagic group than the nondysphagic group while VHI (ND: 16.79  $\pm$  11.54; D: 10.59  $\pm$  10.48) scores were not significantly different. Mean age for the dysphagic group was 74, nondysphagic was 74. 15/19 nondysphagic patients and 12/17 dysphagic patients were female.

**Conclusions** While aging commonly causes presbyphagia, our patient questionnaire data indicates that not all elderly patients suffer from dysphagia. The patient's subjective account of dysphagia was validated by the EAT-10 and PILL-5 patient questionnaires. In contradiction to our hypothesis, no significant difference in aerodynamic or acoustic measurements between dysphagic and nondysphagic elderly patients indicates that glottic insufficiency may not be a significant contributor to presbyphagia in this population.

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#### ACCESS TO FAMILY PLANNING IN RURAL COMMUNITIES PRIMARILY SERVED BY CATHOLIC HOSPITALS: A MYSTERY CALLER STUDY

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10.1136/jim-2018-000939.304

**Purpose of study** Catholic hospitals account for one in six acute care hospital beds. A total of 46 hospitals are considered sole community hospitals, a designation that generally refers to care in remote locations, and three are located in Colorado. Catholic hospitals are expected to follow the *Ethical and Religious Directives for Catholic Health Care Services*, which applies the Catholic doctrine to the practice of medicine and results in prohibition of common reproductive services. Little is known about reproductive health care access in rural communities served primarily by Catholic hospitals. The purpose of this study is to understand access to family planning service appointments in three rural communities (Grand Junction, Durango, and Canon City) that are served by Catholic sole community provider hospitals.

**Methods used** We performed an online search of all general obstetrics and gynecology (ob/gyn), family practice, and midwifery practices in Grand Junction, CO. For each practice in Grand Junction, we called five different times, each one week apart, and queried about availability of (1) short-acting reversible contraception (pill, injection), (2) long-acting reversible contraception (intrauterine device [IUD], implant), (3) emergency contraception (EC), (4) tubal ligation (interval, postpartum), and (5) abortion using structured telephone scripts. We are conducting similar calls in Durango and Canon City.

**Summary of results** We reached all of the 25 eligible practices for each of the calls. Nine practices were ob/gyn, 15 were family medicine, and one was a midwifery practice. Amongst these, 96% offered a birth control or contraceptive pill appointment, 88% injectable contraception, 78% IUD, 65% implant, 8% EC, 20% tubal ligation, and 4% abortion. No practices offered all services. Most denials to appointments were based on the practice not having a trained provider (e.g. a family medicine practice that cannot provide surgical services) and Catholic affiliation was rarely cited as a reason for denial (4%–16% of denials).

**Conclusions** There was little restriction to family planning services secondary to Catholic health care affiliation in Grand

Junction, CO. We will survey two other rural communities to determine if this pattern is consistent.

**306 ABILITY OF OPIOID-IMPAIRED USERS TO INTERACT WITH A SMARTPHONE**

J Carlile, J Sunshine. *University of Washington School of Medicine, Anchorage, AK*

10.1136/jim-2018-000939.305

**Purpose of study** The United States is experiencing an opioid overdose epidemic. Since 2010, overdose deaths have increased by more than 200% due in part to the introduction of illicit fentanyl which can cause acute respiratory failure. The overdose rescue drug naloxone has saved thousands of lives. Yet illicit opioid users often use alone, which increases risk of fatal overdose by decreasing opportunity for intervention. One potential solution (developed by our research team) is a contactless self-monitoring smartphone app which can detect respiratory depression and call naloxone-equipped friends, family or emergency medical services. A key challenge of self-monitoring is minimizing false alarms; to address this, we sought to measure opioid users' ability to interact with a smartphone after an opioid injection (and thus their ability to terminate a false alarm). We hypothesized that when users were impaired but not in acute distress, they would be able to interact with a smartphone.

**Methods used** We conducted a pilot study at the InSite Supervised Injection Facility in Vancouver, Canada. Opioid users were consented by InSite staff and taught how to turn off a smartphone alarm. Participants were monitored for 30 s prior to injection, and a 2 min smartphone countdown alarm was set upon injection completion. Monitoring continued for 30 s post-alarm. Then researchers explained the concept of a smartphone-based self-monitor which could call for help if an overdose was detected. Participants were asked if they would use such a device and how many 'false alarms' they could reasonably tolerate.

**Summary of results** Of 42 participants who successfully injected, 83% turned off the alarm within 30 s, 7% tried to turn it off but had interface challenges, and 9% made no effort. None of the participants experienced an overdose. Of 50 participants asked if they would use such an app, 72% responded 'yes', 12% 'maybe', and 6% 'no' (the remaining 10% declined to answer).

**Conclusions** Our pilot study tested opioid users' ability to interact with a smartphone while impaired. Results suggest that >90% of opioid users are able to interact with a smartphone in the minutes following self-injection. We conclude it would be reasonable to expect users to turn off a smartphone alarm if they were not experiencing life-threatening respiratory depression.

**307 EVALUATION OF A DIGITAL ANGLE MONITOR TO IMPROVE ULTRASOUND SKILLS IN NOVICE MEDICAL STUDENTS**

B Gow-Lee, S White, V Dinh, J Daughety, C Vongchaichinsri, S Rammell, R Krause, M Alschuler, M Holsclaw, B Austin, D Ramsingh. *Loma Linda University, Loma Linda, CA*

10.1136/jim-2018-000939.306

**Purpose of study** A difficult component in ultrasound training is understanding the ultrasound plane within the body.

**Abstract 307 Table 1** Comparison of time to image acquisition, probe placement, and image quality between angle and no angle groups

| Total Participant                   |                    | 45          |            |             |         |  |
|-------------------------------------|--------------------|-------------|------------|-------------|---------|--|
| Count                               |                    |             |            |             |         |  |
| Count                               | 23:22              | Views       | Angle      | No Angle    | P Value |  |
| Angle: No Angle                     |                    |             |            |             |         |  |
| Time to Image Acquisition (seconds) | Median (IQR)       | Apical 4    | 21 (12)    | 49 (26.25)  | <0.0001 |  |
|                                     |                    | Chamber     | 51 (32.5)  | 60 (34.75)  | 0.8357  |  |
|                                     |                    | Parasternal | 37 (33)    | 33.5        | 1       |  |
|                                     |                    | SAX         | 40 (36.5)  | (39.25)     | 0.4227  |  |
|                                     |                    | RUQ         | 40 (32)    | 40.5 (33.5) | 0.3172  |  |
|                                     |                    | Abdominal   |            | 60 (25.25)  |         |  |
| Appropriate Probe Placement         | Count (Percentage) | Apical 4    | 5 (22%):18 | 22          | <0.0001 |  |
|                                     |                    | Chamber     | (78%):1    | (100%):0    | <0.01   |  |
|                                     |                    | Parasternal | 13         | (0%)        | 0.03311 |  |
|                                     |                    | SAX         | (57%):10   | 21 (95%):1  | 0.2362  |  |
|                                     |                    | RUQ         | (43%)      | (5%)        | 0.02196 |  |
|                                     |                    | Abdominal   | 10         | 17 (77%):5  |         |  |
|                                     |                    | Subxiphoid  | (43%):13   | (23%)       |         |  |
|                                     |                    | Suprapubic  | (57%)      | 12          |         |  |
|                                     |                    |             | 8 (35%):15 | (55%):10    |         |  |
|                                     |                    |             | (65%)      | (45%)       |         |  |
| Image Quality Score                 | Count (Percentage) | Apical 4    | 10         | 19 (86%):3  | <0.01   |  |
|                                     |                    | Chamber     | (43%):13   | (14%)       | 0.1868  |  |
|                                     |                    | Parasternal | (57%)      | 21 (95%):1  | 0.2837  |  |
|                                     |                    | SAX         | 18 (78%):5 | (5%)        | 0.05736 |  |
|                                     |                    | RUQ         | (22%)      | 19 (86%):3  | <0.01   |  |
|                                     |                    | Abdominal   | 16 (70%):7 | (14%)       |         |  |
|                                     |                    | Subxiphoid  | (30%)      | 18 (82%):4  |         |  |
|                                     |                    | Suprapubic  | 12         | (18%)       |         |  |
|                                     |                    |             | (52%):11   | 21 (95%):1  |         |  |
|                                     |                    |             | (48%)      | (5%)        |         |  |
|                                     | 13                 |             |            |             |         |  |
|                                     | (57%):10           | (43%)       |            |             |         |  |

Instruction of the proper probe angle with the skin is commonly based on crude probe movements (e.g. tail up/tail down), whose meanings are variable among learners. This study sought to evaluate if the addition of a digital angle monitor would remove this subjectivity and improve training of clinical ultrasound scans.

**Methods used** First year medical students were randomized, after IRB approval, into either a digital angle monitor group or a non-digital angle monitor group (control). Participants were given a handout on how to obtain five (5) point-of-care ultrasound views on an ultrasound simulator (CAE Vimedix). An additional handout was given to the angle monitor group explaining the optimal angle for image acquisition. Time to image acquisition and image quality scores were compared between the groups. In addition, all subjects underwent 3-D tracking of their arm movements for analysis.

**Summary of results** Results demonstrated that the participants given the digital angle information had shorter image acquisition time and improved image quality scores for certain

ultrasound scans (table 1). Correlation was shown between image quality and time to image acquisition for the digital angle group. Visualization of 3-D tracking movements showed less range of motion in the digital angle group.

**Conclusions** The addition of a digital angle monitor allows novice users to acquire higher quality images in a shorter amount of time, thus overcoming some of the learning barriers found in ultrasound education.

Descriptive statistics and statistical analysis for primary and secondary markers. The angle group shows statistically lower values for time to image acquisition (primary marker). Moreover, the angle group have significantly higher image quality scores as well as proportion of accepted images than the non angle group (secondary markers).

### 308 INVESTIGATION OF SELINEXOR AND MARIZOMIB'S SYNERGY IN PEDIATRIC HIGH-GRADE GLIOMA

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10.1136/jim-2018-000939.307

**Purpose of study** This study aims to elucidate the mechanism of action leading to the synergistic relationship between selinexor, a small molecule nuclear export inhibitor, and marizomib, a proteasome inhibitor, in pediatric high-grade glioma (HGG), including diffuse intrinsic pontine glioma (DIPG). DIPG affects mostly younger children and carries a 100% mortality rate. Due to its location in the pons and diffuse nature, DIPG is not surgically resectable and there are no effective chemotherapeutic options. Radiation therapy can usually shrink the tumor briefly, but it is not a curative or long lasting treatment option.

**Methods used** Through a previous drug screen, the Green Lab has shown that selinexor and marizomib behave synergistically against DIPG cells. Using RNA-Seq data, GSEA (gene set enrichment analysis) was used to establish the hypothesis that cell death through enhanced cell cycle regulation leads to the synergistic relationship between selinexor and marizomib. A caspase assay and flow cytometry were used to analyze apoptosis and the cell cycle respectively, and qPCR was used to validate the relative gene expression seen in the RNA-Seq data.

**Summary of results** The caspase assay showed increased apoptotic activity in all cell lines treated with the combination drug therapy. Cell cycle analysis showed the majority of combination-treated cells in either G1 or S phase, although increased levels of G2 were also seen in one cell line. qPCR yielded results similar to that of the RNA-Seq data, including major downregulation of E2F1 and MYC.

**Conclusions** The increased levels of cells in G1/S when treated with the combination therapy of selinexor and marizomib indicates a potential cell cycle arrest at this phase. The caspase assay confirms an increase in apoptosis in cells treated with a combination therapy and the qPCR data points to E2F1 as a potential mediator of these cell cycle effects through possible apoptotic control. Further work including protein expression confirmation and additional cell cycle analyses needs to be done to clarify the pathways that are causing these results in order to better understand what is resulting in the synergistic increase in cell death seen here.

### 309 COST AND LENGTH OF STAY FOR NEONATES WITH HYPOPLASTIC LEFT HEART SYNDROME

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10.1136/jim-2018-000939.308

**Purpose of study** To identify differences in healthcare resource utilization between survivors and non-survivors, and predictors of length of stay (LOS) and cost for neonates with hypoplastic left heart syndrome (HLHS), which the most common form of functional single ventricle heart disease.

**Methods used** Neonates  $\leq 28$  days old with HLHS were identified from the Healthcare Cost and Utilization Project Kids' Inpatient Database (2003–2012). Surgical admissions were identified by Stage 1 palliation as either Norwood with modified Blalock-Taussig shunt (BTS), Norwood with Sano modification, or Norwood with both. Multivariate regression with year random effects was used to compare survivors vs. non-survivors and to identify predictors of LOS and hospital cost.

**Summary of results** We identified 2,226 HLHS surgical admissions with a neonatal mortality of 20.6%. Survivors had longer median LOS (34 vs. 21 days,  $p=0.007$ ), less ECMO use (8.6 vs. 43.9%,  $p<0.001$ ), and higher proportion of Norwood with both BTS +Sano (18 vs. 9.7%,  $p<0.001$ ). Median encounter costs were similar for survivors vs. non-survivors (\$1 46 097 vs. \$150,204,  $p=0.22$ ). Overall, hospitals in the Midwest and South had significantly longer LOS compared to those in the Northeast (9.82 and 12.88 more days, respectively,  $p<0.01$ ), and ECMO use (12.69 days,  $p<0.0001$ ). Significant differences in total costs were noted by hospital region (\$85,392, \$68,932, and \$51 867 more for Midwest, South, and West vs. Northeast,  $p<0.05$ ), hospital size (\$59 240 less for large vs. small hospitals,  $p=0.01$ ), and ECMO use (\$129,909,  $p<0.0001$ ).

**Conclusions** HLHS is associated with significant resource utilization in the first 28 days of life; despite significantly shorter LOS, non-survivors incur similar costs to survivors due to high ECMO use. Significant differences in costs and LOS by hospital region and bed size may underlie differences in healthcare delivery in this population.

## Hematology and Oncology II

### Concurrent Session

10:15 AM

Friday, January 25, 2019

### 310 RACIAL DIFFERENCES IN PROSTATE CANCER INFLAMMATORY MARKERS

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10.1136/jim-2018-000939.309

**Purpose of study** Prostate cancer (PC) is the most common non-cutaneous cancer in men and a leading cause of cancer death. In the US, black men are disproportionately affected with higher incidence of and mortality to PC than any other race. We hypothesize that different inflammatory cells may

**Abstract 310 Table 1** T-cell markers by region in black (BM) and white men's (WM) prostate biopsies (Bx)

|                            | BM Bx<br>Negative | BM Tumor Adjacent<br>Negative | BM PC |
|----------------------------|-------------------|-------------------------------|-------|
| WM Bx Negative             |                   | CD3, CD4, CD8                 | FOXP3 |
| WM Tumor Adjacent Negative | CD4, CD8          | CD3, CD4, CD8                 |       |
| WM PC                      | CD4, CD8          | CD3, CD4, CD8                 | CD8   |

stimulate or inhibit PC development, and that black men have more pro-tumor inflammation contributing to the health disparity seen in PC in the US.

**Methods used** Prostate biopsies were obtained from 84 men, 50% black/50% white men, with and without PC on biopsy. Biopsy tissue samples were stained for 4 T-cell markers (CD3, CD4, CD8, and FOXP3) and 3 regions were examined (prostate tumor, tumor-free areas surrounding the tumor, and controls or biopsy negative samples). Using T-tests, data were analyzed for type of cell (marker) and cells/mm<sup>2</sup> by region. Analysis were stratified by race. An alpha of 0.0125 (after Bonferroni correction  $p=0.05/4$ ) was used.

**Summary of results** Prostate biopsies of black and white men showed several significant differences. Prostate biopsies in black men had statistically significant higher levels of CD8 T-cell expression compared to those of white men ( $p=8.9 \times 10^{-8}$ ). Table 1 summarizes the markers that had statistical significant differences by race and in the 3 regions examined. Black men prostate biopsy tissues displayed higher levels of all markers studied.

**Conclusions** Prostate biopsies showed statistically significant differences in T-cell markers, particularly when compared between the tumor-free region surrounding PC in black men against all 3 regions in white men. These data suggest black men have higher expression of T-cells surrounding PC regions, generating a pro-tumor inflammatory micro-environment, which may in part contribute to PC racial disparity.

### 311 INFLUENCE OF MICROBIOME CHANGES ON ANTI-TUMOR RESPONSE

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10.1136/jim-2018-000939.310

**Purpose of study** The microbiome is the entirety of the microorganisms and their genomes colonizing the human body. Changes in the microbiome impact the innate and adaptive immune system, which both play an important role in anti-tumor responses. NK cells, specifically, take part in tumor defense through their ability to exhibit antibody dependent cell-mediated cytotoxicity (ADCC). It has not been sufficiently researched how microbiome manipulation effects ADCC in terms of anti-tumor response.

We studied the effects of microbiome changes on the efficacy of anti-tumor response in a Burkitt lymphoma model using the human CD20<sup>+</sup>Daudi cell line. Rituximab is an anti-CD20 monoclonal antibody and is given to treat lymphoma, along with chemotherapy.

**Methods used** Severe combined immunodeficient mice were subcutaneously challenged with Daudi cells and divided into 4 groups: no treatment, Rituximab treatment, antibiotic treated

(oral Ciprofloxacin/Metronidazole) or treated with antibiotics and Rituximab.

Fecal samples were repeatedly collected from mice, and used for 16S rRNA amplification and microbiota analysis. Tumors were measured twice a week to monitor tumor burden. To evaluate potential changes in ADCC, spleens were harvested and splenocytes cultured in IL-2 to be used as effector cells in the *in vitro* ADCC killing assay. Daudi cells labeled with radioactive chromium were used as targets.

**Summary of results** Antibiotic treatment did not influence spontaneous tumor growth or the efficacy of Rituximab treatment (See figure 1). However, the ADCC assay did show differences in NK cell killing activity via measured cell lysis and flow cytometry analysis. All stool samples were submitted for 16S rRNA amplification and microbiota analysis; however results are pending from the microbiome facility.

**Conclusions** It is clear from previous research that the microbiome plays an important role in anti-tumor response and this project is off to a promising start using the Daudi cell line as a Burkitt lymphoma model. In the future I plan to use the same experimental design in SCID mice injected with the humanized CHL20 neuroblastoma and the ch14.18 MAb for treatment. It is very exciting to imagine the possibilities of microbiome influence on immunotherapies, especially with an aggressive pediatric cancer like neuroblastoma.

### 312 A CASE OF AML AND TRISOMY 8 WITH CONCOMITANT FACTOR VII DEFICIENCY

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10.1136/jim-2018-000939.311

**Purpose of the study** AML is rapidly lethal unless treated with intensive chemotherapy and/or targeted therapies together with supportive care. Trisomy 8 is the most frequent cytogenetically gained aberration in AML. Here, we share our findings of mosaic trisomy 8 in a leukemia patient with a translocation of chromosome X and 8.

**Methods** Retrospective chart review.

**Summary of results** 41-year-old Hispanic female with no past medical history presented with fever, severe headache, fatigue, bleeding gums, menorrhagia, and severe pancytopenia. Blast was found in the peripheral blood smear guided our suspicion of an underlying hematological abnormality. Biopsy showed 70% bone marrow cellularity with evidence of acute undifferentiated leukemia, decreased megakaryocytes, and atypical plasma cell. Daunorubicin and cytarabine were used for chemotherapy induction. After completing seven days of induction, she developed neutropenic fever. Her course was complicated with bloodstream infection from central line with *Klebsiella pneumoniae*, esophageal candidiasis, severe mucositis, and neutropenic enterocolitis. Her serum was positive for CMV and stool for blastocystis hominis. She was placed on antibiotics, micafungin, ganciclovir. Fever resolved and neutropenia recovered after 16 days post induction. Bone marrow cytogenetic analysis revealed mosaic trisomy 8 with translocation of chromosome X and 8 (47, x, t(x:8)(q13;q24.1),+8(6)/46,XX[14]). Flow cytometry showed blasts dim CD38+, CD117+, dim HLA-DR+, HLA-B27, and negative for lymphoid markers. Furthermore, gene mutations were detected CEBPA, IDH1, JAK2 V617F, and U2AF1

which confirmed the presence of abnormal neoplastic clone, consistent with AML. Additionally, patient had consistently isolated elevated PT without bleeding events. Factor VII level was deficient.

**Conclusion** While trisomy 8 is the most common trisomy in AML, this is the first reported case to the best of our knowledge of t(8,X) translocation resulting in AML, as well as an incidental finding of factor VII deficiency. Most commonly, factor VII deficiency is congenital but it may be possible to acquire inhibitors of coagulation.

### 313 INTEGRATING SINGLE-CELL GENE EXPRESSION DATA INTO PREDICTIVE MODELING OF BREAST CANCER OUTCOMES

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10.1136/jim-2018-000939.312

**Purpose of study** Breast cancer is currently the leading cause of cancer deaths in women. The cause of death in breast cancer is metastasis, a stage of breast cancer where the cancer cells spread to other organs beyond the primary tumor, resulting in a survival rate drop from 90% to below 25%. Therefore, it is critical to identify gene signatures of high-risk patients and establish treatment targets to prevent this progression.

**Methods used** We identified 28 genes with differential gene expression in tumor and metastatic cells from the lungs and lymph nodes of triple-negative breast cancer patient derived xenografts using single cell RNA-seq (sc-RNAseq). We used these genes to build logistic regression models for recurrence, distant metastasis, and death on publicly available breast cancer microarray data to determine whether these single-cell metastatic signatures were detectable and predictive in bulk tumor data.

**Summary of results** Preliminary results identified individual genes that predicted outcome in each category but very few that performed well on all three survival metrics. Interestingly, we also found that recurrence was the only outcome that is best predicted using the full gene signature, suggesting that our gene set may be indicative of tumor dissemination.

**Conclusions** This work demonstrates the utility of patient derived xenografts and single-cell sequencing in gene set selection for predictive modeling in breast cancer and has identified promising genes for future prognostic panels.

### 314 ABSTRACT WITHDRAWN

### 315 DIFFERENTIATING FOLLICULAR LYMPHOMA FROM NODAL MARGINAL ZONE LYMPHOMA BY FLOW CYTOMETRY

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10.1136/jim-2018-000939.313

**Purpose of study** Flow cytometry (FC) has become an effective tool for the diagnosis and staging of hematologic neoplasms, a group of cancers which includes non-Hodgkin lymphomas (NHLs). Yet several of these diseases remain difficult to distinguish from each other by immunophenotype alone, in particular follicular lymphoma (FL) and its rarer counterpart, nodal

marginal zone lymphoma (NMZL). The discovery of one or more antigens with distinct expression in FL vs. NMZL would provide greater diagnostic precision for evaluation of NHLs by flow cytometry.

**Methods used** Prior to experimentation, potential surface markers were identified by reviewing the medical literature. A final list of antigens included CD44, CD82, TACI, IRTA1, and JAM-C. Patient tissue samples of FL, NMZL, and benign follicular hyperplasia controls were thawed, washed, and stained with a 9-color antibody panel: CD40-BV421/Kappa-FITC/X-PE/CD19-PE-CF594/Lambda-PerCP-Cy5.5/CD44-PE-Cy7/CD38-A594/CD82-A647/CD71-APC-A700, where X represented, at various points, TACI, IRTA1, and JAM-C. The resulting FC data were analyzed with in-house software and their median fluorescence intensities (MFI) were compared. Effective antigen(s) were added to a previously-established antibody combination, CD40-BV510/Kappa-FITC/CD75-PE/CD19-PE-CF594/Lambda-PerCP-Cy5.5/CD44-PE-Cy7/CD38-A594/CD32-APC/CD71-APC-A700/CD5-APC-Cy7, and verified with the same method.

**Summary of results** Of the antigens screened, CD44 was the only marker showing significant discriminative utility (downregulation in FL vs. NMZL, with median screening MFI values 198.5 vs. 1843, respectively). CD82 may show some promise in distinguishing the two malignancies, but this difference was ultimately inadequate for clinical purposes. TACI, IRTA1, and JAM-C did not show any significant differences in expression between FL and NMZL.

**Conclusions** CD44 appears to be downregulated in most cases of FL and may be useful for differentiating this lymphoma from closely-related NMZL by flow cytometry. This distinction may improve the specificity of multicolor FC assays, increasing their applicability for the diagnosis of NHLs and providing a useful adjunct to morphologic evaluation.

### 316 RECURRENT GALLBLADDER CARCINOMA PRESENTING WITH MALIGNANT ASCITES

T Sharifan, S Ragland, J Patel. *Kern Medical, Laguna Niguel, CA*

10.1136/jim-2018-000939.314

#### Case report

**Introduction** Gallbladder Carcinoma (GBC) accounts for 80%–95% of the malignancies in the biliary tract, making it the most common neoplasm of the biliary system. Gallbladder Carcinoma has a higher incidence in South Americans, American Indians, Southeast Asians, *S. typhi* and *S. paratyphi* infection, and chronic inflammation of gallbladder. Incidental GBC is discovered on 0.19%–2.8% on cholecystectomies. We present a case of incidental GBC discovered after cholecystectomy with GBC recurrence in the peritoneum.

**Case presentation** This is a 62 year old female with history with incidental GBC presented with abdominal distention for 1 month. The patient had poorly differentiated Stage II (pT2 N0 M0) GBC on pathology post cholecystectomy. Patient had re-exploratory laparotomy with radical hilar lymphadenectomy and Segment V liver resection. Based on complete pathologic resection and negative imaging, there was no indication for adjuvant chemotherapy or radiation therapy per current guidelines. The patient presented to ED twenty three months later with complaints of worsening abdominal distention for 1 month. On physical exam the



abdomen was firm, distended, nontender on palpation, with positive fluid wave suggestive for ascites. CT was concerning for peritoneal metastasis. Cytology from fluid collected via paracentesis then revealed strongly positive Cytokeratin 7 indicating metastatic adenocarcinoma most consistent with gallbladder origin.

**Discussion** Cholecystectomy, hepatectomy, and adjacent lymph node resection is the primary treatment for GBC. Peritoneal tumor seeding has been reported to have prevalence 0%–40% with residual disease reported has high as 61%. NCCN recommends no adjuvant chemotherapy for patient with GBC post resection and negative lymph nodes. However surgical resection alone has shown 51% 5 year survival. The role of adjuvant chemotherapy in patient with complete resection is controversial as some benefits have been shown in meta-analysis study done by Byoung Kim. Currently there are no standard guidelines for monitoring GBC recurrence. We suggest a need for more studies to develop new protocols that will lower GBC recurrences either through adjuvant intraperitoneal chemotherapy, serial CT scans, or peritoneal cytology monitoring.

### 317 NK T-CELL LYMPHOMA OF THE SOFT PALATE

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10.1136/jim-2018-000939.315

**Purpose of study** To discuss a unique case of extranodal NK (Natural Killer) T-cell lymphoma.

**Methods used** A 60 year old male presenting with nasal obstruction and epistaxis for 5 months. Patient was treated in Thailand with three courses of antibiotics and prednisone without improvement. At time of presentation patient had a large nasopharyngeal mass originating from the nasal surface of the soft palate. In-office biopsy of the mass showed possible lymphoproliferative disease.

**Summary of results** The patient was brought into the operating room and a biopsy performed of the nasopharyngeal mass which showed an NK T-cell lymphoma. The patient was referred to hematology/oncology for chemotherapy.

**Conclusions** Extranodal NK T-cell lymphoma is rare manifestation of T-cell lymphoproliferative disorders that can be found in various parts of the head and neck, especially within the nasal cavity. Care should be taken to obtain adequate tissue biopsies for masses in the nasal cavity that are suspicious for this clinical entity.

## Infectious Diseases II

### Concurrent Session

10:15 AM

Friday, January 25, 2019

### 318 INNATE IMMUNE PROTECTION GENERATED AGAINST INFLUENZA IN MICE VACCINATED WITH LIPOSOMES CONTAINING ONLY PAM3CAG AND NO INFLUENZA EPITOPES

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10.1136/jim-2018-000939.316

**Purpose of study** Commercial influenza vaccines stimulate an adaptive immune response to yearly mutating influenza proteins. Previous experiments with a liposomal (Lp) influenza vaccine containing Pam3CAG only and no proteins generated a protective innate immune response against H1N1 virus. In this study, we examined the protection provided by different vaccination dosage regimens with liposomes containing only Pam3CAG.

**Methods used** Different doses of a liposomal VesiVax<sup>®</sup> vaccine, provided by Molecular Express Inc., containing the adjuvant Pam3CAG, were used to vaccinate mice (n=9/group) and included: intranasal (IN) d4, d2 pre-challenge; subcutaneous (SC) d2 pre-challenge; IN d2, d4 post-challenge; SC d2 post challenge; SC buffer d2 pre-challenge. Mice were challenged d0 IN with influenza and monitored for morbidity 2X/day to d21.

**Summary of results** Using the Pam3CAG liposomes, the dosing regimen that was significantly better than all other groups (89% survival) was the IN d4 and d2 pre-challenge (p<0.0006).

**Conclusions** The innate immune response generated by the VesiVax liposomes with just Pam3CAG and no proteins provided significant protection against the influenza viral challenge, suggesting that this approach could be used to protect animals regardless of the influenza protein mutations.

### 319 RISK FACTORS ASSOCIATED WITH RECURRENT KAWASAKI DISEASE

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10.1136/jim-2018-000939.317

**Purpose of study** The objective of this study was to identify the risk factors during the initial episode of Kawasaki Disease (KD) that may increase the risk of recurrence.

**Methods used** A search of online databases, such as PubMed, Google Scholar, and Cochrane was conducted to find studies related to recurrence of KD. Only articles published after the year 2000 that investigated factors associated with increased risk of recurrence of KD in pediatric patients were included.

**Summary of results** A total of 6 studies satisfied our inclusion criteria (see table 1). All of the studies examined clinical factors associated with recurrence of KD, but three of 6 studies examined laboratory parameters during initial presentation. The incidence of recurrence ranged from 1.7% to 3.5% in different studies. The recurrence rate was highest within the first 2 years of initial episode. Although the risk factors that were evaluated were not uniform across studies, coronary artery abnormalities, atypical KD and longer duration of fever during the first episode were identified as risk factors for recurrence in more than one study. The limitation of this review included the retrospective nature of studies which may not have included the recurrence data on some patients as well as the variation in use of laboratory findings to identify patients at risk for recurrent KD.

**Conclusions** Our review suggests that prolonged fever, atypical KD and coronary artery abnormalities may be associated with increased risk of recurrent KD. To prevent recurrence, it is

Abstract 319 Table 1

| Year Published | First Author | Study Location | Number of Patients | Number of Recurrent Cases | Time Between First and Second Episode | Factors During Initial Episode Associated with Increased Risk of Recurrence  |
|----------------|--------------|----------------|--------------------|---------------------------|---------------------------------------|--|
| 2012           | Chahal*      | Canada         | 1010               | 17 in 16 patients (1.7%)  | Average: 1.5 years                    | Longer duration of fever before diagnosis (p=0.01) and total duration of fever (p=0.02)<br>Lower median albumin (p=0.03)<br>Higher white blood cell count (p=0.05)                                 |
| 2001           | Hirata*      | Japan          | 10 679             | 217 (2.0%)                | Range: 2–11 months                    | Presence of cardiac sequelae within 1 year (hazard ratio: 1.77–4.39)   |
| 2015           | Maddox       | United States  | 5557               | 97 (1.7%)                 | Average: 22.5 months                  | Coronary artery abnormality (p=0.01)<br>Atypical KD cases (p=0.006)  |
| 2015           | Maddox       | United States  | 13 874             | 483 (3.5%)                | Not Reported                          | Being Asian/Pacific Islander (hazard ratio: 1.4–3.7)<br>Rash (p=0.03) and cervical lymphadenopathy (p<0.001)<br>Coronary artery abnormality (p=0.003)<br>Atypical KD (p=0.01)                      |
| 2017           | Sudo         | Japan          | 81 310             | 1842 (2.3%)               | Range: within 2 years                 | Being male (hazard ratio: 1.01–1.21)<br>Steroid therapy (hazard ratio: 1.14–1.70)<br>Resistance to IVIG (hazard ratio: 1.18–1.67)  |
| 2013           | Yang*        | China          | 1173               | 22 (1.9%)                 | Average: 12 months                    | Being female (p=0.026)<br>Longer duration of fever before IVIG treatment (p<0.001)<br>Lower hemoglobin level (p<0.001)<br>Higher ALT (p=0.032) and AST (P<br>Coronary artery abnormality (p=0.035) |

\*Studies that included laboratory values as risk factors for recurrence.

crucial to diagnose and treat KD in a timely matter. In addition, a different treatment strategy and closer follow-up may be warranted in patients with above risk factors. Large prospective studies that focus on both the laboratory and clinical criteria as well as treatment course are needed to further investigate the risks for recurrent KD.

### 320 IDENTIFYING RISK FACTORS FOR *STAPHYLOCOCCUS AUREUS* INFECTION IN RIVER RAFTING GUIDES

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10.1136/jim-2018-000939.318

**Purpose of study** Outbreaks of community acquired *S. aureus* have historically been studied in communities such as football teams and river rafting companies, where individuals frequently suffer minor cuts and abrasions and live or work in close quarters. The aim of this study was to identify risk factors for contracting *S. aureus* infections at a single river rafting company in Northern California during the summer of 2018, where residents reported unusually high incidence of *S. aureus* infections.

**Methods used** Case-control analyses of a brief survey from all 12 cases and a convenience sample of 18 uninfected camp residents were performed.

**Summary of results** There was no significant difference in the odds of *S. aureus* infection for the number of days in residence (p=0.810), blisters on hands and feet (p=0.313), showers taken (p=0.182), or loads of laundry washed (p=0.805). Notably, first-season residents at the camp had much higher odds of *S. aureus* infection than multi-season residents (OR 51, 95% CI 4.61–563.91).

**Conclusions** Several young children contracted *S. aureus* infections, decreasing the likelihood of rafts as fomites for the bacteria, as has been previously suggested. Further investigations could evaluate the protective mechanism of previous experience (seasons worked) against *S. aureus* infection.

### 321 TISSUE RESIDENT MEMORY CD8 T CELL RESPONSE TO VARICELLA-ZOSTER VIRUS AFTER SHINGLES

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10.1136/jim-2018-000939.319

**Purpose of study** A new subset of memory T-cells, termed tissue-resident memory T cells or T<sub>RM</sub>, have been defined at sites of cleared infections. These long-lived cell populations are thought to protect against re-infection, and their placement at appropriate sites is an unmet challenge in vaccinology. VZV can reactivate from ganglia to cause a dermatome-restricted rash, termed shingles. The purpose was to measure if VZV reactivation leads to local deposition of VZV-specific T<sub>RM</sub> at the site of shingles.

**Methods used** Immunocompetent adults with shingles were recruited into an IRB-approved protocol. Serial 3 mm punch biopsies were obtained from shingles and normal skin

Abstract 320 Table 1 Qualitative risk factors for *S. aureus* infection in rafting camp residents

| Risk Factor                   | Odds Ratio (95% CI) |
|-------------------------------|---------------------|
| Female                        | 2 (0.5–8.9)         |
| First Summer Resident >1 Week | 51 (4.6–563.9)      |
| New Footwear                  | 1.9 (0.4–8.7)       |
| Current Rafting Guide         | 0.3 (0.04–1.7)      |

around 45 and 90 days post-rash onset. Skin T cells were expanded as bulk, polyclonal populations. To detect VZV-specific CD8 T cell responses, we created panels of artificial antigen presenting cells (aAPC) expressing subject-specific HLA class I A and B variant proteins, and each individual VZV protein expressed as 70 unique ORFs. Skin T cells were added, and after 1–2 days, their specific activation measured by IFN- $\gamma$  ELISA. Peptide epitopes within some reactive VZV proteins were determined using synthetic 13 AA-long peptides covering the relevant VZV protein, again using HLA-defined aAPC.

**Summary of results** We observed VZV-specific CD8 T cell responses from shingles but not control skin in each of the first 3 persons studied. Within the shingles specimen group, T-cell responses were detected to 9 (13%) of the 70 VZV proteins tested. VZV ORF9 had the highest response rate (3/3 subjects), followed by ORF67 (2/3 subjects), with responses to ORFs 20, 23, 35, 39, 49, 61, and 62 also detected. Determining the exact regions ‘epitopes’ of VZV recognized by VZV-specific CD8 T cells was successful for each subject.

**Conclusions** VZV reactivation leads to the spatially-restricted deposition of virus-specific CD8 T<sub>RM</sub> in human skin for up to 90 days after rash healing with classic properties of HLA class I restriction and viral peptide specificity. Having established the T<sub>RM</sub> phenomenon in a common disorder that is accessible to biopsy, we plan detailed single-cell studies of proven VZV-specific T<sub>RM</sub> to measure the transcriptional and epigenetic signature of these desirable cells.

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#### PREVENTING HIV INFECTIONS IN SEATTLE BY PROMOTING AWARENESS AND ACCESS FOR PRE-EXPOSURE PROPHYLAXIS (PREP) FOR HOMELESS YOUNG ADULTS

T Takami. *University of Washington School of Medicine, Seattle, WA*

10.1136/jim-2018-000939.320

**Purpose of study** The community need that this project design seeks to address is creating awareness in the homeless young adult population about pre-exposure prophylaxis (PrEP) for HIV in the Downtown Seattle area. Seattle is the largest city in King county, and King county has the highest rate of new HIV infections in the state by almost double the next closest county. This coincides with King county having the highest prevalence of HIV infected individuals. In order to prevent new HIV infections in Downtown Seattle, awareness for prevention methods such as PrEP, needs to be increased, which was the goal of this intervention.

**Methods used** In order to explore this health issue a literature review was conducted to examine the efficacy of PrEP for HIV as well as determining patient acceptance of the medication. A partnership was formed with Kelley-Ross Pharmacy and YouthCare homeless shelters in order to promote this intervention. Kelley-Ross is a unique pharmacy as they have a medical director that has signed off on a protocol allowing them to do all the lab testing and prescribing of PrEP so patients can make appointments without a referral. YouthCare is an organization that focuses on assisting young adults who are dealing with homelessness. The partnership

was formed through individual meetings with both organizations.

**Summary of results** A literature review on PrEP was provided to YouthCare. Additionally two separate presentation/training sessions were conducted at two YouthCare shelters. These presentations included information about the PrEP medication, where to get the medication subscribed, and how to get the medication and test expenses covered. It also included delivery of brochures and contact information for Kelley-Ross Pharmacy as well as information about the Washington State Drug Assistance Program for PrEP.

**Conclusions** The strengths of the proposed project were that it targets an at-risk population and provides valuable educational information. The challenges of promoting such a project are the location of shelters in relation to PrEP knowledgeable locations such as Kelley-Ross Pharmacy. Potential next steps include spreading training to other homeless aid organizations as well as working with other pharmacies create models similar to Kelley-Ross to allow them to be an all-in-one PrEP location.

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#### THE EVOLUTION OF NUCLEOPORIN 153 AND ITS EFFECT ON HIV NUCLEAR ENTRY

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10.1136/jim-2018-000939.321

**Purpose of study** Hundreds of host proteins are crucial for HIV replication in host cells, and Nucleoporin153 (Nup153) is important due to its role in HIV nuclear entry. Nup153, an essential component of the nuclear pore complex interacts with the capsid core of HIV, allowing nuclear ingress. Nup153 is under positive evolutionary selection in primates. This means that the genetic code of Nup153 has potentially changed over time because of viral parasitism that essentially marks regions of Nup153 that directly interact with viruses. While most of the genetic code for Nup153 between species is similar, the differences due to positive selection are key to determining which amino acid residues interact with the HIV capsid. This rapid evolution of Nup153 has previously been described in the literature, but the relevance of these evolutionary signatures have never been tested in the laboratory. The goal was to find if Nup153 would interact with the HIV capsid differently because of variation in the amino acid residues between different species of primates.

**Methods used** Throughout the research process I learned and performed lab techniques including: plasmid growth in *E. coli*, plasmid purification, restriction digests, TOPO-TA and Gateway™ cloning, agarose gel electrophoresis, DNA quantification, passaging adherent human cells, counting cells, transient transfection of human cells, and recombinant HIV production.

**Summary of results** My results included: successful cloning of TRIM-NUP153C into mammalian expression vectors by Gateway™ cloning, passaging of HeLa and Human Embryonic Kidney Cells (293T), transfection of 293 T cells with Green Fluorescence Protein (GFP), HIV virus creation by transfection, and infection of 293 T cells by pseudotyped HIV-1 in a laboratory setting.

**Conclusions** During this project I learned a great deal about molecular biology and mammalian tissue culture and improved my skills in laboratory research. The biggest issue I ran into was the low number of GFP expressed cells after virus infection. Through adjustments in the current lab protocols, GFP expression has increased a great deal and the project continues to yield useful data. In future projects, the goal will be to improve transfection/infection efficiency through improving cell health, quality of reagents, and improving protocols.

### 324 PROBING THE EFFICACY OF LIPOSOMAL GLUTATHIONE AS A SUPPLEMENT FOR MYCOBACTERIUM TUBERCULOSIS TREATMENT

B Robinson, S Munjal, V Venketaraman. *Western University of Health Sciences, Pomona, CA*

10.1136/jim-2018-000939.322

**Purpose of study** *Mycobacterium tuberculosis* (*Mtb*) is the causative agent of tuberculosis (TB) and accounts for 1.7 million deaths annually. The effectiveness of the Bacillus Calmette-Guérin (BCG) vaccine has remained controversial. Current antibiotic therapy for TB requires treatment for 6–9 months and is often with side effects. Glutathione (GSH), an essential intracellular antioxidant, is deficient in peripheral blood mononuclear cells (PBMCs) of patients with active TB. This study tests the hypothesis that supplemental GSH in conjunction with suboptimal concentrations of first line antibiotics against TB will restore cytokine balance and will improve the ability of *in vitro* granulomas to control *Mtb* infection.

**Methods used** Groups of BCG-vaccinated and unvaccinated individuals were recruited for blood donation. PBMCs isolated were infected with *Mtb* to initiate *in vitro* granuloma formation. Infected cells were subjected to treatment with varying sub-optimal concentrations of antibiotics with and without liposomal GSH (LGSH) supplementation. Supernatants and lysates were collected from granulomas terminated at 8 and 15 days to determine *Mtb* survival and cytokine production.

**Summary of results** LGSH supplementation improved the ability of the antibiotics to reduce *Mtb* infection as evidenced by a significant reduction in colony forming units. In comparison to the non-vaccinated group, LGSH treatment of *in vitro* granulomas derived from BCG-vaccinated individuals resulted in a significant decrease in the levels of IL-10 and IFN- $\gamma$ . Furthermore, LGSH treatment of *in vitro* granulomas derived from BCG-vaccinated individuals resulted in an increase in the levels of IL-2 when compared to the non-vaccinated group, demonstrating an increased T-cell response.

**Conclusions** Results suggest that LGSH administration in combination with suboptimal concentrations of antibiotics might be a viable TB treatment option. Given the significant side effects of TB treatment, reduction of antibiotics would be of great benefit. These promising initial results justify expansion of this study to confirm the observed results in larger patient groups.

### 325 PNEUMOCYSTIS JIROVECI DETECTION IN PRETERM INFANTS ADMITTED TO THE NEONATAL INTENSIVE CARE UNIT: A PILOT STUDY

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10.1136/jim-2018-000939.323

**Purpose of study** *Pneumocystis jirovecii* (*P. jirovecii*) causes PCP pneumonia (PCP) in immunocompromised patients and malnourished infants. We hypothesize that this organism infects preterm infants admitted to the Neonatal Intensive Care Unit (NICU) via the nosocomial transmission route, leading to negative clinical outcomes, including prolonged mechanical ventilation, increased hospital stay, and need for ongoing respiratory support. Early reports have demonstrated neonatal colonization rates ranging between 12%[i]–25.7% [ii] and potential association with respiratory distress syndrome; however, this has not been studied in the United States.

- Nevez, Gilles et al. *Pneumocystis* Is Still Involved in Nonimmunosuppressed Preterm Infants in Europe. *Clin Infect Dis.* 2017;67(4):645–646.
- Rojas P, Friaza V, Garcia E, de la Horra C, et al. Early acquisition of pneumocystis jirovecii colonization and potential association with respiratory distress syndrome in preterm newborn infants. *Clin Infect Dis.* 2017;00:1–6.

**Methods used** This is a prospective, longitudinal study at the LAC+USC NICU using a validated Quantitative Polymerase Chain Reactions (qPCR) assay to identify the organism via amplification of a 506 base pair region of the highly conserved Major Surface Glycoprotein (MSG) gene.

**Summary of results** To this date, 36 endotracheal samples have been collected from 16 patients. 25 samples from 6 patients have been tested with a positive rate of 0%. Of the samples tested patients ranged from 24 to 33 weeks and 360 to 2525 grams. 5 of the 6 patients were intubated at birth and 5 of the 6 neonates received antenatal steroids.

**Conclusions** Currently, there is not enough statistical power to determine the rate of colonization in this population therefore samples from neonates of various gestational and postnatal ages are continuing to be collected. This pilot study is anticipated to be finished by the end of this year with a minimum of 25 patients enrolled.

### 326 EXTRAPULMONARY COCCIDIOIDOMYCOSIS PRESENTING AS PERITONITIS

<sup>1</sup>C D'Assumpcao, <sup>1</sup>S Burcovschi, <sup>1</sup>C Clark, <sup>1</sup>L Moosavi, <sup>1</sup>M Kalluri, <sup>1</sup>E Gunz, <sup>1</sup>J McFarland, <sup>1</sup>J Patel, <sup>1,2</sup>A Heidari. <sup>1</sup>Kern Medical – UCLA, Bakersfield, CA; <sup>2</sup>Valley Fever Institute, Bakersfield, CA

10.1136/jim-2018-000939.324

**Purpose of study** Coccidioidomycosis is a fungal infection caused by *Coccidioides immitis* or *posadasii*. While most commonly presenting as pulmonary infection, dissemination can occur in 0.4%–0.7% of cases. Intraabdominal dissemination

have been reported but very few cases had peritoneal involvement. This is a case of disseminated coccidioidomycosis presenting as peritonitis.

**Methods used** Retrospective case report.

**Case description** A 23 year old Hispanic male presented to an outside hospital with one month history of fever, weight loss, blood in stool, abdominal pain and distension. He was discharged after paracentesis without any further treatment. He presented to another hospital with more severe abdominal pain and distension. Imaging found a small bronchopulmonary fistula with extension into left chest wall with associated left lung volume loss and a left loculated pleural effusion, diffuse mediastinal lymphadenopathy, splenomegaly and abdominal ascites with omental caking. A cervical lymph node biopsy originally performed to rule out lymphoma instead showed coccidioidomycosis spherules with endosporeulation. Intravenous liposomal amphotericin B was started and he was transferred to our institution for higher level of care. Upon arrival his coccidioidal complement fixation (CF) titers were greater than 1:512. He developed small bowel obstruction with progression of ascites and a large pelvic abscess. Catheters placed into pelvic abscess drained purulent fluid that grew *C. immitis*, *Escherichia coli*, and *Bacteroides ovatus*. Small bowel obstruction improved with abscess drainage and antibiotic therapy. After seven hospital days he was discharged with daily outpatient treatment at our infusion center, ambulating and tolerating a regular diet. His amphotericin treatment was tapered to 5 times a week for 2 weeks and then to 3 times a week aiming to finish a 12 week course. His most recent CF titers improved to 1:256.

**Conclusion** Physicians in areas endemic to coccidioidomycosis should be aware of the possibility of abdominal and peritoneal dissemination as the presenting symptom of disseminated coccidioidomycosis. Surgical intervention should be avoided by all means.

## Morphogenesis and Malformations

### Concurrent Session

10:15 AM

Friday, January 25, 2019

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#### EMBRYOPATHY DUE TO TREATMENT OF ECTOPIC PREGNANCY WITH METHOTREXATE

A Lebedoff, D Viskochil, JC Carey. *University of Utah/Primary Children's Hospital, Salt Lake City, UT*

10.1136/jim-2018-000939.325

**Case report** Methotrexate (Mtx) is a folic acid antagonist used therapeutically to treat ectopic pregnancy. Mtx impairs growth and DNA repair by competitive inhibition at the catalytic site of dihydrofolate reductase blocking the production of purine nucleotides in rapidly dividing cells. The success rate for multi-dose protocols is 93% and 88% for single dose therapy. In surviving embryos, Mtx can lead to impaired morphogenesis when taken between gestational weeks 4 to 9. We describe a patient with methotrexate embryopathy and heart defects due to

1st trimester exposure to Mtx for treatment of ectopic pregnancy.

The patient is a term female infant born at 37+3 weeks by c-section, who had prenatal concerns for anomalies on ultrasound. At estimated 6–8 weeks of pregnancy, her mother had symptoms concerning for ectopic pregnancy and received a dose of Mtx through her prenatal provider. Repeat labs after the Mtx administration showed that bHCG continued to rise. The mother went for laparoscopy for further investigation and was found to have bicornuate uterus with fetus found in the uterus. The mother was started on folate to mitigate effects of Mtx as parents desired to continue the pregnancy. Fetal ultrasound showed IUGR, abnormal head shape, proptosis with right orbital mass, micrognathia, mesomelia, oligodactyly, bilateral absence of fibulae, and concern for hypoplastic heart consistent with exposure to methotrexate.

The child was born via c-section to a 28 year old G3P3 with APGARs of 8, 8. Her initial examination showed cleft palate, midface hypoplasia, proptosis, radial polysyndactyly, hypoplastic limbs, and anteriorly placed anus. Echocardiogram showed balanced AVSD and PDA. Head ultrasound did not show any gross abnormalities.

Common manifestations of first trimester Mtx exposure include prenatal growth deficiency, microcephaly, hypoplasia of the cranial bones with synostoses, wide fontanelles, micrognathia, maxillary hypoplasia and limb defects. Less common findings include cleft palate, renal anomalies, neural tube and heart defects.

The critical period for the development of the typical embryopathy has been posited to be 6–9 fetal weeks. The exposure in our case was a single dose of Mtx at 4–6 fetal weeks, suggesting that this window may be earlier.

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#### BIALLELIC *DNAJC21* VARIANTS & INHERITED BONE MARROW FAILURE: REPORT OF THREE AFFECTED SIBS

L Carter, D Stevenson. *Stanford University, Stanford, CA*

10.1136/jim-2018-000939.326

**Purpose of study** Biallelic variants in *DNAJC21* have recently been proposed to cause a novel recognizable syndromic bone marrow failure condition with only 15 cases published thus far, some with limited clinical information. *DNAJC21* is thought to play a role in ribosome biogenesis. In addition to review of the literature, we present a consanguineous family with three individuals with discrete phenotypes, one with confirmed pathogenic variants in *DNAJC21*, to clarify the phenotype of these patients with this newly described disorder.

**Methods used** Whole exome sequencing identified a homozygous c.544C>T (p.R182\*) pathogenic variant in *DNAJC21* in the proband. The proband's consanguineous parents were heterozygous for this change. Targeted testing of the proband's sibs is pending. We present phenotype data for these 3 individuals in addition to review of the literature.

**Summary of results** The proband was evaluated by medical genetics at 13 years. He has short stature, microcephaly, low weight, leg length discrepancy secondary to presumed Legg-Calve-Perthes, and bone marrow failure. He had history of developmental delay and poor school performance. There was increased echogenicity of the pancreas. Minor anomalies

included synophrys, broad nasal bridge, overbite, and persistent fetal finger-tip pads. The proband's older sister has hearing loss, short stature and learning disabilities. The proband's younger brother has aplastic anemia, short stature and dental problems. There is family history of consanguinity as parents are first cousins once removed. The three affected individuals had a similar facial gestalt different from their parents.

**Conclusions** Homozygous *DNAJC21* variants have recently been suggested to cause bone marrow failure. D'Amours et al (*Clin Genet*, 2018) discussed 15 known individuals and suggested that they have a unique type of bone marrow failure syndrome with clinical overlap with Shwachman-Diamond syndrome and dyskeratosis congenita. Based on review of the phenotypes of our patients and the 15 reported we suggest that the phenotype is distinct from other bone marrow failure conditions.

### 329 IMPACT OF CARDIAC ALGORITHM ON CYTOGENETIC TESTING

<sup>1</sup>BJ Floyd, <sup>2</sup>SR Hintz, <sup>2</sup>CJ Suarez, <sup>2</sup>A Cherry, <sup>2</sup>L Yu, <sup>1</sup>W Benitz, <sup>1</sup>JR Priest, <sup>1</sup>GE Wright, <sup>1</sup>S Bhombal, <sup>1</sup>A Davis, <sup>1</sup>VY Chock, <sup>1</sup>N Weigel, <sup>1</sup>D Kobayashi, <sup>1</sup>B Fluharty, <sup>1</sup>D Stevenson. <sup>1</sup>Stanford Children's Hospital, Palo Alto, CA; <sup>2</sup>Stanford Hospital, Palo Alto, CA

10.1136/jim-2018-000939.327

**Purpose of study** Congenital heart defects (CHD) are the most common type of congenital malformation, and may be observed in patients with chromosomal abnormalities or syndromic disease. Cytogenetic tests such as karyotype, CGH microarray, and FISH are frequently utilized in the neonatal intensive care unit (NICU) for molecular evaluation of CHD. Appropriate utilization of cytogenetic testing is a component of high-value care, however inappropriate selection of tests is common, whether due to the growing complexity of these tests or due to redundant testing. Therefore, our aim was to develop an algorithm for genetic evaluation of CHD to reduce redundant cytogenetic testing in the NICU.

**Methods used** An algorithm was developed with providers from neonatology, cardiology, medical genetics, and molecular pathology. Briefly, the algorithm stratified patients based on clinical features – isolated CHD vs multiple congenital anomalies and conotruncal vs other CHD – and incorporated prenatal testing and parental preference. The algorithm was shared at meetings and by email, and posted in the workroom. Cytogenetic testing orders were reviewed and rates were compared before and after the intervention.

**Summary of results** Testing rates prior to the introduction of the algorithm (n=243, pre) vs after implementation (n=77, post): FISH, karyotype, and microarray – 7% pre vs 4% post; FISH and karyotype – 25% vs 6%; karyotype and microarray – 16% vs 11%; FISH and microarray – 4% vs 0%; single test – 48% vs 79%. The rate of diagnosis remained stable (21% vs 23%), despite a decrease in the mean number of tests per patient (1.60 vs 1.24 tests/patient, Mann-Whitney p-value<0.00001).

**Conclusions** Implementation of an algorithm in the NICU for CHD decreased redundant cytogenetic testing without decreasing rates of molecular diagnosis. These results show the benefits of engaging multiple stakeholders in order to systematically reduce misorders and unexpected results, to improve efficiency in treatment, and to decrease financial burden.

### 330 FACIAL MEASUREMENTS FROM 3D IMAGING OBTAINED USING A MOBILE DEVICE FOR USE IN GENETIC EVALUATION

A Kumar, E Kravets, J Bernstein. *Stanford University, Palo Alto, CA*

10.1136/jim-2018-000939.328

**Purpose of study** Conventional dysmorphology involves measuring specific facial features to aid in identifying individuals with rare diseases. Future approaches may leverage computer assisted evaluation of facial images. However, 2D-image-based techniques are limited by artifacts related to projection distortion and head pose affecting measurement accuracy. Capturing 3D images can circumvent these limitations, but many current devices are bulky and difficult to use.

Infrared-based sensors used for facial recognition in mobile phones (e.g. iPhoneX) can now capture 3D images and their inherent portability and ubiquity may overcome major limitations of current 3D technologies. Before use in clinical practice, evaluation of their measurements under ideal and clinical circumstances is needed to identify and address sources of error.

**Methods used** Under ideal circumstances, a mannequin head labeled with markers was used to examine accuracy of the 3dMD system (3dMD, Atlanta GA) as compared to an iPhoneX face-capturing application (Bellus3D, Sunnyvale CA). Three facial images were captured using both devices. Facial meshes from 3dMD and iPhoneX were overlaid and aligned using a computational algorithm. Point-point distances of facial landmarks (palpebral fissure length, inner/outer canthal distance, ear length, mouth width) were calculated in triplicate for each image using MeshLab software. Error was calculated by comparing point-point distances and comparing the alignment of each facial mesh.

**Summary of results** Alignment and comparison of the mesh obtained from 3dMD and the iPhoneX revealed a global alignment error of 0.42–0.60 mm. The average differences in linear measurements from 3dMD and the iPhoneX ranged from 0.07–1.47 mm for various landmarks with measurements of lateral features more error prone than measurement of features in the anterior face. Additional studies in humans are underway.

**Conclusions** In this pilot study, the accuracy of an iPhoneX facial scanner was evaluated for use in a genetics clinic. The ease of use and portability of the system are clear advantages. Limitations include the need for cooperation during scanning as well as reduced accuracy over specific facial landmarks. Additional studies are needed before the platform can be adopted as an addition to manual anthropometry and 2D photography.

### 331 PRENATAL DETECTION OF CEREBELLAR HYPOPLASIA ASSOCIATED WITH A NONSENSE VARIANT IN *DLL1*, A NOTCH LIGAND

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10.1136/jim-2018-000939.329

**Case report** The Notch pathway is a highly conserved pathway in cell differentiation and fate in metazoan species. NOTCH is a cell-surface receptor that transduces signals by interacting with ligands such as Delta-like (*DLL*). We describe the clinical

features of a child with mutation in *DLL1* and a small cerebellum that was identified prenatally.

A 3-year-old female was born to non-consanguineous parents. Abnormal cerebellar formation was noted at 19 weeks gestation and ultrasound showed a cerebellum that measured small for gestational age at <2%. Fetal MRI showed a subjectively small cerebellum that measured at the lower limits of normal. Subsequent ultrasounds showed cerebellum consistently lagging in growth at 10%. All other biometrics were normal. At birth, hypotonia was noted and the child developed speech and motor delays with difficulty in coordination. Examination revealed mild hypertelorism but otherwise normal. Parents declined postnatal MRI. Whole exome sequencing showed a *de novo* nonsense variant, c.1492 G>T, predicting p. Glu498X, in the *DLL1* gene.

*DLL1* is a human homolog of NOTCH ligand which interacts with the FGF pathway that is critical for multiple developmental processes. Notably, in murine studies, *DLL1* missense mutations result in vertebral column defects resembling spondylocostal dysostosis (Schuster-Gossler et al., 2016). Furthermore, missense variants in *DLL1* have been identified in patients with holoprosencephaly or autism (Dupe 2010, Pinto 2014). However, our patient's nonsense variant is more consistent with haploinsufficiency for this gene. Additional evidence linking haploinsufficiency with abnormal cerebellar development comes from a report of a deletion at chromosome 2q37 that includes *DLL1* in association with cerebellar hypoplasia (Peddibhotla et al., 2015). Similarly, conditional deletion of *DLL1* in unipolar cerebellar astrocytes (Bergmann glial cells) in the mouse resulted in disorganization of the Bergmann fibers and a reduction in number and ectopic location of the Bergmann cells (Hiraoka et al., 2013) implying defective cerebellar development.

This is the first description of a *DLL1* variant that is predicted to be deleterious associated with cerebellar hypoplasia identified prenatally. Our findings suggest that *DLL1* should be considered as a cause of cerebellar hypoplasia.

### 332 TREATMENT WITH CHOLIC ACID LEADS TO RESOLUTION OF RENAL CYSTS IN CONGENITAL BILE ACID SYNTHESIS DISORDER TYPE I

PJ Leahy, C Lee, S Schelley. *Stanford, Mountain View, CA*

10.1136/jim-2018-000939.330

**Case report** Diagnostic clues to the etiology of renal cysts in infants include the laterality of the cysts, the size of the kidneys, the presence of renal cysts in other family members, and the presence of other anomalies. While ADPKD and ARPDK are at the top of the differential, defects in bile acid synthesis should be considered especially in the presence of liver or biliary involvement. We report a term infant with normal development who presented with bilateral renal cysts at the age of 20 months. Sequencing and deletion/duplication analysis of *PKD1* and *PKD2* revealed a maternally inherited variant of uncertain significance in *PKD1* not thought to be related to the proband's renal cysts given mother's phenotype.

The patient went on to develop dark green stools and renal cyst number and size remained unchanged. Whole exome sequencing revealed likely pathogenic variants *in trans* in *HSD3B7*. Bile acid analysis confirmed elevation of 3 $\beta$ -hydroxy $\Delta$ 5 bile acids, and the diagnosis of congenital bile acid synthesis defect type I (CBAS1) was made. Treatment with cholic acid lead to nearly complete resolution of the renal cysts one year after treatment and they have not returned. Stool color is normalizing. This is the second report of the resolution of renal cysts after therapy with cholic acid in a patient with CBAS1. While the mechanism is unknown, bile acid synthesis defects should be considered in the differential diagnosis of bilateral renal cysts as cholic acid is an effective treatment option for these patients.

### 333 IL6ST RELATED IMMUNODEFICIENCY DISORDER: A CASE REPORT AND REVIEW OF LITERATURE

<sup>1</sup>F Velez-Bartolomei, <sup>1</sup>D Zastrow, <sup>1</sup>C McCormack, <sup>1</sup>J Kohler, <sup>2</sup>N UD, <sup>1</sup>P Fisher, <sup>1</sup>E Ashley, <sup>1</sup>M Wheeler, <sup>1</sup>J Bernstein. <sup>1</sup>Stanford University-School of Medicine, Stanford, CA; <sup>2</sup>NIH-Undiagnosed Disease Network, Stanford, CA

10.1136/jim-2018-000939.331

**Case report** The IL6ST gene codes for the GP130 cytokine receptor subunit, which is a signal transducer molecule shared by many cytokines, including Interleukin 6 (IL6), Interleukin 11 (IL11), ciliary neurotrophic factor (CNTF), Leukemia inhibitory factor (LIF) and oncostatin M (OSM). Atsumi et al. showed in mice that the p.Tyr759Phe point mutation in the gp130 cytokine receptor can induce autoimmune disease resembling Rheumatoid Arthritis. Recently, Schwerd et al. reported a female patient with biallelic mutations in the IL6ST gene, who presented with elbow contracture, limited finger extension, multiple episodes of pneumonia, cellulitis and eye infections associated with Hyper IgE, eosinophilia and craniosynostosis. We present a 9 year old male patient who is a compound heterozygote for mutations in the IL6ST gene who presents with dysmorphic features, chronic osteomyelitis and septic arthritis, eosinophilia and increased IgE.

The patient has demonstrated camptodactyly of his fingers since birth. At 6 months old he had pneumonia with empyema. He additionally has a history of late eruption of primary teeth, mild persistent asthma and has had myringotomy tubes placement due to chronic effusions. At 4 years old he developed chronic osteomyelitis and recurrent episodes of septic arthritis in knees and left elbow. Dysmorphic features include midface hypoplasia and slightly flared ribs. Laboratory findings have included eosinophilia, elevated IgE and decreased IgM. Whole exome sequencing identified compound heterozygous variants c.1549G>C (p.A517P) and c.1552+3A>C in the IL6ST gene.

Our patient has similar features as the previously reported case, with multiple infections including pneumonia. Chronic osteomyelitis and septic arthritis, as seen in our patient, have not been reported in this disorder. Our case reinforces the gene-disease association and extends the spectrum of phenotypes associated with the IL6ST-related Immunodeficiency disorder.

## Neonatology General IV

## Concurrent Session

10:15 AM

Friday, January 25, 2019

## 334 PRENATAL AND POSTNATAL INFLAMMATION-RELATED RISK FACTORS FOR RETINOPATHY OF PREMATURITY

GP Goldstein, SA Leonard, P Kan, E Koo, H Lee, SL Carmichael. *Stanford University, Palo Alto, CA*

10.1136/jim-2018-000939.332

**Purpose of study** Retinopathy of prematurity (ROP) is a disorder of vascular development in preterm infants. Further research is needed to better understand the relationship between inflammation and ROP. We performed a population-based cohort study to assess the association between prenatal and postnatal inflammation-related risk factors and ROP.

**Methods used** We used data collected by the California Perinatal Quality Care Collaborative, representing nearly all preterm births in California. We included infants born between 2007 and 2011 at less than 30 weeks gestational age, and excluded infants with extremes of weight for gestational age and those with missing exposure or outcome data. Multivariable regression models and principal components analysis were used to assess the association between the prenatal and postnatal inflammation-related exposures and severe ROP.

**Summary of results** 14 816 infants were included in the analysis after application of inclusion and exclusion criteria. 10.8% of infants developed stage 3–5 ROP or surgical ROP. Prenatal inflammation-related risk factors significantly associated with severe ROP were prolonged rupture of membranes (RR 1.18, 95% CI 1.05–1.33), preterm premature rupture of membranes or preterm labor (RR 1.35, 95% CI 1.10–1.65), chorioamnionitis (RR 1.33, 95% CI 1.13–1.56), and congenital infection (RR 1.88, 95% CI 1.21–2.92). Principle components analysis found that the risk of severe ROP was higher in infants with prenatal inflammation-related risk factors (RR 1.18, 95% CI 1.06–1.31). After blocking the effect of prenatal inflammation on gestational age at birth, the risk ratio was reduced to 1.03 (95% CI 0.93–1.13). Postnatal risk factors associated with severe ROP included supplemental oxygen use at 28 days of life (RR 3.3, 95% CI 2.7–4.1), late-onset sepsis (RR 1.39, 95% CI 1.26–1.53), intraventricular hemorrhage grades 3–4 (RR 1.22, 95% CI 1.08–1.37), and necrotizing enterocolitis (RR 1.36, 95% CI 1.19–1.55).

**Conclusions** In summary, we found that postnatal inflammation-related risk factors have a more profound impact on ROP development than prenatal inflammation-related risk factors. The association between prenatal inflammation-related risk factors and ROP was largely explained by gestational age as a mediating variable.

## 335 DEVELOPMENT OF AI DEEP LEARNING ALGORITHMS FOR THE QUANTIFICATION OF RETINOPATHY OF PREMATURITY

<sup>1</sup>P Touch, <sup>1</sup>Y Wu, <sup>1</sup>Y Kihara, <sup>1</sup>E Zepeda, <sup>1,2</sup>TB Gillette, <sup>1,2</sup>MT Cabrera, <sup>1,3</sup>A Lee. <sup>1</sup>University of Washington, Seattle, WA; <sup>2</sup>Seattle Children's Hospital, Seattle, WA; <sup>3</sup>Puget Sound Veteran Affairs, Seattle, WA

10.1136/jim-2018-000939.333

**Purpose of study** Retinopathy of prematurity (ROP) remains a leading cause of childhood blindness worldwide. Current diagnosis relies on the direct visualization of the retina through burdensome and painful neonatal dilated eye examinations. Recently, handheld spectral-domain optical coherence tomography (SD-OCT) has become more widely used in neonates because it allows for non-invasive, quick *in vivo* imaging of the retinal structures offering more detail than clinical examination. However, objective quantification of SD-OCT images are difficult because they require time-consuming human expert interpretation. We sought to create a fully automated algorithm to identify and quantify the ROP clinical features in SD-OCT images from neonates.

**Methods used** 4,687 SD-OCT images from 54 neonates were collected. A fully automated pipeline was created 1) to segment the border between the vitreous and internal limiting membrane and 2) detection of vitreous hyperreflective opacities (VHO) using deep learning and Gaussian convolutions, respectively. The data was partitioned by neonate into training, validation, and test sets. A total of 4 independent expert graders created the ground truth for each image in the test set, which were used to validate the models. We tested the performance of the automated pipeline using Dice coefficient and F1 score.

**Summary of results** The mean Dice coefficients for the human interrater reliability and the models for the vitreous border segmentation were 0.95 (SD=0.12) and 0.90 (SD=0.21), respectively (Wilcoxon  $p < 0.05$ ). The mean F1 scores for the human interrater reliability and the models for VHO detection were 0.75 (SD=0.25) and 0.68 (SD=0.33), respectively (Wilcoxon  $p = 0.60$ ).

**Conclusions** Deep learning models can achieve high accuracy in identifying and detecting certain clinical features of ROP. Features with subjective manual quantification such as VHO may eventually be screened using fully automated algorithms. Further studies are needed to extend the pipeline to include other clinical features such as cystoid macular edema and vitreous bands.

## 336 LENGTH OF STAY AND HOSPITAL COSTS AMONG NEONATES WITH PATENT DUCTUS ARTERIOSUS AND BRONCHOPULMONARY DYSPLASIA IN THE UNITED STATES 2003–2012

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10.1136/jim-2018-000939.334



Abstract 336 Table 1 Comparison of length of stay, hospital costs, and co-morbidities in neonates with PDA and BPD stratified by ligation

|  | Ligation (N=4775)           | No Ligation (N=11661)      | p-value |
|--|-----------------------------|----------------------------|---------|
| <b>Length of stay; median (IQR)</b>              | 103 (81-126)                | 81 (61-103)                | <0.001  |
| <b>Total hospital cost; median (IQR)/\$1000*</b> | \$221,000 (154,000-310,000) | \$150,000 (98,000-225,000) | <0.001  |
| <b>Clinical co-morbidities</b>                   |                             |                            |         |
| <b>Any necrotizing enterocolitis</b>             | 2580 (54.0)                 | 6156 (52.8)                | 0.15    |
| <b>Bowel perforation</b>                         | 391 (8.2)                   | 311 (2.7)                  | <0.001  |
| <b>Severe intraventricular hemorrhage</b>        | 757 (15.8)                  | 1093 (9.4)                 | <0.001  |
| <b>Periventricular leukomalacia</b>              | 206 (4.3)                   | 339 (2.9)                  | <0.001  |

\* Costs are in 2012 U.S. dollars.

**Purpose of study** There is controversy regarding the management of patent ductus arteriosus (PDA). Prolonged patency may lead to adverse clinical outcomes whereas surgical ligation (SL) may also independently contribute to neonatal morbidities. We describe patient characteristics and resource utilization of neonates with PDA *and* bronchopulmonary dysplasia (BPD) comparing those who had SL and those who were not ligated (NL).

**Methods used** Retrospective data analysis of the Kids' Inpatient Database from 2003–2012. We used ICD-9-CM discharge codes to identify diagnoses and procedures. Bivariate analysis was used to compare those who had SL and NL. A multivariate linear regression model with year random effects was done to identify predictors of LOS and costs.

**Summary of results** We identified 16 436 neonates with a diagnosis of PDA and BPD, 29% with SL. The SL group had a higher median (IQR) hospital cost of \$221 k (154 k–310 k) compared to \$150 k (98 k–225 k) in the NL group. SL was also associated with a longer median (IQR) length of stay (LOS) of 103 days (81–126) versus 81 (61–103). Higher rates of co-morbidities were observed in the SL group (table 1). After adjusting for patient demographics and co-morbidities, the SL group still had statistically significant increased LOS and costs.

**Conclusions** Neonates who required SL had longer LOS and higher hospital costs, but were also more likely to have adverse clinical outcomes. Our adjusted analyses suggest that the increased LOS and costs in the SL group are attributed to factors other than patient characteristics and co-morbidities we tested.

intraventricular hemorrhage (IVH), and periventricular leukomalacia (PVL).

**Methods used** We included infants born between January 2010 to July 2016 with birth weight  $\leq 1500$  g who survived for at least one week and did not have congenital malformations. Descriptive statistics, Chi square analysis, and multivariate logistic regression were analyzed using SPSS (v25, IBM). The logistic regression model was built utilizing gestational age, birthweight, gender, inborn status, SNAPPE-II (done at onset of treatment) and CRIB-II (done at birth). We calculated odds of mortality and prevalence of BPD, NEC, IVH and PVL.

**Summary of results** 560 infants were analyzed: 133 (23%) did not receive any treatment, 159 (28%) infants received only indomethacin, 172 (30%) infants underwent ligation, and 96 (17%) infants underwent ligation following failed indomethacin therapy.

Gestational age and birthweight were lower in both surgical groups compared to the non-treatment and indomethacin group. There was a higher proportion of outborn infants in the surgical ligation group. The logistic regression showed reduction in mortality in all treatment groups compared to the no treatment group ( $p=0.021$ ) Severity of illness by either SNAPPE-II or CRIB-II did not contribute to any of the outcomes.

BPD was 2.4 times more likely in infants who underwent surgical ligation ( $p<0.005$ ). Infants who received only indomethacin had a decreased likelihood of developing necrotizing enterocolitis (Bell's stage II and III) ( $p<0.01$ ). There were no significant differences in the likelihood of IVH or PVL for infants in any group.

**Conclusions** In our population of infants  $\leq 1500$  g, treatment of the ductus decreased likelihood of mortality compared to no treatment. Prevalence of BPD was higher in infants who underwent surgical ligation and prevalence of NEC was lower in infants treated with indomethacin independent of SNAPPE-II or CRIB-II.

### 337 IMPACT OF MANAGEMENT OF PATENT DUCTUS ARTERIOSUS ON LOW BIRTH WEIGHT INFANTS

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**Purpose of study** Management of the patent ductus arteriosus in low birth weight infants remains elusive due to lack of randomized control trials. We evaluated the impact of management approaches of patent ductus arteriosus (PDA) in infants born with birth weight  $\leq 1500$  g on mortality and prevalence of bronchopulmonary dysplasia (BPD), Bell's stage II/III necrotizing enterocolitis (NEC), grade III/IV

### 338 VALIDATING ESTIMATION OF FREE WATER NEEDS BASED ON SERUM SODIUM IN THE ELBW DURING THE FIRST WEEK OF LIFE

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10.1136/jim-2018-000939.336

**Purpose of study** To evaluate and validate the use of serum sodium for managing free water status in extreme low birth weight (ELBW) infants by predicting the next serum sodium based on a starting serum sodium value and change in free water delivery using the free-water deficit formula.

**Methods used** Retrospective chart review of ELBW infants born in between January 2015 to December 2017 and admitted to Kapiolani Medical Center for Women and Children Neonatal Intensive Care Unit. All the data were collected in Microsoft excel spread sheet. The free water deficit formula was used to predict the next serum sodium based on the starting serum sodium and change in free water delivery over the period between the two measured sodium values. Further, a statistical model was developed by using the same data set and several influential covariates to calculate next serum sodium. The error of prediction was quantified by the absolute difference between measured and predicted sodium values. Also, the probability of agreement on the predicted *direction* of sodium change was measured. We felt the ability to predict within 2 mEq/L over 12 hours would be a reasonable target.

**Summary of results** 97 ELBW infants defined as birth weight less than 1000 grams were included in this study. The average prediction error over 12 hours was 5.15 mEq/L and 3.35 mEq/L by free water deficit formula and statistical formula, respectively. Probability of agreement on the measured direction of change was 47% and 73%. There was an interesting observation of increase in average serum sodium values in first 47–72 hours of life despite the typical practice of increasing free water delivery over that time.

**Conclusions** Free water deficit formula, using serum sodium value and free water delivery, cannot predict the next serum sodium value within a range that would be practical for targeting. Also, it can predict the direction of change in next serum sodium values less than 50% of the time. The statistical model was better, but still inadequate at predicting next serum sodium values and the direction of change. Prospective study including measuring variables that can be used in a more comprehensive prediction formula in ELBW infants is needed before a study targeting sodium ranges can be undertaken.

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### LACK OF TREATMENT OF PATENT DUCTUS ARTERIOSUS IN EXTREMELY IMMATURE INFANTS INCREASES MORTALITY

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10.1136/jim-2018-000939.337

**Purpose of study** The optimal management of patent ductus arteriosus (PDA) in premature infants is controversial due to a lack of evidence for any specific treatment including non-intervention. We compared clinical outcomes of different management approaches for PDA in infants born at gestational age  $\leq 25$  weeks.

**Methods used** We performed a retrospective review of medical records of neonates born at gestational age  $\leq 25$  weeks between Jan 2010 through July 2017, without congenital malformations. We divided them into four groups based on

their therapeutic intervention: no intervention, indomethacin alone, ligation alone, ligation following failed indomethacin. We analyzed the effect of management type on survival and the prevalence of BPD, NEC (Bell's Stages II/III), IVH (grades III/IV), and PVL while adjusting for severity of illness using SNAPPE-II and CRIB-II scoring systems. Descriptive statistics and chi-square were calculated using SPSS, (v25, IBM). Logistic regression was performed to ascertain the effects of treatment type on likelihood of survival or specific disease. The logistic regression model was built using gestational age, birthweight, gender, inborn status, SNAPPE-II (done at onset of treatment) and CRIB-II (done at birth).

**Summary of results** We identified 210 infants  $\leq 25$  weeks gestational age with a PDA. These divided into four groups: no intervention 17 (8%), indomethacin alone 30 (14%), ligation alone 101 (48%), ligation following failed indomethacin 62 (30%). Birthweights and gestational ages were similar between the four groups. The distribution of gender and inborn status were similar in all groups. There was a significantly higher mortality rate in the no treatment group (47%) compared with the three treatment groups: indomethacin (7%), ligation (9%), ligation following failed indomethacin (10%) The prevalence of BPD, NEC (Bell's Stages II/III), IVH (grades III/IV), and PVL were similar in all groups. The logistic regression showed reduction in mortality in all three treatment groups compared with the no treatment group. Severity of illness by either SNAPPE-II or CRIB-II did not contribute to any of the outcomes.

**Conclusions** In our cohort of infants born  $\leq 25$  weeks gestation the lack of treatment for PDA significantly increased mortality.

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### CARDIOVASCULAR AND ORGAN PERFUSION CHANGES IN NEONATES UNDERGOING GASTROSCHISIS REPAIR

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10.1136/jim-2018-000939.338

**Purpose of study** The objective of this study is to determine the hemodynamic and organ perfusion effects of surgical intervention for gastroschisis in neonates.

**Methods used** This is an ongoing prospective, observational study of newborns with gastroschisis admitted to Children's Hospital Los Angeles. The results of 10 subjects are reported. Ultrasounds were performed one hour before and after final surgical closure. Measurements included indices of cardiac output and function, and superior mesenteric artery (SMA), celiac artery (CA), renal artery (RA), and middle cerebral artery (MCA) flows. Near infrared spectroscopy measured splanchnic, renal, and cerebral regional oxygenation (rSO<sub>2</sub>). Data were analyzed using paired t-test.

**Summary of results** Of 10 subjects (birthweight 2345  $\pm$  549 g, gestational age 36.8  $\pm$  1.1 weeks), 3 had immediate primary repair and 7 had silo placement with serial reductions and delayed closure. There was no difference in left and right ventricular output or shortening fraction before and after surgical closure. While there were no differences in CA, RA, and MCA mean flow velocities before and after surgery, there was a trend toward increased SMA mean flow velocity post-

operatively ( $36.2 \pm 18$  cm/s vs.  $59.2 \pm 34.3$  cm/s,  $p=0.08$ ). There was an increase in cerebral rSO<sub>2</sub> postoperatively ( $74\% \pm 5\%$  vs  $81\% \pm 10\%$ ,  $p=0.049$ ), but there were no differences in splanchnic or renal rSO<sub>2</sub>.

**Conclusions** The trend toward increased SMA mean flow velocity without a change in splanchnic rSO<sub>2</sub> suggests increased intestinal perfusion postoperatively. The increase in cerebral rSO<sub>2</sub> without a change in MCA mean flow velocity may represent a transient change in brain flow-metabolism coupling associated with waning effects of anesthesia. Gastroschisis repair was associated with hemodynamic changes that deserve further exploration in a larger sample size.

## Nephrology and Hypertension

### Concurrent Session

10:15 AM

Friday, January 25, 2019

#### 341 **IVIG REDUCES EFFICACY OF THERAPEUTIC MONOCLONALS THROUGH FC NEONATAL (FCRN) INTERACTIONS**

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10.1136/jim-2018-000939.339

**Purpose of study** Awareness of drug-drug interactions is critical in management of organ transplant recipients. However, there is little understanding of the possibility of biologic agents interfering with the efficacy of other concomitantly administered monoclonal antibodies. Here, the use of high dose IVIg for immune modulation may have an important impact.

**Methods used** This was a single center open label, parallel group, partially randomized, non-confirmatory study to explore a potential effect of IVIg on the PK and PD of the human anti-C5 monoclonal (LFG316). The study investigated the safety, tolerability, pharmacokinetics and pharmacodynamics of LFG316 +IVIg group compared to LFG316 alone (NCT02878616).

**Summary of results** The pharmacokinetics of LFG316 was evaluated separately where LFG316 was administered immediately after high dose IVIG ( $n=6$ ) and LFG316 alone ( $n=2$ ). The PK parameters obtained from both groups were consistent. In the LFG316 +IVIg group, the mean value for AUC<sub>inf</sub>/D decreased by 34%, CL increased by 63% and t<sub>1/2</sub> decreased by 41% compared with the LFG316 alone group. This difference in clearance/elimination characteristics was evident from 3 days to 21 days where faster elimination of LFG316 was observed. In the subsequent weeks, the influence on clearance by IVIG diminished. LFG316 suppressed the complement pathway as measured by the Wieslab assay and CH50 in serum. The rapid elimination of LFG316 in the LFG316 +IVIg group allowed more rapid recovery of complement activity.

**Conclusions** LFG316 alone and LFG316 +IVIg were found to be safe and well tolerated. High dose IVIg administered immediately before infusion of LFG316 has a significant

impact on the pharmacokinetics and pharmacodynamics of LFG316 resulting in a significant decline in which inhibition of complement activity is maintained. The effect of high dose IVIG on LFG316 clearance is most profound in the first 2 weeks after IVIg infusion. This suggest a significant impact of IVIg on clearance of monoclonal antibodies that limits efficacy. This is likely due to of IVIg blocking Fc neonatal receptor (FcRn), increasing clearance of monoclonals. These findings also reveal an important therapeutic pathway for IVIg administration in enhancing elimination of pathogenic antibodies in humans.

#### 342 **IN A MOUSE MODEL OF AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE (ADPKD), BOTH SIROLIMUS AND AN MTOR KINASE INHIBITOR DECREASE CYST VOLUME AND IMPROVE KIDNEY FUNCTION DESPITE DIFFERENTIAL EFFECTS ON SIGNALING AND APOPTOSIS**

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10.1136/jim-2018-000939.340

**Purpose of study** Sirolimus indirectly inhibits mTORC1 and reduces cyst growth in rodent models of autosomal dominant polycystic kidney disease (ADPKD). The novel ATP competitive mTOR kinase inhibitors (TORKs) e.g. Torin2 directly inhibit mTOR kinase resulting in inhibition of both mTORC1 and 2. The purpose of the study was to perform a head-to-head comparison of Torin2 versus sirolimus in a hypomorphic mouse model of PKD.

**Methods used** C57Bl/6 *Pkd1* p.R3277C (ADPKD) mice were treated with 0.5 mg/kg Sirolimus (SIR) or 10 mg/kg Torin2 (TORK) daily from 50 to 120 days of age. Serum BUN was analyzed using an enzymatic assay. Cyst area was quantified from H and E stained kidneys. Kidneys were immunoblotted for mTORC1 and mTORC2 substrates, pS6Ser235/236 and pAktSer473. IHC was performed for mTORC1 substrate 4E-BP1, in addition to proliferation (PCNA) and apoptosis (TUNEL) assessments.

**Summary of results** See table 1. Kidney weight, BUN and cyst area were significantly decreased by both SIR and TORK compared to vehicle (VEH). pAKT was decreased in both TORK and SIR treatments. pS6 staining, p4E-BP1 isoform T70, and PCNA staining were significantly decreased by both SIR and TORK in PKD kidneys. TORK but not SIR significantly decreased p4E-BP1Thr 37/46 isoform and increased TUNEL staining in PKD kidneys. No side effects

Abstract 342 Table 1

|      | KW/<br>BW<br>(%) | BUN<br>(mg/<br>dL) | Cyst<br>area<br>(%) | pS6  | pAKT | pS6<br>(%) | 4E-<br>BP1<br>T70<br>(%) | 4E-<br>BP1<br>Thr<br>37/47<br>(%) | PCNA<br>(%) | TUNEL<br>(%) |
|------|------------------|--------------------|---------------------|------|------|------------|--------------------------|-----------------------------------|-------------|--------------|
| VEH  | 2.6              | 30                 | 32                  | 1.3  | 0.8  | 9.9        | 6.6                      | 7.3                               | 2.3         | 5.5          |
| TORK | 2.1*             | 19*                | 22*                 | 1    | 0.3* | 0.8*       | 2.1                      | 4.1*                              | 1.5*        | 9.5*         |
| SIR  | 2.3*             | 18*                | 20*                 | 0.7* | 0.2* | 1.3*       | 2.6                      | 6.6                               | 1.4*        | 5.3          |

\*p

were noted on gross examination in either treatment group.

**Conclusions** For the first time, we have shown in a head-to-head study that the TORK, Torin2, is as effective as sirolimus in decreasing kidney size and BUN in a hypomorphic ADPKD mouse model. Both drugs inhibited pAKT, p4E-BP1T70 isoform and proliferation. TORK but not SIR significantly decreased p4E-BP1Thr 37/46 isoform and increased apoptosis staining in PKD kidneys. In conclusion, both SIR and TORK are equally effective in decreasing PKD and improving kidney function, but have differential effects on 4E-BP1 signaling and apoptosis.

### 343 UNILATERAL NEPHRECTOMY FOR RECALCITRANT CHILDHOOD NEPHROTIC SYNDROME

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10.1136/jim-2018-000939.341

**Purpose of study** Nephrotic syndrome (NS) is a common childhood kidney disorder. Recalcitrant nephrotic syndrome (RNS) cases are resistant to therapy and experience debilitating edema. Unilateral nephrectomy (UN) has been used to improve the quality of life of these children. The purpose of this report was to analyze our center's experience, with the hypothesis that UN reduces proteinuria and improves clinical outcomes.

**Methods used** This was a single-center retrospective case series study from January 1998 to December 2017. We included patients aged 1–17 years with RNS requiring symptomatic treatment with albumin infusions. Data collected in 3 month intervals for 2 years before and after UN included urinary protein concentration (Uprot), serum albumin level, number of albumin infusions, glomerular filtration rate (eGFR), number of hospital admissions, and growth (Z-scores). Results were expressed as medians and differences among groups analyzed using the Kruskal Wallis test.

**Summary of results** We identified 6 patients, with a median age at diagnosis of 25 mos (range 1–25) and UN at a median age of 42 mos (range 5–85). All had therapy-resistant RNS, 4 had focal segmental glomerulosclerosis (FSGS) and 2 had congenital nephrotic syndrome. While standard measures of nephrotic syndrome severity did not change significantly after UN, including Uprot excretion (13.9 vs 13.9 g/L, pre vs post UN,  $p=0.61$ ) and serum albumin (14 vs 19 g/L, pre vs post UN,  $p=0.87$ ), there was a clinically significant decrease in albumin infusion requirements (29 vs 13 infusions in the 3–6 mos period pre and post UN,  $p=0.34$ ) and in hospitalization rate for co-morbidities (2.8 vs 1.3 hospitalizations per patient per year, pre vs post UN). Notably, in the 3 mos after UN there was a significant decrease in eGFR from 98 to 49 ml/min/1.73 m<sup>2</sup> ( $p=0.02$ ), decreasing to <60 in 3 FSGS patients.

**Conclusions** UN is a radical intervention in patients with RNS. Although UN does not decrease urine protein excretion (g/l) or increase serum albumin levels it does improve the patient's quality of life in the short term by decreasing albumin infusions requirements and hospitalizations for co-morbidities, in part by hastening the progression to ESRD. Although based on a small cohort, these data will help inform parents and caregivers around the decision to proceed with UN.

### 344 KNOWLEDGE, ATTITUDES, AND BELIEFS ABOUT HYDRATION IN MARATHON RUNNERS

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10.1136/jim-2018-000939.342

**Purpose of study** The incidence of exercise-associated hyponatremia (EAH) continues to rise in parallel with the popularity of marathon running. When runners drink fluids beyond thirst and gain weight during a race, they are at risk for developing EAH, sometimes with fatal consequences. Since the revised 2015 statement from the 3rd International EAH Consensus Conference to 'drink to thirst', research specifically on the hydration plans of marathon runners and their knowledge of EAH has not been conducted.

**Methods used** Full marathon runners were approached 1–2 days before the marathon and asked to complete a pre-race survey and give a pre-race weight. Follow up post-race weights were measured at the finish line. Race times were pulled from the public race website. Statistical analysis of data was done using chi-square and ANOVA tests.

**Summary of results** 210 marathoners were enrolled in the study. Post-race weights were obtained for 43 runners at which point an active shooter threat forced research team evacuation. Experienced marathon runners had a hydration plan (82%) compared to first time marathon runners (53%) ( $p<0.01$ ). When the participants were all split into 3 equal groups by race times, the group with longer racing times intended to drink every mile/station (60%) while the group with shorter racing times preferred to drink every other mile or less often (60%). Most runners (84%) claim to have heard of EAH, but only 32% could prove understanding of hyponatremia. Both experienced marathon runners and the tertile of runners with shorter racing times significantly ( $p<0.05$ ) proved to have increased knowledge of hyponatremia compared to first-time marathon runners and the tertile of runners with longer racing times respectively.

**Conclusions** Many first-time marathoners and those with longer racing times who intend to drink at every mile have less knowledge of EAH. From previous studies, this appears to put them at high risk of developing EAH. Increased efforts to disseminate information to 'drink to thirst' and educate marathon runners are necessary to keep them healthy and safe.

### 345 ACUTE KIDNEY INJURY AND ADMINISTRATION OF ALBUMIN IN HOSPITALIZED CHILDHOOD NEPHROTIC SYNDROME PATIENTS

<sup>1</sup>R Humphreys, <sup>2</sup>C Zurbier, <sup>1</sup>J Sibley, <sup>1</sup>M Catapang, <sup>1</sup>D Matsell, <sup>1</sup>C Mammen. <sup>1</sup>BC Children's Hospital, Vancouver, BC, Canada; <sup>2</sup>University of Amsterdam, Amsterdam, Netherlands

10.1136/jim-2018-000939.343

**Purpose of study** Childhood nephrotic syndrome (NS) is often associated with significant edema. Infusions of intravenous (IV) albumin and diuretics can be used to aid fluid removal. NS patients with edema are at risk of acute kidney injury (AKI); however, the epidemiology of AKI during these episodes is not well described. The aims of this study were to describe AKI epidemiology in this population and to compare the clinical features of patients with and without AKI.

**Methods used** This was a retrospective cohort study of 51 hospital admissions for edema from 41 NS patients seen at BC Children's Hospital (Vancouver, Canada) from 2000–2012. Readmissions <2 weeks were excluded. All patients received albumin with or without furosemide. AKI was defined per Kidney Disease Improving Global Outcomes (KDIGO) creatinine criteria. The modified Schwartz equation was used to estimate baseline creatinine using a 'normal' eGFR of 120 ml/min/1.73 m<sup>2</sup>. Patients with and without AKI were compared for AKI course, amount of albumin received, and complications.

**Summary of results** Of 51 admissions 27% (14/51) met criteria for AKI; 57% (8/14) of these met criteria for Stage II or III. AKI was seen in 71% (10/14) upon admission; by discharge 57% (8/14) had resolved. Between groups, AKI admissions were associated with older patients (14 vs 8 years,  $p=0.02$ ) and higher hemoglobin values (mean  $159 \pm SD 27$  g/L vs  $142 \pm 18$ ,  $p=0.03$ ) [RAH1]. There was no significant difference between AKI and non-AKI in subsequent weight loss (9% vs 7%,  $p=0.33$ ), or length of stay (median 7 [IQR 7] days vs 5 [3] days,  $p=0.08$ ).

**Conclusions** AKI is a common feature of admissions for edema in NS patients, representing ~25% of our cohort. Hypovolemia on admission, supported by evidence of hemoconcentration, was likely a contributing factor in the AKI. AKI resolved in nearly 60% of our cohort, suggesting albumin offers benefit for both edema and renal function. Further study is warranted to analyze complications in this cohort including pulmonary edema.

### 346 PREDNISONE DOSING IN CHILDHOOD NEPHROTIC SYNDROME: COMPARISON OF LONG AND SHORT INDUCTION CLINICAL PATHWAYS

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10.1136/jim-2018-000939.344

**Purpose of study** Nephrotic syndrome (NS) is a common childhood kidney disorder. All children with new-onset NS have been managed as per our local NS clinical pathway (CP), which features standardized prednisone dosing at induction. Since the inception of our CP in 2013, new evidence emerged suggesting non-inferiority of short versus long induction dosing. In 2016 we therefore reduced our CP-recommended induction duration from 24 to 12 weeks with concomitant reduction in cumulative prednisone dosing from 4095 to 3360 mg/m<sup>2</sup>. We hypothesized that relapse outcomes would be similar in both the long and short induction CPs.

**Methods used** All children diagnosed with new-onset NS from Jan 2013–Jun 2017, initiated on the CP, and with at least 1 year of follow-up were eligible ( $n=58$ ). After excluding cases with non-minimal change disease, steroid resistance by 6 weeks, and early relapse by 12 weeks, children were stratified into short (SD:  $n=14$ ) and long (LD:  $n=28$ ) duration groups as per their intended CP induction protocol. Primary outcomes included time to first relapse, number of relapses, and the proportion of children with frequently relapsing NS ( $\geq 2$  relapses within the first 6 months of therapy or  $\geq 4$  relapses by 1 year). **Summary of results** A total of 42 children (29% female, median age 4.5 years [IQR 4.1]) were included. The median

dose of induction prednisone was significantly higher in the LD vs. SD group (3995 mg/m<sup>2</sup> vs. 3442,  $p=0.02$ ). The SD group had a shorter time to first relapse (median 135 days vs. 174), more relapses in the first year from diagnosis (median 3 vs. 2), and a higher proportion of frequently relapsing NS (62% vs 36%) than the LD group; however, all between-group differences lacked statistical significance ( $p>0.05$  for all).

**Conclusions** Standardized clinical pathways are effective tools that allow for implementing and evaluating change. Although reducing our CP-recommended induction duration from 24 to 12 weeks suggested poorer short-term relapsing outcomes, there were no statistically significant differences. Ongoing monitoring of our shortened CP is warranted as more patients and longer follow-up periods become available. Results will be used to inform future CP dosing recommendations.

### 347 RADIATION DOSE REDUCTION OF UNENHANCED CT SCAN LIMITED TO THE KIDNEYS FOR FOLLOW UP OF ASYMPTOMATIC PATIENTS WITH KNOWN NEPHROLITHIASIS

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10.1136/jim-2018-000939.345

**Purpose of study** To identify the bony landmarks and associated radiation dose reduction for a limited CT scan of the kidneys in patients requiring renal calculi follow up.

**Methods used** This IRB-approved, HIPAA-compliant retrospective study included all adult patients who underwent a CT under the exam description 'CT abdomen +pelvis renal stone' during 2017. A total of 299 patients were included. The total z-axis length of the original CT scan was recorded, and the radiation dose was recorded. The upper and lower limits of the kidneys on each scan was recorded based on the sagittal scout vertebral body endplates, and the new reduced z-axis length was measured. A commercially available software package was used to provide whole body estimates and individual organ equivalent dose for both the original CT scan as well as the limited CT scan with the new prescribed z-axis.

**Summary of results** The new prescribed upper and lower limits of the CT scan to include the kidneys was the superior endplate of T11 and the inferior endplate of L5. This led to an average scan length reduction of approximately 50%. The whole body mean effective dose was reduced by 41%, and the breast, gonadal, and bladder reduction was 72%, 74%, and 86%, respectively.

**Conclusions** In asymptomatic patients with need for imaging of the kidneys to evaluate for renal calculi growth and new stone formation, the prescribed upper limit of the superior endplate of T11 and lower limit of the inferior endplate of L5 provide a sizeable reduction in scan length and radiation dose.

### 348 PEDIATRIC RENAL BIOPSIES: CURRENT PRACTICE AND COMPLICATIONS AT A TERTIARY CARE CENTER

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10.1136/jim-2018-000939.346

**Purpose of study** Renal biopsies are common diagnostic procedures for patients with renal diseases. At our institution, interventional radiologists perform percutaneous renal biopsies under ultrasound guidance for both native and transplant (tx) kidneys. Study objectives were: 1) to evaluate the incidence of complications following renal biopsies and 2) to compare complications between native and tx biopsies.

**Methods used** Our retrospective study at BC Children's Hospital (Vancouver, Canada) included 404 biopsies performed on 239 patients (median age: 14.2 years, range: 8 months–20.6 years) from Jan 2010–Aug 2018 by 5 interventional radiologists. Data was obtained through patient charts and review of ultrasound imaging. Minor complications were: perinephric hematomas  $\geq 2$  cm or labelled as at least 'moderate', arteriovenous fistula (AVF) or pseudoaneurysm. Major complications were: any complication requiring blood transfusion, embolization or surgery. Chi-squared and Mann-Whitney U tests were used to compare native and tx renal biopsies.

**Summary of results** 203 and 201 biopsies were performed on native and tx kidneys, respectively. 33 complications were identified in 31 biopsies, with only 1 defined as a major complication (significant hematuria requiring blood transfusion). Median number of biopsies per patient for native vs tx biopsies was 1 vs 3 (range: 1–4 for native biopsies, 1–11 for transplant biopsies) ( $p < 0.001$ ). Complication incidence for all biopsies was 7.7% and 10.3% vs 5.0% in native vs tx biopsies, respectively ( $p = 0.043$ ). In biopsies with complications, the most common was perinephric hematoma for native kidneys (86%) and AVF for transplant kidneys (90%). Median number of days from biopsy to the complication finding was 0 days (range: 0–12 days) and 11 days (range: 0–154 days) for native and tx biopsies, respectively ( $p < 0.001$ ).

**Conclusions** Ultrasound guided renal biopsies appear to be a relatively safe procedure in the pediatric population with a low incidence of complications. Native and tx biopsy complications differ in regards to incidence, most common types and timing of identification. This analysis has led to a recent local quality improvement initiative to standardize our renal biopsy practices.

## Neuroscience II

### Concurrent Session

10:15 AM

Friday, January 25, 2019

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#### CATECHOL-O-METHYLTRANSFERASE POLYMORPHISM VAL<sup>158</sup>MET IS ASSOCIATED WITH DISTAL NEUROPATHIC PAIN IN HIV-ASSOCIATED SENSORY NEUROPATHY

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10.1136/jim-2018-000939.347

**Purpose of study** Despite the efficacy of antiretroviral therapies in viral suppression and immune recovery, many of those who age with HIV develop HIV-associated sensory neuropathy (HIV-SN). While some with HIV-SN remain asymptomatic, others experience debilitating symptoms of neuropathy such as distal neuropathic pain

(DNP). A single-nucleotide polymorphism of the gene for catechol-O-methyltransferase (COMT) results in the variant Val<sup>158</sup>Met, which has reduced enzymatic activity and results in higher synaptic dopamine levels. Prior studies have implicated Val<sup>158</sup>Met in numerous pain contexts. Here we examine the role of Val<sup>158</sup>Met as a predictor for DNP in HIV-SN.

**Methods used** We explore the relationship between Val<sup>158</sup>Met and DNP in HIV-SN in 1044 HIV-infected individuals enrolled in CHARTER, an observational study across 6 US institutions. Participants underwent neurologic examination, neurophysiologic testing, and whole-genome genotyping. The signs used to diagnose neuropathy were diminished ability to recognize vibration, reduced sharp-dull discrimination in the feet and toes, and reduced ankle reflexes. Neuropathy symptoms assessed included bilateral loss of sensation, paresthesias, and dysesthesias or DNP. The role of Val<sup>158</sup>Met in the presence of confounders was evaluated by multivariable logistic regression. Participants were stratified into European, African, and admixed Hispanic ancestry groups in order to evaluate the contributions of genetic background to the observed effect of Val<sup>158</sup>Met.

**Summary of results** Of the 591 participants with HIV-SN, 227 (38%) endorsed DNP. Val<sup>158</sup>Met was significantly related to the development of DNP in HIV-SN (OR=1.6) but not to non-painful symptoms. The association remained significant after controlling for other risk factors for DNP: lifetime diagnosis of depression, older age, female gender, total d-drug exposure, diabetes, and nadir CD4. Stratified by genetic ancestry, the association between Val<sup>158</sup>Met and DNP was only significant in the European group.

**Conclusions** Val<sup>158</sup>Met may be an important genetic marker for susceptibility to DNP in those of European ancestry with HIV-SN. Neuropathic pain remains a prevalent cause of disability and reduced quality of life among individuals with HIV and merits continued research efforts.

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#### POST TRAUMATIC INDUCTION OF GUILLAIN BARRÉ SYNDROME

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10.1136/jim-2018-000939.348

**Introduction** Guillain Barré Syndrome (GBS) is an ascending demyelinating polyneuropathy with paralysis and areflexia that is typically associated with preceding respiratory or gastrointestinal infections. Other etiologies are less frequently reported. We present a case of atypical acquired GBS following physical trauma.

**Case presentation** A previously healthy 64 year old male presented following a traumatic accident with no loss of consciousness. Acute injuries included multiple fractures of the 4th–6th ribs on the right, a small hemopneumothorax, and fracture of the right clavicle. Upon presentation, the patient had no neurological abnormalities. Initial CT of the head without contrast was clear of acute intracranial abnormalities. In addition to the aforementioned injuries, spinal imaging showed multilevel cervical and thoracic degenerative changes

with no evidence of cervical cord edema or myelopathy. 24 hours after admission, the patient rapidly decompensated, developed altered mental status, and required intubation for respiratory compromise. Subsequently, the patient's mental status improved but he continued to exhibit weakness and flaccid quadriplegia. MRI illustrated punctate acute subcortical infarcts bilaterally in the posterior frontal regions with no evidence for intracranial hemorrhage. Electrodiagnostic studies showed diffuse acute axonal sensory and motor polyneuropathy consistent with GBS. Cerebrospinal fluid showed albuminocytologic dissociation with elevated protein at 67 mg/dl and WBC count of 3 k/uL. The patient was started on treatment for GBS with a five day course of plasmapheresis followed by IVIG. The patient responded with significant improvement, including increased motor tone and voluntary movement in his extremities. He was discharged with outpatient neurology follow up.

**Discussion** Occurrence of trauma leading to subsequent GBS is rarely reported and is mainly limited to cases involving traumatic brain injuries or spinal cord injuries. Early identification and treatment of GBS with plasmapheresis/IVIG can prevent respiratory failure and accelerate time to recovery by 40%–50%. Therefore, it is essential to consider this diagnosis in patients presenting with acute polyneuropathy and flaccid paralysis following physical trauma with lack of identifiable precipitating factors.

**351** **TRANSCUTANEOUS NEUROMODULATION OF SPINAL CORD RESTORES BLADDER AND BOWEL FUNCTION AFTER SPINAL CORD INJURY**

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10.1136/jim-2018-000939.349

**Purpose of study** Following a spinal cord injury (SCI), lower urinary tract (LUT) and bowel dysfunction are universal and significantly impacts this population's health, quality of life and are high priorities from the patients' perspective. Current therapies focus on managing complications associated with the

dysfunction without attempting to normalize or restore function. This study investigates the use of non-invasive spinal cord stimulation and its ability to modulate both bladder and bowel function.

**Methods used** Patients with SCI at T11 or above who rely on clean intermittent catheterization were recruited. 10 individuals (7 male; 3 female) participated in a two-day initial period where the LUT was mapped to spinally evoked responses at T11 and L1. Baseline urodynamic data were recorded, as well as urodynamic data with the stimulation to measure acute changes. Three (2 male; 1 female) returned for long term stimulation over 8 weeks. This group received stimulation three times a week and maintained bladder diaries to track changes. Validated bladder and bowel questionnaires as well as urodynamic data were collected at the beginning and end of the long-term stimulation period.

**Summary of results** During the initial testing period, stimulation to T11 at 1 Hz acutely increased voiding efficiency (42% vs 22%;  $p < 0.05$ ) while stimulation at 30 Hz increased bladder storage capacity (259 ml vs 151 ml,  $p < 0.05$ ). Long term stimulation showed a significant inverse correlation between the time of study and incontinence episodes between all three patients ( $r = -0.301$ ,  $p < 0.05$ ). Two out of the three patients reported improvements in overall bowel movements with lower time needed to complete (e.g. 75 min pre-therapy to 20 min during therapy) or reduced reliance on digit stimulation and reduced reliance on suppository.

**Conclusions** This study provides initial data supporting the ability of non-invasive spinal stimulation to improve both bladder and bowel function in patients with SCI both acutely and long term. Such a modality has the potential to improve quality of life and overall health in this population and can be synchronized with routine rehabilitation that these patients undergo.

**352** **INTERNET GAMING DISORDER (IGD): ASSOCIATIONS WITH CHANGES IN GRAY MATTER AND BEHAVIORS**

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10.1136/jim-2018-000939.350

**Abstract 352 Table 1** Association of IGD and Changes in Brain Matter Structure and Behavioral Outcomes

| First Author, Year Published | IGD Subjects (n) vs. Healthy Controls (n) | Changes in Structure   | Behavioral or Mood Outcomes   |
|------------------------------|---|--|---|
| Seok JW, 2018                | 20 vs 20                                  | GMD increase in left caudate (P)   | Internet addiction scores (severity) were positively associated with depression scores ( $p < 0.001$ ); impulsiveness scores ( $p < 0.001$ ). |
| Choi J, 2017                 | 22 vs 24                                  | GMD lower DLPFC in IGD subjects, P   | In IGD group: Lower DLPFC correlated with depression ( $p = 0.001$ )  |
| Lee D, 2018                  | 45 vs 35                                  | GMV smaller in the singulate and orbitofrontal cortex w/IGD (P)  | IGD group with higher motor impulsivity: $p < 0.001$  |
| Weng CB, 2013                | 17 vs 17                                  | GMV decreased in right orbitofrontal cortex and bilateral insula (P)   | Barret Impuliveness Scale higher in patients with IGD ( $p < 0.05$ )  |
| Wang H, 2015                 | 28 vs 28                                  | GMV decreased in the bilateral anterior cingulate cortex, precuneus motor area, superior parietal cortex, left DLPFC, left insula and bilateral cerebellum in IGD subjects, ( $p < 0.05$ ) | Stroop task: the IGD group committed more errors than the control group during the incongruent condition ( $p < 0.05$ )                       |
| Cai C, 2016                  | 27 vs 30                                  | GMV increase in the right caudate and right nucleus accumbens (NAc) of subjects with IGD ( $p < 0.05$ )  | Stroop task incongruent errors higher in IGD compared to controls ( $p < 0.05$ ),   |
| Yuan K, 2016                 | 43 vs 40                                  | 15–23 Increased volume of right caudate and nucleus accumbens (NAc) in subjects with IGD ( $p < 0.05$ )  | Stroop task incongruent errors higher in IGD compared to controls ( $p < 0.05$ )  |

GMD=Grey Matter Density, GMV=Grey Matter Volume, DLPFC=dorsolateral prefrontal cortex (DLPFC)

**Purpose of study** IGD is now characterized as an addictive disorder. To gain a better understanding of IGD, the objective of this study was to evaluate any associations between IGD and changes in brain gray matter and its impact on mood and behavior.

**Methods used** Only studies of IGD subjects that included a control group were included in our analysis. The studies also must have included both a structural assessment (via voxel-based morphometry or magnetic resonance imaging) of the brain as well as a behavioral analysis.

**Summary of results** We found 7 studies that satisfied our inclusion criteria (table 1 below). Most studies were cross sectional and included teenagers or young adults. Diagnosis of IGD varied in different studies, some were based on the standard Internet Addiction Testing and others based on DSM-V criteria. Common changes in brain structure in IGD subjects compared to controls included: smaller volume and/or density in pre-frontal or orbitofrontal area, increased density or volume in the caudate cortex and nucleus accumbens. These alterations were associated with severity of IGD. Mood or behavioral assessment were consistent with increased incidence of depression, impulsive behavior and impairment of cognitive control in IGD subjects compared to controls.

**Conclusions** Our literature review suggests that IGD is associated with structural alterations mainly in the frontostriatal areas that control impulsivity, reward based learning and mood. These findings were confirmed by behavioral assessments. However due to the cross-sectional nature of the studies cause-and-effect relationships remains unclear. Answering this question is critical for developing treatment strategies for individuals with IGD. Larger longitudinal controlled studies are needed to substantiate these findings.

### 353 GREATER OCCIPITAL NERVE BLOCK FOR THE TREATMENT OF CHRONIC MIGRAINE HEADACHES: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**Purpose of study** Few treatment options exist for chronic migraine headaches, with peripheral nerve blocks having long been used to reduce frequency and severity of migraines. Although the therapeutic effects have been observed in clinical practice, the efficacy has never been fully studied. In the past decade however, several randomized clinical controlled trials have been conducted to assess the efficacy of greater occipital nerve (GON) block in the treatment of chronic migraine headaches. The goal of this study was to analyze the currently available data and establish clinical guidelines for the use of GON block in the treatment of chronic migraines.

**Methods used** A systematic review of the literature was performed in the citation databases PubMed, Embase, Medline and The Cochrane Library. The initial search of databases yielded 259 citations of which 33 were selected as candidates for full-text review. Of these, 9 studies were selected for inclusion in this meta-analysis.

**Summary of results** Studies were analyzed that reported mean headache days per month in both intervention and control groups. A total of 417 patients were studied, with a pooled mean difference of  $-3.60$  headache days (95% CI= $-1.39$  to

$-5.81$ ). This demonstrates that GON block intervention significantly reduced the frequency of migraine headaches compared to control ( $p < 0.00001$ ). Secondary analysis was also performed on mean visual analog scale (VAS) pain scores of study participants. Pooled mean difference in VAS pain scores of  $-2.20$  (95% CI= $-1.56$  to  $-2.84$ ) demonstrated significant decrease in headache severity compared to control ( $p = 0.0121$ ). Two studies also reported patients that experienced a greater than 50% reduction in headache frequency. Risk ratios were calculated in these two studies, and the average risk ratio was found to be  $0.76$  (95% CI= $0.97$  to  $0.55$ ). This demonstrated a significant decrease in headache frequency ( $p < 0.00001$ ).

**Conclusions** GON block should be recommended for use in migraine patients, in particular those that may require future surgical intervention. GON block may act as an important stepping stone for patients experiencing migraine headache, in its ability to potentially assess surgical candidates for nerve decompression.

### 354 A CASE OF ACUTE SPONTANEOUS EPIDURAL HEMATOMA

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10.1136/jim-2018-000939.352

**Purpose of study** Spontaneous spinal epidural hematoma is a rare condition requiring early recognition and intervention and is considered a neurosurgical emergency.

Spontaneous epidural hematomas are mostly associated with coagulopathies, vascular malformation, anticoagulation therapy, neoplasms and trauma. However in half of the cases the etiology remains unclear. We are describing a case of spontaneous cervical spine epidural hematoma in a patient with underlying lupus.

**Method** Retrospective case report

**Case presentation** 26 year old African American male with diagnosis of Lupus in remission presented with sudden onset of burning pain at the left scapula with radiation to right scapula associated with bilateral arms numbness and weakness.

He denied any preceding trauma or invasive procedures and presented to a local hospital but was discharged with pain and muscle spasm medication, which provided minimal relief. Two days later his symptoms worsened to the extent of difficulty walking and eventually paraplegia with decreased sensation from abdomen to legs, and urinary retention.

Neurological assessment on admission indicated 3/5 left upper extremity strength, 2/5 left lower extremity strength, decreased sensation to light touch and pinprick in left upper and lower extremity, and positive Babinski. Within a few hours, his weakness and sensory defects had progressed to include the right lower extremity as well.

MRI of cervical spine indicated a large extradural mass in the posterior portion of cervical spine between C5-T2 with significant left lateral compression of the spinal cord. Patient was emergently taken for intervention and had C6-T1 laminectomy for evacuation of what was found to be a spinal epidural hematoma. Postoperatively, patient reported persistent numbness and tingling in fingertips and lower extremities, however, reported regaining 85% motor function of right arm, 80% of the right leg, 75% of left arm, and 40% of left leg.



**Conclusion** Diagnosis of Spontaneous spinal epidural hematoma should be suspected with sudden onset neurological deficits. MRI is the diagnostic modality and emergent neurosurgical decompressive laminectomy should be performed to avoid permanent neurological deficit.

**355 ISOLATED OPHTHALMOPLEGIA WITH POSITIVE GQ1B ANTIBODY TITERS**

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10.1136/jim-2018-000939.353

**Case report** The presence of GQ1b antibodies in acute inflammatory demyelinating syndromes has been well established. These syndromes are closely related, forming a spectrum with similar underlying pathophysiology but varying clinical presentation. Recognizing these variations facilitate quick and accurate diagnosis.

A previously healthy 57 year-old male presented with a three day history of painless binocular diplopia. These symptoms were preceded by an isolated bout of mild, non-bloody, diarrheal illness while in Costa Rica two weeks prior. Upon admission, he reported no blurry vision, loss of vision, or eye discharge. Two days after onset of the diplopia, he experienced a severe throbbing frontal headache with mild nausea. Review of systems were otherwise negative. Examination revealed isolated bilateral CN VI palsy, with intact reflexes throughout. Initial CT/MRI revealed no abnormalities. AChR antibody titer was negative and his CSF demonstrated normal values. CSF was sent for further analysis and the patient was discharged after receiving a course of IV Solu-Medrol, which relieved only his headache, and follow up.

The next day, he reported worsening diplopia with new onset mild axial ataxia and was readmitted to the hospital. He exhibited horizontal ophthalmoplegia, with restricted upward vertical gaze. Examination of the patient demonstrated an A and O male with normoreflexia in all extremities, intact motor and sensation in all extremities, and an abnormal finger-nose-finger test with both eyes opened attributed to his

diplopia, with no cerebellar signs. CSF demonstrated positive GQ1b antibodies, EMG/NCS studies of all extremities were not suggestive of demyelination.

In this case, the patient developed bilateral ophthalmoplegia associated with serum GQ1b IgG antibodies. AIDP processes were pursued because of his presentation and history, however, the patient remained normoreflexive. In addition, EMG/NCS studies did not reveal a peripheral demyelinating process. This case of isolated bilateral ophthalmoplegia illustrates a rare presentation on the spectrum of GQ1b syndromes. Recognizing that AIDP syndromes may present in a non-typical manner is crucial to facilitating prompt clinical diagnosis and initiation of appropriate immunotherapy.

**356 SURGICAL TREATMENT OF SEIZURES REFRACTORY TO ANTI-SEIZURE MEDICATION IN THE PEDIATRIC POPULATION: A CLOSER LOOK AT THE LITERATURE**

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10.1136/jim-2018-000939.354

**Purpose of study** Published literature on the success rates of epilepsy surgery in pediatric patients is limited. The objective of this study was to perform a compilation of studies available on the effectiveness of surgery in pediatric patients with epilepsy refractory to anti-seizure medications.

**Methods used** We used search engines, such as Pubmed, Google Scholar and Cochrane to identify the studies. Only studies of pediatric patients <18 years of age that included a control group (medication alone) were included in our analysis.

**Summary of results** More than 60 articles were found and of those, 7 studies satisfied our inclusion criteria (see table 1). Seizure freedom was higher in the surgical group compared to the medical treatment group in all studies. The location of seizure focus and the duration of seizures were not well defined in some studies. But in those studies that characterized the location, there was a higher surgical success rate in children with focal or unilateral epileptogenic pathologies. Adverse outcome in the surgical group included monoparesis

**Abstract 356 Table 1** Comparison of surgical and non-surgical management of epilepsy in children

| 1st Author, Year | Subject (n) in Surgery Group                  | Control (n) in Non-Surgery Group | Age at Surgery (years) | Localization of Seizures                  | % Seizure Free: Surgical vs. Non-Surgical                         | Follow-Up Time (years) |
|------------------|---|----------------------------------|------------------------|---|---|------------------------|
| Dwivedi, 2017    | 57  | 59                               | ≤18                    | Temporal: 24.6%<br>Extra-Temporal: 75.4%  | 77% vs. 7% (p<0.001)  | 1                      |
| Puka, 2016       | 71  | 37                               | 12.98 (Mean)           | Temporal: 53.85%<br>Extra-Temporal: 46.2% | 92.8% vs. 57% (p=0.001)   | 6.98 (Mean)            |
| Otsuki, 2015     | 31 resective surgery<br>36 palliative surgery | 250                              | <6                     | All Extratemporal                         | Surgical 52.4%<br>Palliative 32.1%<br>Medical 15.7%               | 3                      |
| Edelvik, 2013    | 88  | 13                               | ≤18                    | Temporal: 43%<br>Extra-Temporal: 57%      | 44.0% vs. 0.00% (p<0.0005)  | 10                     |
| Mikati, 2010     | 19  | 19                               | 2–14                   | Temporal: 36.8%<br>Extra-Temporal: 63.2%  | 78.9% vs. 21.1% (p=0.01)  | 3.44–3.84 (Mean)       |
| Skirrow, 2010    | 42  | 11                               | 12.3–13.3 (Mean)       | All Temporal                              | 86.0% vs. 36.0% (p=0.002)   | 9                      |
| Rausch, 2003     | 44  | 8                                | Not Stated             | Left Side: 47.7%<br>Right Side: 52.3%     | 88% of non-surg and 50% of surg had at least one seizure (p<0.05) | 12                     |

and hemiparesis in minority of patients that improved over time. One study (Rausch) reported that at the 12 year follow-up, all non-surgical patients and 71% of the surgery patients were taking anti-seizure medications. However, the number of medications was less and quality of life was better in the surgical group.

**Conclusions** Our review suggests that epileptic resective surgeries were associated with higher rate of seizure freedom compared to medical treatment alone. Large controlled trials are needed to delineate the most optimal time for surgery as well as long-term outcome for different seizure types in patients with drug-resistant epilepsy.

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### AN EXAMINATION OF NEURAL NETWORKS IN ADOLESCENTS WITH AND WITHOUT SEVERE WORRY

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**Purpose of study** Severe worry involves persistent thoughts about potential negative events, is present across anxiety and mood disorders, and frequently emerges during adolescence. The neural underpinnings of worry are poorly understood, particularly among adolescents. The current study sought to identify patterns of brain activity underlying the experience of worry in adolescents.

**Methods used** Forty-five adolescents (ages 13–18) with mild to severe worry were recruited from an urban children's hospital and the larger community. Worry severity was assessed via self-report on the Penn State Worry Questionnaire for Children (PSWQ-C). Participants underwent functional magnetic resonance imaging (fMRI) during which they completed an emotional anticipation task to isolate regions of the brain activated during the anticipation and viewing of emotional images. Negative and neutral images were presented following a negative, neutral, or ambiguous cue, and participants pressed a button to classify the image as either negative or neutral. We examined blood oxygenation level-dependent (BOLD) responses in the anterior cingulate cortex (ACC), insula, and amygdala across groups during viewing of negative images preceded by a negative cue, and contrasted these against BOLD responses to neutral images preceded by a neutral cue (threshold at  $p < 0.001$ ,  $k > 5$ ). Beta weights were extracted and correlations were performed to examine associations between activation in regions of interest (ROI) and PSWQ-C scores.

**Summary of results** Group analyses revealed significant activation of the ACC and insula in response to negative versus neutral images, with no significant activation of the amygdala. A marginally significant negative association was found between PSWQ scores and activation in the insula ( $r = -0.266$ ,  $p = 0.077$ ) during emotional image viewing.

**Conclusions** Our findings are largely consistent with previous studies, suggesting that the insula and ACC are implicated in the anticipation and processing of negative emotion, and are likely to be central to worry. Surprisingly, activation in the insula was negatively associated with worry severity, although this finding was only marginally significant. It may be that other brain regions, outside our collection of ROI, are more central in determining the intensity and severity of worry.

## Surgery IV

### Concurrent Session

10:15 AM

Friday, January 25, 2019

358

### HISTORY OF RENAL TRANSPLANT DOES NOT PORTEND TO INCREASED MORTALITY IN DE NOVO BLADDER CANCER

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10.1136/jim-2018-000939.356

**Purpose of study** Immunosuppression following solid organ transplant is associated with an increased incidence of secondary malignancies. Several reports in the literature have suggested an increased risk of *de novo* bladder cancer in renal transplant recipients. However, it remains unknown if *de novo* bladder cancer in renal transplant patients portend increased mortality as with other known secondary malignancies.

**Methods used** We performed retrospective review of cystectomy patients between 2014 and 2016 at The University of Colorado Cancer Center. Inclusion criteria was any patient with bladder cancer that underwent radical cystectomy with or without adjuvant/neoadjuvant chemotherapy and radiation therapy. Exclusion criteria were patients lost to follow-up or incomplete medical records. A renal transplant cohort was created from those patients meeting inclusion criteria. Additional variables were age, gender, pathological stage, chemotherapy status, radiation status, and recurrence. The two cohorts were then compared with logistic regression and chi-square tests to identify any significance in all-cause mortality, 60 day mortality, cancer recurrence, and pathologic stage at time of cystectomy.

**Summary of results** 449 patients met inclusion criteria and 9 of these patients were found to have a history of renal transplant prior to the development of bladder cancer. Transplant status was not significant for all-cause or 60 day mortality, and age was the only significant variable with regard to all-cause mortality ( $p = 0.0018$ ). Of the 173 patients with cancer recurrence following cystectomy, there was no significance between recurrence rates and transplant status ( $OR = 0.180$ ). Regarding pathological staging, there was no significant difference between transplant status and non-transplant status ( $p = 0.62$ ).

**Conclusions** Our data suggests that the incidence of *de novo* bladder cancer in the setting of immunosuppression following renal transplantation is not associated with an increase in mortality as seen in other secondary malignancies. This suggests that management of bladder cancer in the setting of chronic immunosuppression should not deviate from the standard of care in non-immunosuppressed patient, but further validation of our findings is warranted.

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### DIFFERENCES IN MUSCLE QUALITY BETWEEN INDIVIDUALS WITH ACUTE AND CHRONIC SPINE PATHOLOGY

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10.1136/jim-2018-000939.357

Abstract 359 Table 1

| Model                | L. Multifidus |       | R. Multifidus |       | L. ES        |       | R. ES        |       |
|----------------------|---------------|-------|---------------|-------|--------------|-------|--------------|-------|
|                      | Std. $\beta$  | P     | Std. $\beta$  | P     | Std. $\beta$ | P     | Std. $\beta$ | P     |
| Age                  | 0.43          | 0.005 | 0.44          | 0.009 | 0.41         | 0.017 | 0.43         | 0.020 |
| Gender               | 0.33          | 0.025 | 0.39          | 0.019 | 0.34         | 0.045 | 0.27         | 0.132 |
| Chronicity           | -0.63         | 0.000 | -0.52         | 0.003 | -0.53        | 0.004 | -0.50        | 0.009 |
| Model R <sup>2</sup> | 0.68          | -     | 0.60          | -     | 0.55         | -     | 0.49         | -     |

Abstract 359 Table 2

| Model                | % Muscle     |       | % Fat        |       | % Collagen   |       |
|----------------------|--------------|-------|--------------|-------|--------------|-------|
|                      | Std. $\beta$ | P     | Std. $\beta$ | P     | Std. $\beta$ | P     |
| Age                  | -0.49        | 0.030 | 0.24         | 0.268 | 0.48         | 0.025 |
| Gender               | -0.16        | 0.447 | 0.13         | 0.549 | -0.05        | 0.806 |
| Chronicity           | 0.31         | 0.158 | -0.47        | 0.040 | 0.23         | 0.264 |
| Model R <sup>2</sup> | 0.28         | -     | 0.25         | -     | 0.35         | -     |

**Purpose of study** Individuals with lumbar spine pathology (LSP) have been observed to have degeneration and fatty infiltration of the paraspinal muscles. However, aging is known to cause similar changes and thus, distinguishing disease progression from natural aging has been difficult to determine. The purpose of this study was to determine the differences in muscle fatty infiltration and tissue composition in individuals with acute and chronic symptoms associated with LSP, in an age and gender matched cohort.

**Methods used** 26 patients with LSP were studied. 13 had a symptom duration <6 months and 13 for >6. T2-weighted MRIs were used to measure the fat fraction of the multifidus and erector spinae (ES) muscles at the L4 vertebra. Additionally, biopsies of the multifidus from each patient were analyzed for tissue composition (muscle, collagen, and fat) via trichrome staining. Multivariable linear regression models were created for the dependent variables of MRI fat fraction and histology-based tissue composition, using age, gender, and chronicity as independent predictor variables.

**Summary of results** For MRI fat fraction analyses, age, gender, and chronicity were all significant predictors with the exception of gender for the right ES. Older individuals and females had higher fatty infiltrate while individuals in the chronic group had lower levels (table 1). For biopsy-based tissue composition analyses, chronicity was the only significant predictor of percent fat, with acute patients having higher fat proportions. Age was the only significant predictor of the %muscle and %collagen, with older people having less muscle and more collagen (table 2).

**Conclusions** These results demonstrate that age, gender, and chronicity are significantly related to muscle fatty infiltration and that age and chronicity are significantly related to tissue compositional changes. Thus, paraspinal muscle quality is affected by symptom duration in individuals with lumbar spine pathology. Even when adjusting for age and gender, individuals with acute symptoms have higher levels of fatty infiltration.

360 THE SCALP DONOR SITE FOR SPLIT-THICKNESS SKIN GRAFTING: A SYSTEMATIC REVIEW

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10.1136/jim-2018-000939.358

**Purpose of study** Several considerations may influence a surgeon's choice of donor site for autologous split-thickness skin grafting (STSG) of acute burns. The scalp is an appealing donor site for STSG coverage of acute burns due to its hidden nature upon hair regrowth and excellent healing potential, but it is often reserved for massive burns with limited donor site availability. This systematic review aims to evaluate outcomes of scalp donor sites for STSG coverage of acute burns to elucidate its viability as a first-line option for coverage of smaller total body surface area (TBSA) burns.

**Methods used** A systematic review across MEDLINE, Embase, CENTRAL, CINAHL and LILACS databases and grey literature was conducted. Original research assessing cohort outcomes of STSG coverage of acute burns using a scalp donor site was included. Non-human studies, non-clinical studies and studies that did not specify the donor site(s) used were excluded. Outcome measures included donor site healing time, complications (namely alopecia and folliculitis) and quality of healed skin (including pigmentation changes and hypertrophic scars). Studies discussing scalp STSG coverage for non-burn patients were reviewed but did not meet inclusion criteria.

**Summary of results** Of 1201 citations identified for review, 15 met the inclusion criteria. Combining retrospective and prospective cohort studies, 1761 patients (mean age=15.36 years, mean TBSA=36.93%) underwent split thickness skin grafting with scalp donor sites. Of these, 29 (2.78%) developed folliculitis and 72 (4.60%) developed alopecia, with higher rates in De La Mettrie hair types VI-VIII. Other complications, including 'concrete scalp deformity' and hair transfer, were noted with very low incidence. Further, rapid donor site healing times (mean=7.84 days) and capacity for re-harvest (mean=2.32 harvests/patient) were noted.

**Conclusions** Published literature supports the scalp as a viable first-line option for split-thickness skin grafting of acute burns irrespective of TBSA. The scalp offers low complication rates, robust capacity for repeated harvest and little to no long-term aesthetic detriment to patients. Further studies elucidating the role of hair type in STSG complications are required to optimize surgical options for each patient.

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### A 5 YEAR RETROSPECTIVE STUDY COMPARING RESULTS OF LAPAROSCOPIC VERSUS ROBOTIC INGUINAL HERNIA REPAIR

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**Purpose of study** The progression of minimal invasive surgery is revolutionizing common surgical procedures. Previous studies have compared the outcomes of laparoscopic versus robotic inguinal hernia repairs but they have not evaluated outcomes beyond 30 days after surgery. The purpose of this study is to compare the short and long term outcomes of non-emergent laparoscopic transabdominal preperitoneal (TAPP) inguinal hernia repairs to robotic-assisted TAPP inguinal hernia repairs.

**Methods used** A retrospective chart review of patients who underwent key-hole inguinal hernia repair at a single tertiary institute between 2012 to 2017 was performed. A total of 279 patients were reviewed whose surgeries were performed by 5 surgeons. 32 patients were excluded due to incomplete medical records, the emergent nature of presentation, gross contaminations, or when hernia repair was not the primary surgery. Data collected per patient began from initial consultation up until one year post-operation. Clavien-Dindo Surgical Complication scores were calculated. Costs analysis data was gathered and compared to insurance reimbursements per subject. Long term outcomes were measured by using a validated inguinal pain questionnaire and validated quality of life questionnaire. All subjects were consented. Data analysis was performed using SAS version 9.4.

**Summary of results** Preliminary data using Chi-Square analysis showed no difference in 30 day Clavien-Dindo surgical complications (P-value=0.78). Chi-Square test also showed no significance between the two groups of patients which required secondary innervations at one year interval (P-value=0.94). There was no significant difference in mortality after 1 year between the two groups (P-value=0.53).

**Conclusions** Our study showed, as of now, that there is no difference between laparoscopic versus robotic approach in performing an elective inguinal hernia repair. Further work with regards to cost analysis is pending. Analyzing surgeon preference and surgical ergonomics using validated tools will add value to this investigation. We propose that either techniques provide safe and durable surgical outcomes for all patients in an elective setting.

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### COMPREHENSIVE ANALYSIS OF RADIATION USE IN SURGERY AT A TERTIARY ACADEMIC HEALTHCARE SYSTEM

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10.1136/jim-2018-000939.360

**Purpose of study** There is burgeoning understanding of radiation use in the surgery. In the era of growing image guided surgeries, the analysis of radiation use in the operating room at a systems based level can help identify high use factors that

can lead to quality improvement initiatives for both patients and health care professionals.

**Methods used** A retrospective review was undertaken of all operative fluoroscopic guided surgical procedures from three hospitals in a tertiary academic health care system from 2010–2017. Radiation usage metrics and cases were categorized based on surgical subspecialty, type of c-arm used, surgical fields, and surgical procedure.

**Summary of results** 1252 cases were analyzed and notable trends in all radiation usage metrics were identified across the surgical subspecialty, type of c-arm used, surgical field location and surgical procedure. Overall, vascular surgery averaged 40 times higher radiation exposure per patient than other surgical subspecialties (613.3 mGy vs 15.6 mGy, p=0.001). Statistically significant higher radiation exposures were correlated with fixed c-arm usage (1229 mGy vs 331 mGy, p=0.001), abdominal/pelvic procedures (429.2 mGy vs 274.0 mGy, p=0.002), and embolization (2450.6 mGy vs 328.2 mGy, p=0.019). Analysis of dose reduction techniques also demonstrated notable trends.

**Conclusions** A system wide healthcare analysis identified notable trends in operative radiation usage. Specifically, cases that involve vascular surgery, use of a fixed c-arm, abdominal/pelvic procedures, and embolization cases have the highest radiation exposure. These types of variables can be targeted for future dose modification techniques or staged procedures. This data can serve as baseline information for future quality improvement initiatives for patient and operating room exposure safety.

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### HEAD SHAPE AFTER SAGITTAL CRANIOSYNOSTOSIS SURGERY: OPEN VS ENDOSCOPIC STRIP CRANIECTOMY WITH HELMET THERAPY

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10.1136/jim-2018-000939.361

**Purpose of study** Sagittal craniosynostosis is a skull deformity that occurs when the sagittal suture fuses prematurely. To improve cosmesis, prevent future psychological impact, and address any raised intracranial pressure, different surgical techniques are used. This study compares outcomes of open surgery versus endoscopic strip craniectomy with helmet therapy.

**Methods used** A retrospective chart review was conducted of patients with non-syndromic sagittal craniosynostosis treated surgically from 2011–2016. Patients were divided into 2 groups: open or endoscopic surgery. Head shape was assessed using pre and post operative cephalic index (CI). Complications and operative details were compared.

**Summary of results** A total of 51 children (36 male, 15 female; 13 open, 38 endoscopic) were included with an average length of follow up of 27.2 months (4–60). The average age at surgery was 6.9 months (2–23) for open and 3.6 months (2–6) for endoscopic, p=0.0389. There was no significant difference in preoperative CI between endoscopic and open groups (0.67 vs 0.66). The largest improvements in CI were seen 3–6 months postoperatively. The CI at the last follow up was 0.74 with open and 0.75 with endoscopic. There was no statistical difference for operative time or complications (endoscopic vs open): dural tears (11% vs 0%), sinus laceration (0% vs 8%), wound infection (3% vs 8%),

unplanned reoperation (0% vs 8%) and meningitis (0% vs 8%). Mean estimated blood loss was 38 mL for endoscopic and 74 mL for open ( $p=0.031$ ). There were no transfusions, brain injuries or deaths. The mean hospital stay for open was 1.7 days vs. endoscopic, 3.1 days,  $p<0.001$ .

**Conclusions** Early (3 months) endoscopic (with helmet therapy) and later (7 months) open surgical techniques are both effective treatments for non-syndromic sagittal synostosis, with no statistical differences in post-operative CI or complications. These findings support the use of either technique and corroborate literature. A larger study may provide further evidence on how these and other surgical techniques improve head shape, as well as explore factors that may influence procedure selection.

**364 RISK FACTORS FOR MORTALITY IN PATIENTS WITH BLUNT MECHANISM AORTIC TRAUMA AT UCH: UC DENVER, MEMORIAL HOSPITAL COLORADO SPRINGS, MEDICAL CENTER OF THE ROCKIES**

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10.1136/jim-2018-000939.362

**Purpose of study** To describe the population affected by blunt aortic injury in Colorado and answer the question: What mechanistic, temporal and clinical factors are associated with mortality in BAI for patients in the UCHealth hospital system?

**Methods used** The study sites are University of Colorado Hospital, Memorial Hospital and Medical Center of the Rockies. Subjects  $\geq 18$  at time of injury, identified by ICD-9 were gathered by chart review for 1/1/06–9/11/17. Variables for demographics, injury and treatment were collected. Data were stored in RedCap and statistics performed with SPSS. Descriptive statistics, chi-square and ANOVA were performed as appropriate for variables. Binomial logistic regression was performed to determine the effect of multiple concurrent variables on mortality.

**Summary of results** Subject ( $n=65$ ) mechanisms of injury were motor vehicle collisions 60%, motorcycle collision 16.9%, motor vehicle vs pedestrian 12.3%, falls 7.7%, other 3.1%. 50.8% of patients presented with GCS  $> 8$ . 35.4% were transfer patients. ANOVA showed subject mortality was not dependent on time to first medical care  $F(32,17)=1.509$ ,  $p=0.186$ ,  $\eta^2=0.74$  and not dependent on time to study hospital  $F(39,14)=2.092$ ,  $p=0.069$ ,  $\eta^2=0.854$ .  $\chi^2$ -square showed no significant difference in mortality for airbag deployment or seat belt use ( $\chi^2(1,39)=0.009$ ,  $p=0.925$  and  $\chi^2(1,39)=0.022$ ,  $p=0.882$ ). Binary logistic regression indicates that RTS is trending towards a significant predictor of mortality ( $\chi^2(12,54)=0.009$ ,  $p<0.05$ ). Other predictors of mortality ISS, TRISS, mechanism, transfer status, GCS, race and sex are not significant in the current model. RTS was significant at the 5% level (Wald=4.937,  $p=0.026$ ). The odds ratio for RTS was 0.485 (95% CI 0.257 to 0.918). The model correctly predicted 90.9% of cases of no mortality and 81% of cases of mortality (87% correct overall).

**Conclusions** The data is fairly representative of Colorado as only UCHealth hospitals treat BAI, but the sample size is small as it is a rare injury. Data is still being collected for some fields and autopsy reports could provide additional subjects and data for certain subjects. The current regression

model predicts mortality 87% correctly but further adjustment will be done to predict mortality more accurately and without a burdensome number of variables.

**365 NOVEL STRATEGIES TO COMBAT SURGICAL SITE INFECTION USING MICRONUTRIENTS**

EY Choi, DD Gordon, CP De Guzman, R Newhall, G Harding, S Gupta. *Loma Linda University School of Medicine, Loma Linda, CA*

10.1136/jim-2018-000939.363

**Purpose of study** Surgical site infection is a common hospital acquired infection. Currently, topical antimicrobials are applied to surgical sites as a standard of care. Anecdotal evidence indicates antimicrobial properties of commercially available topical products containing micronutrients such as vitamin A, vitamin D, zinc oxide, and silver.

**Methods used** An agar well diffusion assay and agar surface assay were used. Calcipotriene, Desitin, Acticoat, SSD, Tretinoin were used as proxies for the antimicrobial properties of vitamin D, zinc oxide, silver, and vitamin A. Bacitracin ointment was used as a control. In the well diffusion experiment, each product was dispensed into a 6 mm well on Mueller-Hinton agar (MHA) inoculated with *Staphylococcus epidermidis*. For the surface experiment, a one inch slit was made on MHA inoculated with *S. epidermidis*, then a line of cream or a strip of Acticoat was applied over the slit. The plates were stored at 37°C and the zone of inhibition was measured at 24 hour and 72 hour.

**Summary of results** The well diffusion experiment indicated that all the creams except Calcipotriene had antimicrobial properties by the development of zones of inhibition and suppression. For day one, the average diameter of zone of inhibition (in mm) was  $20.67 \pm 2.3$ ,  $19.83 \pm 1.83$ ,  $21.42 \pm 1.62$ ,  $21.25 \pm 1.54$  for Calcipotriene, Desitin, SSD, and Tretinoin respectively. Compared to the zone of inhibition of bacitracin ointment,  $20 \pm 1.6$ , none except Calcipotriene were significantly different. In the surface experiment, Acticoat, Desitin, and SSD showed zones of inhibition. For day one, the average width of inhibition (in mm) was  $4.65 \pm 2.6$ ,  $0.55 \pm 0.8$ ,  $4.95 \pm 3.82$  for Acticoat, Desitin, and SSD respectively. Compared to the Bacitracin, which did not show any antimicrobial activity, all of them showed significantly larger zones of inhibition.

**Conclusions** This study showed that topical products with micronutrients or silver had antimicrobial properties that were not significantly different from that of bacitracin. Acticoat and SSD showed promising results when applied on the surface as better than the standard of care. Further testing with larger sample sizes needs to be done along with assessing the duration of effect of each agent.

**366 ASSOCIATION BETWEEN RETINAL MICROVASCULATURE ACROSS RACE AND AXIAL LENGTH**

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10.1136/jim-2018-000939.364

**Purpose of study** To examine race-related differences in microvasculature density and retinal tissue thickness across axial

length using optical coherence tomography angiography (OCT-A) in healthy eyes.

**Methods used** 25 subjects of African descent (AD) and 55 subjects of European descent (ED) were included. All patients underwent a complete ophthalmological evaluation including OCT-A testing. Vessel density examination of the superficial vascular plexus and more deep vascular plexus were evaluated in the optic nerve head and macula. Linear regression analyses were also conducted to assess the association between axial length and OCT-A measured vessel density while controlling for age. Comparisons of measures between races were conducted using non-parametric clustered Wilcoxon signed-rank tests.

**Summary of results** Analyses identified racial differences in deep macula whole image vessel density (AD mean: 51.54 and ED men: 49.76, in  $p=0.04$ ) and in deep macula parafoveal vessel density (AD mean: 53.38, ED mean: 51.51,  $p=0.030$ ). Axial length was not significantly related to either measure when controlling for age and race. A non-significant trend identified differing relationships between axial length and deep macula parafovea vessel density between AD and ED subjects ( $p=0.067$ ). There were no differences in optic nerve head whole image or peripapillary vessel density with and without large vessel removal between races. Axial length was significantly related to optic nerve head vessel density measures, although no evidence of differing relationships by race was found. In a stratified analysis, each measure remained significantly related to axial length in subjects of ED but not in those of AD, largely reflecting a limitation in sample size.

**Conclusions** Retinal microvasculature differences by race were found in the deep but not superficial macular layers. Axial length was more strongly related to vessel density in the optic nerve head than in the macula. This information can inform the development of normative reference databases of vessel density measures.

## Joint Plenary Session

### WAFMR, WAP, WSCI, AND WSPR

Friday, January 25, 2019

1:30 PM – 3:30 PM

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#### IMPACT OF ERYTHROPOIESIS STIMULATING AGENTS ON BEHAVIORAL MEASURES IN SCHOOL AGE CHILDREN BORN PRETERM

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10.1136/jim-2018-000939.365

**Purpose of study** We previously reported that children who as preterm infants were randomized to receive ESAs had better scores on externalizing behaviors (i.e. hyperactivity, conduct problems, aggression) and fewer behavioral problems than those randomized to placebo, as measured through parental report at 3.5–4 years (Lowe et. al, J Pediatrics 2017).

**Methods used** Children born preterm (birth weights 500–1250 grams) randomized to ESAs (n=41) or placebo (n=15) as infants were enrolled around 3 years of age. Healthy controls

born at term were recruited at 4 years of age. Children were seen at 3.5 to 4 years of age (visit 1) and 5.5 to 6 years of age (visit 2). We evaluated the impact of treatment on the four composite scales of the BASC-2 for visit 2: externalizing problems, internalizing problems, behavioral symptoms, and adaptability. Standardized composite scores were used for the subscales of BASC-2. Higher scores indicate lower behavioral performance, except for adaptability where higher scores indicate better performance. All BASC questionnaires were completed by a parent during the child's testing session. BASC subtest scores were analyzed among groups, controlling for maternal education.

**Summary of results** Term and preterm groups were significantly different in birth weight, gestational age and maternal education. Term and preterm groups were significantly different on three of the four BASC subscales. Term and placebo groups were significantly different for Externalizing ( $p=0.02$ ) and Behavioral Symptoms ( $p=0.01$ ). Term and ESA groups were significantly different for Adaptability. Adjusting for Maternal Education, Preterm and ESA groups differed on Internalizing ( $p=0.01$ ), Externalizing ( $p=0.05$ ) and Behavioral Symptoms ( $p=0.04$ ).

**Conclusions** The term group scored significantly better on all BASC scales compared to the preterm group (combined ESA and placebo groups). The beneficial effects of ESAs on childhood behavior were maximal in children of mothers with lower maternal education. ESAs seemed to ameliorate the adverse impact of lower maternal education (lower SES) on the behavioral domains seen in the placebo group. These findings are consistent with BASC scores obtained at 3½ to 4 years of age.

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#### IDEAS FOR CHANGE: FAMILY VIEWPOINTS FOR IMPROVING FOLLOW-UP AFTER NICU DISCHARGE

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10.1136/jim-2018-000939.366

**Purpose of study** In the U.S., nearly 5 00 000 infants are annually hospitalized in the NICU. The burden of infant health and developmental sequelae related to infants with medical complexity is widely recognized, but we have minimal information on parental perspectives for improving follow-up. We sought to understand families' experiences after discharge to better inform interventions.

**Methods used** Open-ended semi-structured interviews were conducted with English or Spanish speaking families enrolled in Medicaid in an urban high-risk infant follow-up clinic at a safety-net center, which serves preterm and high-risk term infants. We generated salient themes using modified grounded theory. Interviews were conducted until thematic saturation was reached.

**Summary of results** Twenty-one participants completed the study. The infant's median (IQR) birth weight was 1750 (1305, 2641) grams. 47% of infants required medical

equipment. 68% were Hispanic. 14% were Black non-Hispanic. 62% reported living in a neighborhood with 3–4th quartile economic hardship. The analysis revealed six major themes describing families' experiences and ideas to support follow-up: (1) comparison to normal babies, (2) concern for maternal mental health, (3) looking for peer support systems, (4) feeling empowered with health literacy, (5) including mobile technology into discharge materials and (6) home nursing/respite care.

**Conclusions** Families often compare their preterm or high-risk infant to their peers and mothers feel anxiety and stress. However, families often found hope and resilience in peer support and cited that in addition to health literacy, interventions using mobile health technology and respite/nursing care could better support families after discharge.

### 369 TUMOR-STROMAL INTERACTIONS IN COLORECTAL CANCER TREATMENT

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10.1136/jim-2018-000939.367

**Purpose of study** Cancer is a complex adaptive system orchestrated by the interactions between tumor cells and their microenvironment. In particular, cancer-associated fibroblasts (CAFs), the dominant cellular component of the tumor stroma, are often associated with a poor prognosis for a number of cancers. While significant literature has highlighted the influence of CAFs on tumor cell proliferation and invasion, the role of CAF heterogeneity on treatment response remains largely understudied. To advance our biological understanding of cancer and improve treatment efficacy, we are utilizing quantitative high-content imaging coupled with more physiologically-relevant patient-derived model systems to interrogate the dynamic interactions between cancer cells and their microenvironment. These studies are aimed at increasing our understanding of the functional and therapeutic utility of CAFs by leveraging expertise across disciplines. We focus our initial efforts in colorectal cancer (CRC), where the five-year survival rate for metastatic disease remains around 10% despite the introduction of novel therapies.

**Methods used** We have established a biorepository of patient-matched molecularly and clinically annotated CRC preclinical models, including tumor organoids and respective CAFs. We utilized high-content imaging workflows, along with machine learning and other image analysis techniques, to dynamically phenotype thousands of single cells or multicellular aggregates during drug treatments. Traditional molecular biology assays (i. e., qPCR, cytokine arrays, and western blots) were employed for mechanistic interrogation into CAF-induced drug resistance.

**Summary of results** Our preliminary work demonstrates that drug-treated CAFs alter colorectal cancer cell response to anti-EGFR targeted therapy highlighting a novel mechanism of environment-mediated drug resistance. Specifically, we discovered that patient-derived CAFs increase their secretion of EGF when treated with the anti-EGFR therapy cetuximab. This increased level of EGF is sufficient to sustain the EGFR signaling axis in tumor cells and organoid models, even in the presence of cetuximab – thus resulting in continued cancer growth.

**Conclusions** We have identified CAFs as a source of environment-mediated cetuximab resistance in colorectal cancer.

## Behavior and Development II

### Concurrent Session

8:00 AM

Saturday, January 26, 2019

### 370 CROSSFIT KAMP: AN INTERVENTION TO IMPROVE SOCIAL SKILLS IN CHILDREN WITH AUTISM

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10.1136/jim-2018-000939.368

**Purpose of study** The Centers for Disease Control and Prevention estimate that 1 in 59 U.S. children have been diagnosed with an autism spectrum disorder (ASD). Peer relationships and social skills are core challenges for those with ASD. Previous studies of structured exercise programs, like karate, have shown positive effects on social skills and reduction of stereotypical behaviors. CrossFit Kids provides a scalable structured physical exercise program based on a group training atmosphere that incorporates combinations of core functional movements and strength exercises that children can perform with basic equipment. CrossFit Kids could potentially promote social skill development; however CrossFit Kids has yet to be studied in children with ASD.

**Methods used** CrossFit KAMP is a wait-list randomized control study for children with ASD ages 8–11 years old. The intervention is a 14 week twice weekly CrossFit Kids exercise program with the specific aims of improving social skills, self-esteem, and behavioral symptoms measured by coding observed social interactions via video recording and parent and participant social and behavioral functioning rating scales. The rating scales will be administered at baseline, after each 14 week session, and 8 weeks post-intervention. Video recording with coding will be done in the second week and the last week of exercise sessions. Primary assessment of treatment effects will be measured by comparing treatment and wait-list control groups on baseline-adjusted mean outcomes at the first follow-up.

**Summary of results** We are currently enrolling our first intervention group and baseline characteristics will be presented.

**Conclusions** The results from this study is potentially beneficial in creating a program for children with ASD to promote social skill development, improve self-esteem and reduce stereotypical behaviors while also providing improved health through exercise. If successful, CrossFit KAMP could easily be implemented on a larger scale.

### 371 PHYSICAL ACTIVITY AND QUALITY OF LIFE IN ADOLESCENT GIRLS WITH TURNER SYNDROME

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10.1136/jim-2018-000939.369

**Correction: Risk factors for mortality in patients with blunt mechanism aortic trauma at UCH: UC Denver, Memorial Hospital Colorado springs, Medical Center of the Rockies**

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J Wehrend. Risk factors for mortality in patients with blunt mechanism aortic trauma at UCH: UC Denver, Memorial Hospital Colorado springs, Medical Center of the Rockies. *J Investig Med* 2019;67:222. doi: 10.1136/jim-2018-000939.362.

Since the publication of abstract 364 on ‘Risk factors for mortality in patients with blunt mechanism aortic trauma at UCH: UC Denver, Memorial Hospital Colorado Springs, Medical Center Of The Rockies’, the authors have noticed that a co-author name was omitted from the final version.

L Ferrigno should have been listed as an author alongside J Wehrend. L Ferrigno is also affiliated with the University of Colorado School of Medicine, Denver, CO.

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