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

Purpose of study Women with Turner syndrome (TS) have a high risk of cardiac disease, diabetes, and psychiatric conditions. Regular exercise has both physical and mental health benefits, but women with TS exercise less than peers. The objective of this study was to examine physical activity and other domains of health-related quality of life (QOL) in adolescents with TS as well as the lived experience with exercise.
Methods used Cross-sectional, mixed-methods study in girls with TS, 13–21 years of age without any exercise restrictions. Adolescents completed PROMIS QOL questionnaires in the domains of Physical Activity, Peer Relationships, and Psychological Stress Experiences and a parent completed the parent-proxy versions in the same domains; raw scores were converted to t-scores. A one-sided t-test was used to compare t-scores to a mean of 50 and paired t-tests compared adolescent to parent t-scores. One-on-one semi-structured interviews that focused on their experience with exercise were conducted; transcripts were coded and then analyzed using phenomenology methodology.
Summary of results Adolescents (n=17) and parents (n=17) both reported lower physical activity than normative data (p=0.01). Parents reported significant concerns for their daughters in Peer Relationships (p=0.002) and Psychological Stress Experiences (p=0.04), and these scores were significantly worse than adolescent reports (p=0.002). Adolescents did not endorse poor QOL in these domains and their t-scores were significantly better than the parent report (p=0.002 for both). Qualitative analysis found that visual-spatial deficits and anxiety were limitations to physical activity. Motivational factors for engaging in physical activity differed between parents and adolescents. Adolescents were driven by socialization, while parents were motivated by long-term health benefits.
Conclusions Adolescents with TS do not get enough physical activity. Visual-spatial deficits and anxiety, well-known components of the TS neurodevelopmental profile, negatively impact experiences with exercise. Addressing these deficits may make experiences more positive. Recognizing the unique motivational factors for exercise can guide targeted counseling. More work is needed to reconcile the finding that adolescents are motivated by socialization but parent-report scores in Peer Relationships were low.

372 EVALUATION OF SOCIABILITY AND ANXIETY-RELATED BEHAVIORS IN A MOUSE MODEL OF ANGELMAN SYNDROME AT TWO AGES

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10.1136/jim-2018-000939.370

Purpose of study Angelman syndrome is a neurodevelopmental disorder characterized by cognitive and motor deficits, along with anxiety and social abnormalities. The maternally derived *Ube3a* mouse model of Angelman syndrome was previously characterized for cognitive and motor deficits; however, other behavioral domains and older ages have not been explored. We investigated locomotor, anxiety-related and social behaviors in *Ube3a* mice and wildtype (WT) littermates at two ages, 6 months and 12 months.
Methods used Two anxiety-related conflict assays to assess exploratory behaviors were employed: elevated plus-maze and light↔dark exploratory transitions. Two social assays were used, male-female interactions and 3-chambered social approach. Open field exploratory locomotion served as a control assay to detect motor abnormalities that could introduce artifacts into the interpretations of social and/or anxiety-related abnormalities.
Summary of results The social assay, 3-chamber social approach, revealed that younger *Ube3a* mice, unlike younger WT mice, failed to show preference for the chamber with a novel mouse over the chamber with a novel object, indicating potential social deficits in this age group. Male *Ube3a* mice in both age groups spent significantly less time following an estrus female compared to WT controls during the male-female interaction test. There was also a strong tendency towards less sniffing behavior (nose-to-nose and nose-to-anogenital) in the younger *Ube3a* males. Although older mice exhibited less exploratory behavior in the anxiety-related assays, this may be due to well-characterized motor deficits that were confirmed in the open field test. Interestingly, younger *Ube3a* mice exhibited no significant difference in exploratory behaviors during the anxiety-related tasks and displayed no motor deficits.
Conclusions This study demonstrates social abnormalities in a mouse model of Angelman syndrome. Future testing should take into consideration the effect of mouse age when interpreting results from behavioral assays. Importantly, this study suggests that the phenotypes of the *Ube3a* mice, as with symptoms of people with Angelman syndrome, may change over the lifespan of the subject.

373 EXPLORING THE ASIEP AS AN OUTCOME MEASURE OF SOCIAL INTERACTIONS IN FXS

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10.1136/jim-2018-000939.371

Purpose of study Differences in social development and ASDs are a core part of the FXS phenotype. Identification of a more efficient measure that directly evaluates social interaction, can monitor change over time, and that can be used across age ranges is an area of need for FXS research and clinical care. The ASIEP-3 Interaction assessment is a standardized measure of social interaction that quantifies spontaneous social responses, reactions to requests, and the individual's social interactions under different conditions. The overall goal of this project is to assess the feasibility of the ASIEP-3 as a potential outcome measures in FXS.
Methods used The ASIEP-3 assessment is a play-based, video recorded session. Responses are scored as interaction, independent play, no response, or aggressive. The ASIEP-3 produces raw scores for all ages, and standard scores for ages 2–13. Materials adapted for an older age group.
Summary of results The ASIEP-3 was successfully administered and completed by all but 2 of the 35 participants enrolled in the study (1 non-compliance, 1 unstandardized administration). To date, results are available for 31 ASIEP administrations (21 males, M=15.44, SD=10.95 years [2–46]). Participants had a range of cognitive abilities (SB-V M(31)=60.34, SD=18.77, [47–109]), behavior symptoms (ABC Total M(13)=33.54, SD=26.12, [2–98]), and autism diagnosis (ASD n=18). Across

all administrations, the average percentage of coded behavior was highest for interaction (42% of codes),
Conclusions The ASIEP-3 was feasibly administered to both males and females with FXS across a wide range of ages, abilities, autism symptoms and behavior ratings by examiners with various levels of education. Most ASIEP scores were in the interaction and constructive independent play categories. The lack of relationship between ASIEP scores and factors such as age and IQ suggest that the measure is appropriate for most, if not all, individuals with FXS. Future directions also include further evaluation of feasibility, clinical validity, and longitudinal trajectory. The ASIEP-3 shows promised as a measure that may fill a significant gap in the ability to reliably index longitudinal social development in FXS.

374 OBSERVED PARENTING AND CHILD ANXIETY IN CHROMOSOME 22Q11.2 DELETION SYNDROME

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10.1136/jim-2018-000939.372

Purpose of study Individuals with Chromosome 22q11.2 Deletion Syndrome (22q) have a higher incidence of anxiety disorders than the general population. There is a known association between parental psychological control (PPC), and child anxiety in the typically developing (TD) population. In children with 22q, we have shown a similar relationship between self-reported PPC (specifically intrusive control) and child anxiety. The purpose of this study was to determine whether the same association exists between directly-observed parenting and anxiety in 22q and TD dyads.
Methods used 63 parent-child (22q: 32 and TD: 31) dyads were videotaped performing joint problem-solving tasks (puzzle and origami folding). Raters blinded to diagnosis coded parenting behaviors (physical assistance, physical intrusion, etc.) on a 1–5 scale every 30 s and consensus scores were obtained. Parents completed the Spence Children's Anxiety Scale. Student's t-test and Pearson's correlation coefficient were used to compare differences in mean parenting scores and determine the strength of correlation between variables.
Summary of results Mean age was 7.78 years and 45% of children were male. FSIQ and adaptive function were significantly higher in TD ($p<0.001$), and children with 22q had significantly higher anxiety scores (22q: 61.3 vs. TD: 46.7, $p<0.001$). Inter-rater agreement ranged from 0.62–0.92 for all codes except for negativity. There were no significant differences in mean ratings of observed parenting between 22q and TD dyads for either task. However, in the 22q dyads, there was a significant positive relationship between physical assistance in the origami task with child anxiety ($r=0.43$, $p=0.02$). In TD, there was a negative relationship between physical assistance (origami) and child anxiety ($r=-0.38$, $r=0.03$). There were no other significant correlations between other parenting ratings and child anxiety.
Conclusions Higher ratings of parental physical assistance is associated with child anxiety in children with 22q, but not TD. This is congruent with prior work documenting a positive relation between self-reported parental intrusiveness and child anxiety. These findings may inform intervention targets in parenting behaviors to decrease child anxiety in a high-risk population such as children with 22q.

375 PRELIMINARY EVALUATION OF DEVELOPMENTAL SCREENING MEASURES IN HIGH-RISK INFANTS WITH SEX CHROMOSOME TRISOMY

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10.1136/jim-2018-000939.373

Purpose of study Sex Chromosome Trisomy (SCT) occurs in 1:500 births and includes XXY/Klinefelter syndrome, Trisomy X, and XYY syndrome. Historically, less than 10% of individuals with SCT are diagnosed before adolescence, however the rate of prenatal diagnosis is increasing exponentially as noninvasive prenatal testing of fetal DNA in maternal blood has evolved to become standard screening in prenatal care. Children with SCT are at increased risk for neurodevelopmental differences including speech-language delays (75%) and motor skills delays (50%). The purpose of this project is to evaluate if developmental screening measures commonly used in the primary care setting identify early developmental delays in the high-risk population of infants with SCT.
Methods used Participants include infants with a prenatal diagnosis of SCT evaluated as part of the eXtraordinarY Babies study. Parents completed the Ages and Stages Questionnaire (ASQ) and the Parents Evaluation of Developmental Status (PEDS) prior to other study procedures, which included the Bayley Scales of Infant Development-3. ASQ and PEDS results will be compared to direct evaluation results from the Bayley-3 in domains of cognition/problem solving, language, and fine/gross motor skills using Pearson correlations of scaled scores in corresponding developmental domains and McNemar's test for dichotomous results (below/above cut-off) for comparison of preliminary sensitivities of screening measure subscales.
Summary of results Participants to date include infants with XXY (n=35), XYY (n=6), XXX (n=5) and XXYY (n=2) seen for visits at 2–4, 6, and 12 months of age. Results of the above analyses will be presented.
Conclusions Identification of the most sensitive developmental screening measures for infants with SCT is important to guide recommendations for primary care developmental screening in this high-risk population in order to facilitate early identification and treatment for developmental delays.

376 PREVALENCE OF PRE-PREGNANCY DEPRESSION AND RECEIPT OF ANTICIPATORY GUIDANCE ABOUT DEPRESSION AMONG COLORADO MOTHERS WITH CHRONIC CONDITIONS

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10.1136/jim-2018-000939.374

Purpose of study The aims of this study are to 1) investigate the co-occurrence of depression and comorbidities such as hypertension (HTN) and chronic diabetes mellitus (DM) prior to pregnancy and 2) assess the association of maternal comorbidities with receipt of anticipatory guidance about depression during pregnancy.
Methods used Data was analyzed from the 2012–2015 Colorado Pregnancy Risk Assessment Monitoring System (PRAMS), a population-based surveillance system that collects data on

pregnancy and postpartum experiences of mothers who have recently delivered a live infant.

Chi-square tests and 95% CI were used to assess differences in maternal characteristics between mothers with and without co-morbidities, including report of depression prior to pregnancy. We calculated adjusted risk ratios (ARR) to evaluate the likelihood of receipt of anticipatory guidance about depression during pregnancy among mothers with and without co-morbidities, controlling for maternal socio-demographic characteristics. All analyses were weighted and standard errors were adjusted to account for the complex survey design of PRAMS

Summary of results 6056 (Weighted n=251,835) Colorado mothers were included in our analysis and 9.6% (95% CI: 8.64–10.63) of mothers reported feeling depressed prior to pregnancy. Of those who were depressed prior to pregnancy, 20.3% also had accompanying comorbidities such as HTN or DM compared to 2.7% of mother who were not depressed (p-value<0.0001). 78.1% (95% CI: 76.7%–79.6%) of all mothers received anticipatory guidance about depression during pregnancy. In the adjusted analysis, there was no difference in receipt of anticipatory guidance about depression between mothers with and without pre-pregnancy comorbidities (ARR 1.06; 95% CI 0.98–1.15).

Conclusions In this population based study, nearly 10% of Colorado mothers reported feeling depressed prior to pregnancy and nearly one-quarter of mothers did not receive anticipatory guidance about depression during pregnancy. While mothers with pre-existing comorbidities (HTN or DM) prior to pregnancy were more likely to be depressed than mothers without chronic conditions, receipt of anticipatory guidance about depression during pregnancy did not vary between these groups.

377 DO MOTION PERCEPTION AND BINOCULAR FUNCTION SHARE COMMON PROCESSING MECHANISMS?

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10.1136/jim-2018-000939.375

Purpose of study Amblyopia is a developmental disorder characterized by one eye having decreased visual acuity that cannot be corrected with glasses (amblyopic eye), while the other has normal visual acuity (fellow eye). Deficits in binocular vision, including depth perception (stereopsis) are common in amblyopia. The Giaschi lab discovered that amblyopia also disrupts motion perception. This deficit is unexpected because it affects both eyes and involves different brain regions than those involved in visual acuity. We hypothesize that deficits in motion perception are related to disrupted binocular vision. The current study was conducted to determine whether motion perception and binocular function are correlated in typical or atypical vision.

Methods used Correlation and regression analyses were run on data obtained from past studies in our lab to determine relationships between measures of visual acuity, motion perception and binocular function, as well as to see which factors predict whether an individual has amblyopia. Data from a total of 299 participants with healthy vision and 70 participants with amblyopia, with an age range of 3 to 32 years old, were included as part of this study. Motion perception was characterized by performance on computer-generated tests of global motion and motion-defined form. Binocular function was characterized by performance on clinical and computer-generated tests of stereopsis.

Summary of results Stereopsis and motion perception were correlated in combined data from both the amblyopia group and the healthy vision group. Stereopsis was shown to be a predictor, independent of visual acuity, of whether an individual has amblyopia.

Conclusions Overall, our results suggest an association between motion perception and binocular function, indicating a shared processing mechanism. Neuroimaging studies may be able to determine which areas of the brain are common to processing both motion perception and binocular function. There are also treatment implications because deficits in stereopsis and motion perception often persist following standard patching therapy for amblyopia. We hypothesize that these deficits contribute to treatment failure and to amblyopia recurrence, and possibly to deficits in hand-eye coordination and reading.

Community Health II

Concurrent Session

8:00 AM

Saturday, January 26, 2019

378 DOES RAPID WEIGHT GAIN IN INFANCY PREDISPOSE TO BEING OVERWEIGHT LATER IN LIFE?

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10.1136/jim-2018-000939.376

Purpose of study Despite increasing rates of both adult and childhood obesity in the United States, the interplay of early risk factors predisposing to obesity remains a topic under investigation. The objective of this study was to determine whether rapid weight gain in infancy is associated with an increased risk of overweight status later in life.

Methods used A literature review was conducted using PubMed, Medline, and Google Scholar. We included cohort studies of infants born at term with weight measurements recorded both within the first year of life and during a follow-up period at least 7 years later.

Summary of results Table 1 below summarizes the results of the 7 studies that met our inclusion criteria. Of the 7 studies, 6 demonstrated a statistically significant relationship between rapid weight gain in infancy and overweight status later in childhood or adulthood. The remaining study demonstrated a statistically significant relationship between rapid weight gain in the first 5 years of life and subsequent higher body mass index (BMI). Limitations included variation in the time period considered 'infancy' and in participant age at follow-up as well as controlling for different confounding variables.

Conclusions Rapid weight gain in infancy is likely related to subsequent overweight status. More research is needed to clarify the most critical time period for weight gain within the first year of life as well as the significance of rapid weight gain in infancy relative to other risk factors associated with overweight status. We are currently developing educational tools to help families and communities to better understand

Abstract 378 Table 1 Rapid Weight Gain in Infancy and Subsequent Overweight Status

First Author; Year of Publication; Location	N Subjects (Initial Phase)	N Subjects (At Time of Follow-Up)	Infancy Age Range of Weight Gain	N% Initial Subjects with Rapid WT Gain	Outcome at F/U in Infants with Rapid WT Gain vs. Infants Without Rapid WT Gain
Salgin B; 2015; South Africa	2352	1208 at 18 years	Birth to 1 year	290 (12.4%)	Average BMI: 22.7 vs. 21.4 (p<0.001) Avg WT: 62.3 kg vs. 57.9 kg (p<0.001)
Ekelund U; 2006; Sweden	2094	248 at 17 years	Birth to 6 months	63 (25.4%)	Avg FM: 17.5 kg vs. 14 kg (p<0.001) Avg WC: 75 cm vs.72 cm (p<0.001) Avg BMI: 22.5 vs. 20.5 (p<0.001)
Stettler N; 2005; USA	952	653 between 20–32 years	Birth to 8 days; Birth to 112 days	Data not provided	Odds Ratio for Group: WT Gain First 8 Days and Adult BMI>25 Absolute Infant WT Gain: 1.28 (95% CI: 1.08–1.52) Infant Change in WT Z Score: 3.62 (95% CI: 1.43–9.18) Odds Ratio for Group: WT Gain First 112 Days and Adult BMI>25 Absolute Infant WT Gain: 1.04 (95% CI: 1.01–1.08) Infant Change in WT Z Score: 1.41 (95% CI: 1.09–1.82)
Sutharsan R; 2015; Australia	6927	2077 at 21 years; 1910 at 5 years	Birth to 6 months; Birth to 5 years	457 (22%) during first 6 months 611 (32%) during first 5 years of life	Odds Ratio for Group: Rapid WT Gain First 6 Months Adult BMI 1.13 (95% CI: 0.86–1.49) Adult WC 1.24 (95% CI: 0.92–1.67) Odds Ratio for Group: Rapid WT Gain First 5 Years Adult BMI: 2.35 (95% CI: 1.82–3.03) Adult WC: 2.20 (95% CI: 1.65–2.95)
Stettler N; 2003; USA	446	300 between 18–22.9 years	Birth to 4 months	86 (29%)	Odds Ratio – Rapid WT Gain in Infancy and Obese in Young Adulthood: 5.22 (95% CI: 1.55–17.6) Odds Ratio – Rapid WT Gain in Infancy and Overweight-Overfat in Young Adulthood: 6.72 (95% CI: 1.93–23.4)
N. Stettler; 2002; USA	27 889	19 397 at 7 years	Birth to 4 months	Data not provided	Odds Ratio – Rapid WT Gain in Infancy and Overweight Status at Pediatric F/U: 1.38 (95% CI: 1.32–1.44)
M. Oyama; 2010; Japan	69	86 between 18–21 years	Birth to 3 months	Data not provided	Correlation Coefficient: Infant WT Change vs Adult BFP: 0.26 (P: 0.034) Correlation Coefficient: Infant WT Change vs Adult BMI: 0.18 (P: 0.132)

WT=Weight; FM – Fat Mass; WC – Waist Circumference; BMI – Body Mass Index; FFM – Fat Free Mass; BFP – Body Fat Percentage

the importance of appropriate feeding and nutrition during infancy.

379 FAMILIES LEARNING TOGETHER: INCREASING HEALTH KNOWLEDGE AND DECREASING BMI BY COMMUNITY CENTERED EDUCATION

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10.1136/jim-2018-000939.377

Purpose of study The purpose of this project is to help improve health knowledge and application within families by providing courses that are community based and culturally conscious. This is in an effort to reduce the obesity rate in Lake County, which is higher than the state rate.

Methods used The primary approach to exploring this health issue was via community interviews. Community members identified that several children in the community had food insecurity, poor support of healthy habits at home, limited access to recreation, and overall lack of health knowledge. They felt that all of these factors contributed towards the obesity rates within the community. These sentiments were supported by the demographic analysis, which revealed increased obesity rates in the county compared to the state and decreased activity rates in the county compared to the state. My community partnership formed from my community interview with Amy Vaughn a coordinator for the Flathead Boys and Girls club. For intervention, she had the ultimate goal of being able to have cooking classes that were family focused at the club. This led to a literature review to see if this would be effective in lowering obesity rates and how to best structure this kind of intervention.

Summary of results Deliverables to my community partner were a literature review, a plan for how community physicians could get involved, identifying potential community partners, and a report regarding community feedback from community interviews.

Conclusions The strengths of the proposed project were that the actual integration of the program Let's Go! 5–2-1–0 into the Boys and Girls club would have been feasible. Additionally, there is evidence-based support that family-based programs can improve child and adult BMI. The weaknesses of this plan were that the construction of the new Boys and Girls clubs had not been completed yet, therefore, implementation of this project is not feasible at the moment. Additionally, this project would require a significant amount of funding and community partners.

380 A POSTCARD INTERVENTION TO LESSEN DEPRESSION IN THE ELDERLY

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10.1136/jim-2018-000939.378

Purpose of study Red Lodge, Montana is home to a rapidly aging population, with the majority of the said population living outside of the town on large isolated tracts of land. A high rate of depression in the elderly is present in Red Lodge, and many of these people attribute their depression to social isolation as a result of their living situations.

The goal of this intervention is to decrease scores on PHQ-9 surveys by engaging in monthly correspondence with intervention participants and providing them with lists of mental health resources in their community.

Methods used In order to identify that depression in the elderly was a problem in Red Lodge, many community interviews were conducted. Interviewees included the Red Lodge Area Community Foundation program director, the local librarian, and multiple people attending a class at the senior center. In addition to this, the nurses at Beartooth Billings Clinic screened all people over 65 years of age with a PHQ-9 form before their visit with a provider. After an extensive PubMed literature review, a postcard intervention was decided on because of its cost-effective nature and ability to reach very isolated people. The Red Lodge Area Community Foundation volunteered to implement the postcard intervention.

Summary of results Explicit instructions regarding what each letter should include, how participants should be recruited, and the duration of the intervention were delivered to the Red Lodge Area Community Foundation. In addition, a thorough demographic analysis of the community and the results of the PubMed literature review were also the to the community partner.

Conclusions The strengths of this intervention are within its reach, simplicity, and cost-effectiveness. Regardless of where someone lives, he or she likely still receives mail, so this intervention has the possibility to reach essentially every individual within the community. The time commitment from the volunteers is only as much time as it takes to write one letter per month, and the cost is also minimal for printing, packaging and shipping the postcard. This project will connect the isolates with their community, resulting in decreased depression and hopefully fostering a stronger sense of community. Next steps will include applying for funding through a Substance Abuse and Mental Health Services Administration (SAMHSA) grant or the Montana Healthcare Foundation grant.

381 A COMMUNITY CONFERENCE: ADVERSE CHILDHOOD EXPERIENCES AND THEIR IMPACT ON SUBSTANCE USE

SM Doe-Williams. *University of Washington School of Medicine, Moscow, ID*

10.1136/jim-2018-000939.379

Purpose of study Monroe, Washington is located in Snohomish County and has a weakness in minority substance use. With a population of 18,789, 25% represents members under 18% and 18% are Hispanic. Research about adverse childhood experiences (ACEs) has been published for a while, yet practices have not changed. This project sets out to address the unfamiliarity of how ACEs affect a person's likelihood of using abusive substances. The rate of excessive drinking is 19% compared to Washington state at 18% and the drug-overdose mortality rate is 17 per 1 00 000 versus the state at 15 per 1 00 000. Community members have expressed concern on substance use, especially about high school youth.

Methods used After a thorough, demographic analysis of Monroe and Snohomish County was performed, a community search to find people to discuss health issues was initiated. These discussions took place at the local library, Monroe Boys and Girls Club and the Monroe Community Coalition (MCC). More outlooks on health issues were taken from clinical observations while participating at the Monroe Sea Mar Clinic. Once these dialogues concluded, a collaborating partnership was created with MCC by discussing their inclination to work on a project about ACEs and substance use. MCC is a federally funded organization that specializes in the prevention of early use of alcohol and other drugs targeted towards youth.

Summary of results A conference to educate health professionals and community members about ACEs and their impact on substance use is the project that is being planned with MCC. This deliverable to the community will hopefully increase the awareness on this topic and facilitate the discussion of incorporating interventions into clinical and community practice. Other deliverables include a detailed literature review, plan of next steps, and an agenda along with a sample power point to utilize in the educational presentation.

Conclusions While searching for partnerships was difficult, it was easy to create a relationship with MCC due to the drive and enthusiasm from the prevention coordinator. This project topic is a passion for this organization and has great meaning to raise awareness in the local community. Next steps for the project would be to advertise and implement the pilot presentation. It would be beneficial to expand this conference to Snohomish County and state-wide.

382 REDUCING DRUG OVERDOSE DEATHS IN BENEWAH COUNTY BY INCREASING TRIBAL POLICE ACCESS TO INTRANASAL NARCAN

B Bergam. *University of Washington School of Medicine, Spokane, WA*

10.1136/jim-2018-000939.380

Purpose of study Substance use disorder is an ongoing epidemic in Native communities. Benewah County, Idaho which encompasses the Coeur d'Alene (CDA) Tribe, is estimated to have double the drug overdose death rates compared to the State as a whole. Narcan is stocked at the local Indian Health Service (IHS) clinic pharmacy, but is only utilized by patients who seek care there. Nationally, first responders are beginning to utilize intranasal Narcan which has shown to reverse overdoses and save lives.

Methods used Through community interviews with social service organizations and discussions with the CDA Tribal Police, substance abuse was identified as the primary health concern in this community. A thorough literature review showed the benefits of integrating medication-assisted treatment (MAT) plans, including the use of intranasal Narcan, into IHS facilities and by tribal police. The CDA Tribal Police Department had taken steps towards obtaining intranasal Narcan through the IHS pharmacy in Benewah County but approval through the Tribal Code had not been obtained and a protocol for the logistics around tracking intranasal Narcan vials had not been formally documented.

Summary of results As part of the implementation process of this project, approval through the CDA Tribal Code was obtained through the Lead CDA Tribal Attorney. In addition, a step-by-step protocol for collaborating with the IHS pharmacy to order, store, and track intranasal Narcan was distributed to the CDA Tribal Police Department. Project development meetings with the CDA Tribal Police Department

and IHS clinic stakeholders strengthened the partnership between these two entities.
Conclusions The CDA Tribal Police Department is in the final stages of getting this project approved through the Bureau of Indian Affairs and solidifying funding through IHS with the goal of distributing intranasal Narcan to their officers by October 2018. A detailed protocol around the approval process for tribal police departments to obtain intranasal Narcan is not well documented in the literature. This is an area for future development for more tribes to easily integrate Narcan into their substance abuse treatment programs.

383 YOU CAN'T BE WHAT YOU CAN'T SEE: A COLLABORATIVE PARTNERSHIP TO IMPROVE SELF-EFFICACY AND RESILIENCE IN IMPOVERISHED MINORITY ADOLESCENT FEMALES

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10.1136/jim-2018-000939.381

Purpose of study Growing up in poverty skews normality, making it difficult to visualize a life outside poverty. It can also result in lowered self-efficacy and decreased resilience due to toxic stress. Although impoverished adolescents want to become healthy and successful adults, it can be difficult to become what they can't see. High-risk minority adolescents thus partnered with pediatric residents/faculty to become change agents within their own community.
Methods used Students anonymously surveyed 223 fellow high school students asking about their personal perceptions of home/school support, their willingness to be involved in community improvement efforts, and whether they felt they had the power to make a difference. Students re-wrote Fresno County's 8 Pillars of Health from a youth standpoint, created vision boards to help visualize their futures, mentored K-6 elementary school students, made 'care packages' for foster care youth, invited a State Assemblyman and guest speakers to visit their classroom, and submitted abstracts of their work to regional and national medical conferences.
Summary of results About 1 in 6 students felt unsupported at home, while only 53% felt supported at school. 22% of students felt that they would be unwilling to work with others to improve their community, 25% felt that they would be unable to make a difference, and only 14% felt that they did not have the power to change their future. Students discussed how they could further impact their community with a State Assemblyman, worked with pediatric residents to develop healthier lifestyles, and met with guest speakers that introduced them to a variety of careers. They gave workshops on 'Amplifying Teen Voices' and presented posters on their community health action research projects both locally and at national medical conferences.
Conclusions Even impoverished minority youth feel that they have the power to make a difference within their own lives and their own communities. However, they need mentors to help them visualize and navigate a future vastly different from their own upbringing. Pediatric residents, faculty, and medical students can successfully help to provide this service in an outside-the-exam-room approach to improving adolescent health and success in life.

384 TRAUMA INFORMED CARE: INCREASING KNOWLEDGE OF TRAUMA INFORMED PRACTICES AMONG MEDICAL STAFF WORKING WITH VULNERABLE POPULATIONS IN SEATTLE, WASHINGTON

A Smith. *University of Washington, Seattle, WA*

10.1136/jim-2018-000939.382

Purpose of study Research supports a strong, graded correlation between childhood traumatic events and social and emotional issues, as well as poor health outcomes as adults. Rates of physical and psychological trauma are high in homeless populations. Seattle and King County has the third largest homeless population in the nation, totaling 11 643 people in 2017. Trauma informed care is one way to help prevent and treat trauma incurred by individuals and communities, however this is not yet standard practice in healthcare settings.
Methods used Interviews with Harborview Family Medicine physicians and local homeless shelter staff identified the need for improved care of patients with trauma histories. Rebekah Demirel, Director of Trauma Integration Programs, was interviewed about trauma informed care and how to conduct trainings. A literature review was further conducted to identify trauma informed practices most relevant to the work of healthcare providers.
Summary of results Trauma informed care training was presented to the Harborview Family Medicine Clinic in August 2018. Twelve attending and resident physicians participated. Training included an introduction to trauma informed care principles, how to identify symptoms of trauma, and specific recommendations to guide interaction with patients.
Conclusions Trauma informed care training was well received by Harborview Family Medicine staff. However, the training was limited to providers who elected to attend at one Seattle clinic. Future work should expand trainings to other healthcare clinics, assess how trauma informed care practices impact patient engagement and health outcomes, and explore funding sources for these efforts.

385 INCREASING BREAST-FEEDING CONTINUATION RATES AMONGST WOMEN, INFANT, CHILD PARTICIPANTS IN CUT BANK, MT VIA PEER COUNSELING

SK Clement. *University of Washington School of Medicine, Bozeman, MT*

10.1136/jim-2018-000939.383

Purpose of study Breast-feeding initiation rates amongst WIC participants average 82.2% in Cut Bank, MT. However, by three months post-partum only 35.6% of mothers are continuing to breast-feed. In addition to lack of self-efficacy, another common reason for breast-feeding cessation is the absence of timely information and guidance due to a constrained Lactation Consultant. To confer maternal and child health benefit, the World Health Organization recommends mothers worldwide adhere to exclusive breast-feeding for the first six months of the infant's life. This project aimed to

implement a multi-modal peer counseling program to increase breast-feeding continuation rates amongst WIC participants.

Methods used A literature review was conducted to explore interventions that were economical and supported the development of a mother's self-efficacy. Additionally, interviews were conducted with community partners including the WIC program coordinators, the county public health nurse, and nurses and physicians at Northern Rockies Medical Center (NRMC), the primary healthcare facility for the community. These interviews identified current resources, barriers, trends, and perceptions of breast-feeding in the community. Thereafter, an adapted peer counseling program was developed based on an existing curriculum developed by WIC, 'Loving Support to Implement Best Practices in Peer Counseling'. The adaptations included multiple modalities of communication and recruitment of local peer counselors.

Summary of results A presentation was delivered to WIC regarding the salient findings from the literature review. Subsequently, a work group was facilitated with the WIC program coordinators to develop an expansion plan to recruit volunteers from the local WIC program. Finally, a template and three chronological peer counseling newsletters were generated: antepartum, one-day and three-months post-partum. These newsletters were then distributed and continued by the WIC office.

Conclusions The primary strength of this project is the economic feasibility of a volunteer-supported program. This model extends the knowledge and support of the Lactation Consultant to reach more community members. Also, the project catalyzed an opportunity for collaboration between the WIC office and NRMC to improve post-partum care.

Endocrinology and Metabolism III

Concurrent Session

8:00 AM

Saturday, January 26, 2019

386 SLEEP DURATION, QUALITY, AND SLEEP-DISORDERED BREATHING ARE ASSOCIATED WITH HEPATIC STEATOSIS AND INSULIN RESISTANCE IN ADOLESCENT GIRLS WITH OBESITY AND PCOS

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10.1136/jim-2018-000939.384

Purpose of study Polycystic Ovarian Syndrome (PCOS) affects 6%–10% of women and is associated with hepatic steatosis (HS). Development of HS in PCOS is likely multifactorial and may relate to poor sleep. We investigated differences in objective markers of sleep in girls with obesity and PCOS with and without HS, and examined relationships with insulin resistance (IR).

Methods used 61 girls with PCOS and obesity (Age 15.7 ±1.7 years; BMI%ile 97.4±2.2) had 1) fasting hormone and metabolic measurements 2) an oral sugar tolerance test for assessment of IR and 3) abdominal magnetic resonance imaging for hepatic fat fraction. All participants wore actigraphy to assess sleep for 7 days at home prior to the study visit. Polysomnography (PSG) was also completed for a subset of 27 girls. Participants were classified as HS (fat fraction ≥5.5%, n=29) and non-HS (NHS, n=32). T-tests were used for group comparisons and Pearson's correlations examined associations between variables.

Summary of results Groups did not significantly differ on demographic and physical characteristics (e.g., age, BMI percentile). Girls with HS had 3 times as much hepatic fat as NHS (12.5%±7.5% vs. 3.5±1.1%) and had worse markers of IR and hepatic inflammation. Actigraphy showed that girls with HS had significantly less sleep, lower sleep efficiency and longer sleep onset latency on weekends, but not weekdays, compared to NHS. Across the cohort, shorter weekday and weekend sleep duration, poorer weekend sleep efficiency and longer sleep onset latency were significantly associated with more hepatic fat ($r=-0.32$, $p=0.02$; $r=-0.27$, $p=0.04$; $r=-0.41$, $p<0.01$; $r=0.29$, $p=0.03$, respectively). Among those with PSG (HS=15; NHS=12), girls with HS had significantly higher apnea–hypopnea index (AHI),% REM sleep, and oxygen desaturation index. Higher AHI significantly correlated with IR ($r=0.62$, $p<0.001$).

Conclusions Among obese girls with PCOS, HS appears to be a risk factor for poor sleep and sleep-disordered breathing, which are associated with IR. Further work is needed to determine if sleep health is a modifiable target to improve HS and IR in girls with obesity and PCOS.

387 PLASMA OXYLIPIN AND ENDOCANNABINOIDS PROFILE IN HISPANIC AND CAUCASIAN SUBJECTS WITH NONALCOHOLIC FATTY LIVER DISEASE: A PILOT STUDY

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10.1136/jim-2018-000939.385

Purpose of study Hispanics (HIS) have higher rate and severity of non-alcoholic fatty liver disease (NAFLD) compared to Caucasians (CAU) and lipotoxicity contributes to its progression via oxidative stress and inflammation. Some bioactive lipid species including oxylipin (OXY) and endocannabinoids (EC) are key inflammatory mediators and thought to play a role in NAFLD progression. We hypothesize that biochemical distinction(s) exist between HIS and CAU subjects with NAFLD to explain the disparity observed in prevalence.

Aim To explore plasma OXY and EC metabolomic profile in HIS and CAU bariatric surgery subjects with NAFLD.

Methods used Plasma (n=18) of HIS and CAU with biopsy-proven NAFLD were matched by age, sex and ethnicity to (n=18) healthy control subjects (HC). Plasma samples were collected on overnight fasting state. Free OXY was profiled with Ultra-performance liquid chromatography/tandem mass spectrometry.

Summary of results Fold change and pathway analysis showed an increased linoleic acid (LA) oxidation products in both ethnicities. However, trihydroxyoctadecenoic acid (Sum TriHOME) were higher in HIS. Both ethnicities showed

increased fold change of arachidonic acid (AA) oxidation products. Thromboxane B2 (TBX2) and hydroxyeicosatetraenoic (12, 15-HETE) were high in HIS only.

Conclusions When comparing to healthy control, HIS and CAU with NAFLD show different pattern of OXY and EC profile. Possible contributing factors include diet and genetics. The impact of the observed differences in OXY and EC on NAFLD state is not elucidated and needs further investigation.

388 DIETARY INTAKE IS ASSOCIATED WITH LIVER FAT IN OBESE ADOLESCENT GIRLS WITH PCOS

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10.1136/jim-2018-000939.386

Purpose of study Obese adolescent girls with polycystic ovarian syndrome (PCOS) have an increased likelihood of developing non-alcoholic fatty liver disease (NAFLD). Dietary carbohydrate consumption contributes to the formation of excess hepatic fat and development of NAFLD in other populations. However, the effect of dietary intake on hepatic fat content is unknown in obese adolescent girls with PCOS.

Methods used Secondary analysis in a cohort of 106 sedentary (<3 hours of exercise/week) adolescent girls (15.6±1.8 years of age) with PCOS and BMI ≥90th percentile for age and sex, who were enrolled in three different cross-sectional studies (AIRS, APPLE, PLUM). Participants underwent fasting laboratory tests to confirm the diagnosis of PCOS per NIH criteria, an abdominal MRI to quantify hepatic fat percentage, and a food frequency questionnaire (FFQ) to estimate dietary intake. NAFLD was defined as hepatic fat ≥5.5%. Correlations were performed in SAS to assess the association between liver fat percentage and dietary intake.

Summary of results The mean BMI percentile was 97.6% ±2.0 and the mean hepatic fat percentage was 7.5%±6.9, with 49.5% percent of participants meeting criteria for NAFLD. Several dietary measurements correlated with increased liver fat percentage: higher servings of bread, cereal, rice, and pasta ($r=0.25$, $p<0.01$); higher servings of bread, cereal, rice, and pasta low in fiber ($r=0.35$, $p<0.01$); more total carbohydrates ($r=0.23$, $p=0.02$); and greater total kcal intake ($r=0.22$, $p=0.02$).

Conclusions We found that total calories, carbohydrate intake, and in particular low fiber carbohydrate foods were related to increased hepatic fat in obese adolescents with PCOS. Due to the increased odds of developing NAFLD in this population, dietary counseling to reduce total calorie and carbohydrate consumption may hold promise in addressing NAFLD in this population.

389 EXCESS DE NOVO LIPOGENESIS MEDIATES HEPATIC STEATOSIS IN OBESE ADOLESCENTS WITH POLYCYSTIC OVARIAN SYNDROME

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10.1136/jim-2018-000939.387

Purpose of study Polycystic ovarian syndrome (PCOS) is a common endocrine disorder and is associated with a high risk of metabolic disease. We demonstrated that 50% of obese girls with PCOS have hepatic steatosis (HS, liver fat >5%) which can lead to increased morbidity. The mechanisms underlying the development of HS in obese girls with PCOS are unknown. We hypothesized that HS in obese PCOS girls is related to excess hepatic *de novo* lipogenesis (DNL).

I think Meridith's abstract used a different definition of HS (I think hers was >5.5) so make sure they are consistent

Methods used Obese adolescents with PCOS but not diabetes were studied: 6 without HS and 5 with HS. Visceral and hepatic fat was assessed via MRI. DNL was measured fasting and throughout an oral sugars tolerance test (OSTT; 75 g glucose +25 g fructose) using IV stable isotope $^{13}C_2$ acetate incorporation into VLDL-triglyceride (VLDL-TG) palmitate. Serum for fasting hormone, lipid and inflammatory markers and OSTT-derived glucose, insulin and free fatty acid (FFA) analyses were collected.

Summary of results Girls without HS were 17±1 years of age, with BMI 34.6±2.1 kg/m^2 and% liver fat 3.5%±0.2%; those with HS were 16±1 years, with BMI 38.5±2.9 kg/m^2 and% liver fat 8.2%±0.8%. PCOS girls with HS tended to have higher fractional OSTT DNL TG (11.7%±2.0% of total palmitate HS vs. 7.52%±1.2 no HS; $p=0.065$).% Liver fat tended to relate to OSTT DNL ($R^2=0.45$, $p=0.173$). Mean OSTT insulin ($R^2=0.49$, $p=0.017$), peak insulin ($R^2=0.59$, $p=0.006$), and ALT ($R^2=0.39$, $p=0.041$) all positively correlated with mean fractional OSTT DNL TG, whereas markers of glycemia including HbA1c ($R^2=0.06$, $p=0.44$) and 2 hour OSTT glucose ($R^2=0.09$, $p=0.36$) or BMI did not ($R^2=0.01$, $p=0.854$).

Conclusions Among girls with PCOS, those with HS tend to have increased DNL which was strongly related to the insulin response to sugars. Upregulated DNL may be influenced by excess postprandial insulin which relates to markers of hepatic inflammation. Future therapies to decrease hepatic steatosis in girls with PCOS may need to target the pathway of DNL.

390 *IN VIVO* MOLECULAR INVESTIGATION OF TAURINE AS A NOVEL THERAPEUTIC APPROACH TO TREATING GLUTATHIONE-DEFICIENT DISEASES IN A MOUSE MODEL OF HOMOCYSTINURIA

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10.1136/jim-2018-000939.388

Purpose of study Due to the important antioxidative and detoxifying effects of glutathione (GSH), GSH-deficiency has been associated with a variety of diseases, including cystic fibrosis, diabetes, neurodegenerative diseases, and classical homocystinuria (HCU). In HCU, cystathionine beta-synthase (CBS) is depleted, leading to decreases of cysteine and GSH levels while increasing homocysteine levels. Recent studies have shown the efficacy of taurine treatment in normalizing GSH levels and GSH-metabolizing enzymes. In addition to the diet, taurine is synthesized *in vivo* but mechanisms regulating endogenous taurine synthesis in the context of HCU

are not well characterized. The main objective of this study was to improve our understanding of taurine synthesis in a pre-clinical mouse model of CBS-deficient homocystinuria (HCU).

Methods used The effect of HCU upon key components of taurine synthesis via the cysteamine pathway was investigated in mouse liver samples using Western blotting analysis of protein expression. Levels of pantothenate kinase (PanK1), coenzyme A synthase (COASY), pantetheinase (VNN1), and cysteamine dioxygenase (ADO) were investigated in WT control animals and HCU mice (designated HO mice) in the presence and absence of betaine, cysteine, and taurine treatment.

Summary of results The results showed 3-fold repression of ADO in untreated HO mice that was increased by betaine and taurine treatment. Betaine-treatment improved ADO levels by bringing them up to 58% of the WT, while taurine-treatment completely normalized ADO repression. PanK1 and COASY protein expression levels were not significantly affected by HCU or by treatments other than betaine, which increased both PanK1 and COASY levels relative to the controls.

Conclusions The repression of ADO suggests that endogenous taurine synthesis is halted when cysteine and GSH are deficient possibly indicating that taurine-deficiency could contribute to the pathologic effects seen in GSH-deficiency. The ability of taurine to restore ADO expression may indicate that this treatment exerts a cysteine sparing effect with the potential to boost tissue GSH levels and may be useful in a wide range of diseases where GSH depletion is an initiating pathogenic factor.

391 ELECTRONIC CIGARETTES EXACERBATE WESTERN DIET INDUCED HEPATIC STEATOSIS: ROLE OF CYP450 FAMILY OF PROTEINS AND ALTERED LIPID METABOLISM

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10.1136/jim-2018-000939.389

Purpose of study Both primary and second hand smoking contributes to the development of diabetes (T2DM) and non-alcoholic fatty liver disease (NAFLD). Epidemiological studies have demonstrated that smoking exaggerates hepatic steatosis in obese people which can increase the rates of mortality and morbidity worldwide. Recently, electronic cigarettes (Electronic Nicotine Delivery System or ENDS) have been promoted as a risk-free alternative to conventional smoking without knowledge of its long-term effects on consumer's health.

Methods used We used Apolipoprotein E knockout (ApoE -/-) mice fed on a western diet (WD), a mouse model of NAFLD, that we have previously used to demonstrate that ENDS treatment for 12 weeks exacerbates WD-induced hepatic steatosis. We monitored differential gene expression using RNA sequence analysis (RNAseq) technique and found that 433 genes were differentially expressed in the ENDS-treated livers compared to saline-treated livers. An analysis was done on this data with a focus on the CYP450 family proteins and genes associated with lipid metabolism. The RNAseq data was validated via RT-PCR and western blotting and immunohistochemistry.

Summary of results The expression of Acyl-CoA synthetase long chain family member 3, Lipoclain-2 associated hepatic lipid breakdown was reduced in ENDS- treated livers compared to saline-treated livers. We found an upregulation of CIDEA, CIDEAC, and MOGAT1 genes involved with lipid droplet formation and storage, suggesting that the lipid mobilization was hampered which favors lipid accumulation in the liver. We also found upregulation of CYP4A10, a gene associated with lipid peroxidation and is a salient feature of hepatic steatosis.

Conclusions Our findings led us to the conclusion that ENDS and WD alter hepatic gene expression in a manner that enhances lipid accumulation, oxidative stress, lipid peroxidation and apoptosis leading to NAFLD. This project was funded by the Tobacco Related Disease Research Program grant # 25Ip-0013 entitled 'Metabolic and Carcinogen Effect of Electronic Cigarettes.'

392 CAPILLARY LIPOPROTEINS BY POINT-OF-CARE ANALYZER VS. VENOUS BLOOD VALUES: CLOSE ENOUGH?

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10.1136/jim-2018-000939.390

Purpose of study Point-of-care (POC) lipoprotein analysis enables prompt feedback to wellness participants (WP) for health counseling for diet, exercise and other interventions including follow-up with primary clinicians. Accuracy of such results is crucial, so we compared POC values with those obtained using venous blood (VB) in two prior years.

Methods used Total cholesterol (TC) and high-density lipoprotein (HDL) concentrations were measured by a POC analyzer in capillary blood obtained by lancet fingerstick in 352 county workers whose previous TC values in VB at a hospital laboratory agreed within 30 mg/dL, and whose HDL levels in VB agreed within 10 mg/dL. The portable POC analyzer was calibrated each morning at the county health facility. Agreements of POC results for TC and HDL with prior VB values were compared with industry standards of POC agreement with reference values of 10 and 12 mg/dL, respectively. Results were provided to each participant in person and by letter, and compared by Bland-Altman plots, t-tests and linear regression analysis.

Summary of results POC group means for TC and HDL (table 1) differed from VB values by only 3.3 and 2.4 mg/dL ($p<0.001$) but many individual comparisons of POC vs. VB lipid concentrations exceeded respective industry norms. For TC, the POC results were either too high or too low in

Abstract 392 Table 1 Total cholesterol and high density lipoproteins: point-of-care (POC) vs. hospital lab

	Point-of-Care Analyzer	Venous Blood, Hospital Lab
Total cholesterol, mg/dL	178.9±36.2	183.2±31.0
POC,% too high	26.4	Reference
POC,% too low	16.8	Reference
High-density lipoprotein mg/dL	48.6±16.0	46.2±11.3
POC,% too high	15.5	Reference
POC,% too low	26.2	Reference

43.2% of workers, and similar disparity was found in 41.7% of HDL comparisons.
Conclusions Group means for TC and HDL comparisons of POC vs. VB results differed by only 4.3 and 2.4 mg/dL, respectively ($p<0.001$). However, individual TC results were either above or below industry standards of agreement with reference values in 42.2% of WP. Individual HDL results were also disparate in 41.7% of WP. Better agreement is needed for appropriate health coaching.

393 TRANSCRIPTIONAL REGULATION OF SPTY2D1, A NOVEL DETERMINANT OF PLASMA CHOLESTEROL LEVELS

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10.1136/jim-2018-000939.391

Purpose of study Plasma cholesterol concentration is a major determinant of cardiovascular disease risk. In recent years, the genetic determinants of cholesterol levels in the population have been investigated by genome-wide association studies (GWAS), which identified dozens of chromosomal regions involved in cholesterol regulation. One reported candidate is SPTY2D1, a gene previously characterized as a transcriptional regulator, but never before linked to lipid metabolism. Through the analysis of epigenetic chromatin marks, we identified a single nucleotide polymorphism (rs794654) within the SPTY2D1 promoter as a candidate to affect SPTY2D1 transcription. Importantly, rs794654 exhibits strong association with plasma cholesterol levels. Based on these results, we hypothesized that cholesterol association at this locus is caused by rs794654 through the modulation of SPTY2D1 expression.
Methods used To begin to test this hypothesis, we used site-directed mutagenesis to generate promoter fragments with alternative alleles of rs794654 and performed luciferase reporter assays in transfected COS7 cells.
Summary of results Our results demonstrate that the rs794654-G allele confers significantly higher promoter activity compared to rs794654-C.
Conclusions These results suggest that rs794654 regulates SPTY2D1 expression and further implicate this gene in the determination of plasma cholesterol levels. Future studies will identify the transcription factor(s) affected by rs794654 and investigate the role of SPTY2D1 in cholesterol metabolism.

General Internal Medicine and Aging

Concurrent Session

8:00 AM

Saturday, January 26, 2019

394 EFFECTS OF FASCIAL STRETCH THERAPY ON PAIN INDEX AND ACTIVITIES OF DAILY LIVING IN PATIENTS WITH CHRONIC NON-SPECIFIC LOW BACK PAIN

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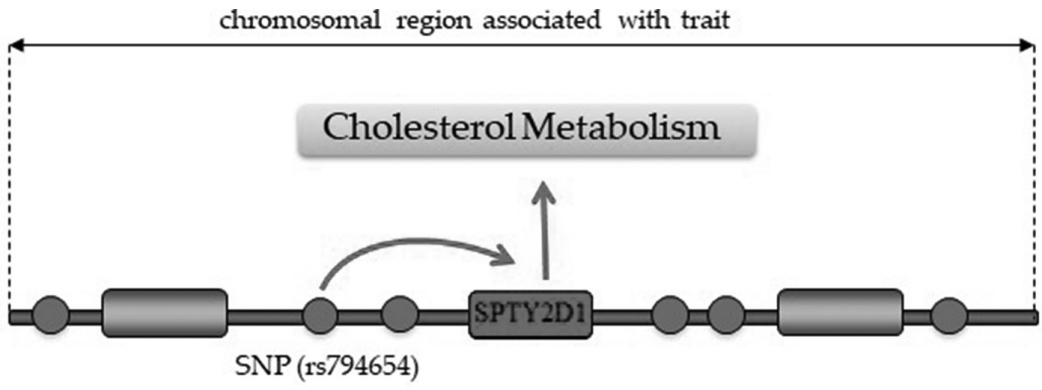
10.1136/jim-2018-000939.392

Purpose of study Numerous fascia-focused therapies are used to treat pain, most relying on direct manipulation and/or tool-mediated techniques. Fascial Stretch Therapy (FST), on the other hand, uses distally applied techniques to yield both local and global desired tissue outcomes and subjective pain improvement, including those related to Low Back Pain (LBP). We hypothesize that subjects receiving FST will have reduced nonspecific LBP and enhanced activities of daily living (ADL) scores.
Methods used Eleven subjects who met study criteria (7F, 4M; Age 22–32 y/o) underwent 1 (n=11), 2 (n=7), or 3 (n=5) successive FST treatments (Tx in table 1 below) which consisted of 30 min of 3-strap stabilization-mediated body stretch (8 per side). Subjects had pain and ADL scores (Bathing: BAT; Car egress/ingress: CEI; Toilet use: TOI; Forward bending: FOB; Dressing: DRE) measured pre- and 1- and 3 day post-FST. We used a linear mixed effects model to ascertain the relative% change in scores over time using the pretreatment time point as the reference group. All p-values were 2-sided and $p<0.05$ was considered statistically significant.
Summary of results Statistically significant improvements in pain and ADL scores (*) were found at the time points shown in the table 1. Score improvements noted in the table ranged between 31% and 57% compared to pretreatment time point. Individuals reported an overall reduction in post therapy back pain ratings as well as a reduction in need for pain medication for back pain.
Conclusions This pilot study shows that both single as well as multiple, successive 30 min FST treatments improve pain and ADL scores, with the highest improvements seen in pain and FOB. Future studies will determine optimal treatment



Abstract 393 Figure 1

Abstract 394 Table 1

SCORE	1 Tx; 1 day post	1 Tx; 3 day post	2 Tx; 1 day post	2 Tx; 3 day post	3 Tx; 1 day post	3 Tx; 3 day post
PAIN	*	*		*	*	
BAT				*		
CEI	*	*	*	*	*	*
TOI						
FOB	*	*	*	*	*	*
DRE	*		*		*	*

frequency and measure additional variables aimed at mechanistic understanding of treatment effects.

395 PERFORMANCE OF THE LOS ANGELES MOTOR SCALE IN THE PREHOSPITAL TRIAGE OF LARGE VESSEL OCCLUSION STROKE

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10.1136/jim-2018-000939.393

Purpose of study Stoke is a leading cause of death and disability, particularly when caused by a large-vessel occlusion (LVO). LVO strokes are treatable with thrombectomy at Comprehensive Stroke Centers (CSCs), whose limited number and geographical distribution requires accurate identification and triage of appropriate candidates by emergency medical services (EMS). We evaluated use of the LA Motor Scale (LAMS) as a triage tool in a metropolitan EMS system, and potential variables that might improve its predictive accuracy.

Methods used We reviewed all EMS-suspected strokes from 1/1/17 – 4/31/18 in King County, WA, with a focus on those with suspected LVO based on a LAMS $\geq$4 and last known well (LKW) <6 hours. We abstracted EMS and hospital records to determine final diagnosis (LVO, ischemic non-LVO, hemorrhagic, or stroke mimic) as well as the National Institute of Health Stroke Scale (NIHSS) findings at hospitalization.

Summary of results Among patients with an EMS-designated impression of stroke, 205 met inclusion criteria. LVOs were diagnosed in 84 (41.0%), ischemic non-LVO stroke in 34 (16.6%), hemorrhagic stroke in 56 (27.3%), and stroke mimic in 31 (15.1%) patients. Those with LVO stroke tended to be older, less likely to have diabetes, and were more likely to have atrial fibrillation. NIHSS data were available for 184 (89.8%) patients. EMS application of LAMS $\geq$4 had a positive predictive value (PPV) of 41.0% for LVO stroke. Increasing triage threshold to LAMS=5 increased PPV to 49.0% but missed 13.1% of LVO strokes. NIHSS parameters that distinguished true LVO from other strokes and stroke mimics included abnormal extraocular movement ($p=0.001$) and extinction/inattention ($p<0.001$).

Conclusions LAMS-based triage of suspected LVO stroke had modest PPV. While not all NIHSS domains are easily replicated in a prehospital setting, the assessment of extraocular movement may be a relatively straightforward and useful adjunct to LAMS for improving prehospital LVO stroke triage.

396 MEDICAL STUDENT PERCEPTIONS OF PARENTHOOD TIMING

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10.1136/jim-2018-000939.394

Purpose of study The practice of delaying parenthood in lieu of professional pursuits is common in career fields such as medicine. While some literature exists on the postponement of parenthood among physician residents, little exists regarding medical students. We aimed to assess medical students' self-perceived fertility and preservation, their attitudes toward delaying parenthood, and whether the desire to have children affects specialty choice.

Methods used A 23-item survey, consisting of yes/no and multiple-choice questions, was distributed to students at two west coast medical schools. Responses to the questionnaire were voluntary and anonymous. 658 total surveys were collected and analyzed between October 2017 and March 2018. 414 surveys were completed in person and 240 were completed electronically. Survey responses of nonparents and parents were separately analyzed using univariate logistic regression and all analyses were conducted in R software using the generalized linear model function.

Summary of results Among all those surveyed, 59.8% were female, 59.3% MD students, 85.1% age 30 or younger, and 88.5% were nonparents. Christians, those aged 26–30, and those wishing to pursue pediatrics most significantly predicted a desire for children. Among nonparents who desire children: 55% wish to have their first child between ages 31–35, 82.6% have concerns about the timing of when to start a family, 72% feel pressure to delay parenthood given career circumstances, and males more than females would consider cryopreservation in the face of subfertility. Regarding fertility awareness, 14.4% of parents and 7.4% of nonparents have had personal experience with infertility.

Conclusions Medical students not only have concerns about the timing of when to have children, many feel the pressure to delay having children due to professional goals. The majority also desire starting families at a time when professional demands are at their peak and fertility begins to precipitously decline. Given the increasing age of matriculating medical students and the intensive time investment to achieve physicianhood, our research suggests that medical educational institutions consider how they can better aid students in balancing the challenges of pursuing medicine with the desire to have children.

397 CLINICIAN RECOMMENDATIONS OF TECHNOLOGY FOR WEIGHT LOSS

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10.1136/jim-2018-000939.395

Purpose of study The purpose of this study was to determine if clinicians in an academic setting recommend technology for weight management and, if so, consider the recommendation to be evidence-based, or if age or personal use of technology related to clinical recommendations.

Methods used 906 clinicians in a University-affiliated medical practice were contacted via email with a link to an anonymous WebQ survey. Participants self-reported whether they recommend apps or other technologies to patients for food

logging, weight loss, fitness tracking, step tracking or other health monitoring, and whether they personally use these tools. Likert scales were used to assess beliefs in efficacy and evidence base. Chi-squared tests (χ^2) were performed using STATA on the first 75 submitted survey results.

Summary of results Of respondents, 64% (48 of 75) had recommended technology for weight loss, food logging, fitness or step recording, or health monitoring. 81% of clinicians (61 of 75) reported personally using these tools. The proportion of respondents recommending any technology for weight loss did not differ based on belief that research supports technology for weight loss ($\chi^2(4)=5.46$, $p=0.24$). The proportion of providers recommending any technology did not differ by age ($\chi^2(3)=0.70$, $p=0.87$), but tended to be higher among clinicians who believed that evidence supports technology's benefit for weight loss ($\chi^2(4)=9.21$, $p=0.06$) and was significantly higher among those personally using technology ($\chi^2(1)=9.38$, $p<0.01$). Respondents personally using apps for weight loss had a higher proportion reporting they believe that apps are effective for weight loss ($\chi^2(3)=21.9$, $p<0.01$) and that research supports the use of apps for weight loss ($\chi^2(4)=9.54$, $p=0.049$).

Conclusions This electronically administered survey showed a significant portion of responding clinicians using technology themselves, although estimates of prevalence are limited by the low response rate. Respondents who personally use technology were more likely to believe in the efficacy of such tools and recommend them to patients. The likelihood of recommending technologies for weight loss was unrelated to belief that evidence supported the use of such technology.

398 LIMITATIONS OF A SYNTHETIC PATIENT POPULATION GENERATOR USING EMR DATA

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10.1136/jim-2018-000939.396

Purpose of study Strict confidentiality rules often prevent data scientists from having access to real-world patient data. Synthetic data designed to replicate real-world patients is one approach to solving this problem. Synthea is a synthetic patient generator which utilizes disease-specific state transition probability modules to synthesize patients on a population level. Although Synthea has been used to model patients at a country, state, and city level, it has not been used to model hospital-specific patient populations. This study focuses on creating Synthea disease modules reflecting observed hospital-specific transition probabilities.

Methods used De-identified electronic medical record (EMR) data from 9 97 235 patients containing 25,640,495 conditions was used as a localized hospital data set. Synthea was utilized to generate patients based upon transition state probabilities computed from the dataset. Due to their simplicity, transition probabilities for Synthea's sinusitis and appendicitis disease modules were implemented.

Summary of results The modules included in Synthea contain disease transition states and probabilities that could not be calculated using available EMR patient data. For example, the Synthea sinusitis module requires probabilities for bacterial versus viral infection (table 1). This distinction was not documented by clinicians in the EMR so no local probability could be calculated. Conversely, clinically relevant transition states occurred in the EMR that were not present in Synthea modules. For example, the appendicitis module does not allow for resolution using antibiotics which was often done in clinical practice; Synthea assumes all appendicitis cases are resolved only with appendectomy.

Conclusions The two disease modules in Synthea could not be modified to represent a local hospital population using EMR data either due to data not recorded in the EMR or clinically important transition states missing in the Synthea models. New Synthea models containing transition probabilities actually recorded in EMR data need to be developed to create localized synthetic patient populations for data scientists.

Abstract 398 Table 1 Disease states not present in EMR but required for Synthea transition probabilities

Name	SNOMED-CT	Instances
Acute bacterial sinusitis (disorder)	75498004	0
Viral sinusitis (disorder)	36971009	0

399 FACTORS AFFECTING FRACTURE-RELATED DISABILITY LEAVE

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10.1136/jim-2018-000939.397

Purpose of study Observe and evaluate trends in fracture-related disability leave as affected by multiple factors, including the physical nature of the work involved, body part injured, age, and biological sex, in hopes of creating more accurate guidelines for determining length of disability leave.

Methods used Records from a major institution containing all fracture-related disability claims from 2006–2017 were analyzed. All claims resulting in at least one day of leave were included (n=657). The effect of physical requirement

Abstract 399 Table 1

Physical Group	Average Days Off	P-Value	Average Age (years)	Age Correlation (R^2)	Male Days Off	Female Days Off	Sex P-Value	Lower Extremity Average	Upper Extremity Average	Extremity P-Value
Overall	81.87	N/A	47.97	0.0022	75.63	85.62	0.31	94.13	71.48	0.03
Sedentary	61.17	0.00002	48.69	0.009	60.68	61.36	0.95	63.5	51.29	0.22
Mixed	98.58	0.06	47.08	0.003	103.65	96.11	0.76	127.18	79.93	0.06
Purely Physical	106.74	0.001	48.7	0.01	75.45	148.89	0.00005	125.32	88.4	0.1

(sedentary, mixed, or purely physical), academic level required, age, sex, and body part injured on length of disability leave were evaluated using regression, t-Test, and ANOVA.

Summary of results Sedentary jobs were associated with significantly shorter leave than mixed or purely physical jobs ($p=0.00002$). Purely physical jobs were associated with significantly longer leave overall ($p=0.001$), but not compared to mixed jobs ($p=0.6$). Age had the strongest influence on leave duration in the purely physical group ($R^2=0.01$). Female sex was associated with significantly longer leave than male only in the purely physical group (148.89 vs. 79.93 days; $p=0.0005$). Lower extremity fractures were associated with significantly longer leave than upper extremity (94.13 vs. 71.48 days lost; $p=0.03$). Workers in occupations requiring undergraduate-level education took significantly fewer days off than those in jobs requiring technical school or high school or lower ($p=0.05$ and $p=0.04$, respectively), however, higher education level was not associated with shorter leave overall.

Conclusions Jobs completed from a sedentary position are associated with shorter leave following fracture compared to those with mixed or purely physical responsibilities. Lower extremity fractures are associated with more days lost from work compared to those affecting upper extremities. Females working in purely physical jobs may need to take longer periods of leave than males in similar occupations.

400 SYSTEMIC REVIEW OF 30 DAY INTERNAL MEDICINE HOSPITAL RE-ADMISSIONS; RISK FACTORS AND PREVENTION

H Saab. *Kern Medical, Bakersfield, CA*

10.1136/jim-2018-000939.398

Purpose of study To examine our current pattern of 30 day re-admission with same diagnosis to identify patients at risk of admission with the same diagnosis. What to do to prevent re-admission and how to improve medicare response by reducing cost.

Methods used Retrospective chart review study of recorded 2016 same diagnosis re-admissions of Internal medicine department.

Summary of results There was a total of 214 encounters of re-admission to internal medicine department in 2016, 106 were admitted for the same diagnosis as discharged. Skin and soft tissue infection diagnosis (14%), followed by urinary tract infections (10%) were the most common diagnoses. Average admission age was 49 years. Dissecting the pool of patients we noticed that average length of stay was 5.4 days, 51% of the patients were of Hispanic race, 80% were females, 48% were unemployed, 58% had below normal albumin level, 42% were drug users, 70% were discharged home compared to 13% to skilled nursing facility. 20 encounters had hospital discharge follow-up prior to re-admission, none of the patients had meds-to beds as the program had not been implemented.

Conclusions Risk factors for readmission to hospitals are multifactorial, however, severity of the disease suggested by albumin level, length of stay, discharge destination, drug use, inconsistent follow-up appointment and medication non adherence seem to have a correlation with same-diagnosis readmission within 30 days.

401 EVALUATION OF END-OF-LIFE PREFERENCES OF PATIENTS WITH AMYLOIDOSIS

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10.1136/jim-2018-000939.399

Purpose of study Patients with amyloidosis experience high rates of morbidity and mortality. Little is known about what matters most to them and their end-of-life (EOL) care preferences. As patients become increasingly ill, many rely on healthcare proxies to make decisions for them. This is particularly challenging as the proxies often do not know the patients' goals and preferences for care. In this pilot study, we sought to address this gap in research by determining the EOL preferences of patients with amyloidosis and exploring proxy understanding of these preferences.

Methods used We used the Stanford What Matters Most Letter template to document patients' EOL wishes. Patients' wishes were divided into 3 categories: 1. What I *do want* at the end of life, 2. What I *do not want* at the end of life, and 3. Yes or No response to the question, 'If my pain and distress are difficult to control, please sedate me even if this means that I may die sooner.' We collected the responses of nine patients with amyloidosis, and present the total percentage of 'yes' answers to each question. In addition, we asked four patient proxies to answer the same questions on behalf of their patient. We determined patient-proxy concordance as the percentage of matching responses.

Summary of results In the *do not want* category, 89% of patients indicated a preference for not being put on a breathing machine, but only 11% indicated not wanting to die at home. Similarly, in the *do want* category 89% indicated wanting a gentle death, 78% to die pain free, and only 11% to spend their last days in the hospital. In the final category, 89% of patients wanted extensive pain control. Notably, only 25% of proxies understood that their patient wanted to be pain free at the end of their life, and patient-proxy concordance was 58% on average.

Conclusions We found common themes among the EOL preferences of patients with amyloidosis and explored patient-proxy concordance. Our results highlight that many patients would prefer a pain-free, gentle death at home without a breathing machine and that the responses to an advance directive are difficult to predict, even for assigned medical proxies. One study limitation is our small sample size. Future work among a larger population of patients with amyloidosis is needed to allow more generalizability.

Genetics II

Concurrent Session

8:00 AM

Saturday, January 26, 2019

402 TESTING READ THROUGH COMPOUND SAFETY TO TREAT HERITABLE PULMONARY ARTERIAL HYPERTENSION

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10.1136/jim-2018-000939.400

Purpose of study Heritable Pulmonary Arterial Hypertension (hPAH) is a progressive fatal disease with no effective treatment and is caused by a nonsense mutation in the *BMPR2 (Bone Morphogenetic Protein Receptor type 2)* gene. This mutation encodes a premature termination codon (PTC) that halts translation and produces either a nonfunctional truncated protein, or no protein at all. Small Molecule Read-Through (SMRT) compounds can read through PTCs in genes with nonsense mutations, which cause at least 10% of all genetic diseases. We propose to test whether our lead SMRT compound **GJ103** can readthrough PTCs in BMPR2 transcripts, and thus be used to effectively treat hPAH.

Methods used To test the efficacy of GJ103, Human Blood Outgrowth Endothelial Cells harboring *BMPR2* nonsense mutations (R584X and R899X) were treated with GJ103 for 24 hour. In addition, using wild-type (C57BL/6J background) mice, we conducted acute (1 week) and chronic (4 weeks) tolerability and toxicology studies to determine the Maximum Tolerated Dose (MTD) of GJ103. Three-month-old female mice were administered escalating doses of GJ103 (10, 25, 50, 250 mg/kg, n=5) via intraperitoneal route one time for the acute, and 4 times (25 and 50 mg/kg, n=5) for the chronic study. Biochemical and histological assays for liver, renal, cardiac, and metabolic functions were performed on blood and tissues collected.

Summary of results *In vitro* study shows that GJ103 efficiently reads through PTCs produces considerable expression of full-length BMPR2 protein in endothelial cells harboring BMPR2 mutation. No clinical signs of overt toxicity, changes in body weight or behavior were observed. Serum biomarkers of liver, kidney and heart function were all within the normal range both in the acute and chronic toxicity study.

Conclusions Since GJ103 showed no toxicity on a wide range of toxicological and safety parameters tested, it sets the stage for testing its efficacy in well-established mouse models (*Bmpr2*$^{+/R584X}$ and *Bmpr2*$^{+/R899X}$) of human hPAH, which otherwise is a rapidly lethal condition.

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403 ABSTRACT WITHDRAWN

404 ATTEMPTED TREATMENT OF NEONATAL LETHAL CPT II

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10.1136/jim-2018-000939.401

Case report We present a case of carnitine palmitoyltransferase II deficiency (CPT II) which illustrates pre- and postnatal features of the most severe Neonatal Lethal form of CPT II including new information about the disease course of this rare disorder.

Our patient was a term female infant born to unrelated parents. Prenatal ultrasound showed bilateral hyperechoic kidneys and ventriculomegaly. The couple's prior pregnancy was electively terminated at 23 wks due to anomalies; polycystic kidneys and corpus callosum agenesis. Newborn screen on that fetus suggested CPT II but autopsy conclusion was sporadic Multicystic Dysplastic Kidney. In this pregnancy, once anomalies were noted, maternal expanded carrier screening was done and positive for CPT II. Given the presumed diagnosis, a plan was developed for treatment of CPT II in the infant after delivery to include high glucose infusion rate, IV carnitine, and introduction of MCT oil with feeds. Infant was vigorous at birth with normal initial labs and normal amplitude-EEG. NBS sent at 12 hours confirmed the diagnosis. Unfortunately, by DOL3 labs suggested multi-organ failure and apnea developed. aEEG showed seizure activity progressing to encephalopathy. Care was withdrawn and death occurred quickly.

This case serves as a reminder that some metabolic disorders can cause morphologic changes which may be recognizable before documentation of metabolic derangement. CPT II most often presents as the myopathic form with exercise intolerance. The infantile hepatocardiomuscular form presents in the first year of life with cardiomyopathy and liver disease. This form is a target for newborn screening as it is treatable with dietary changes and intervention with exacerbations. There are case reports of attempts to treat the most severe cases of CPT II recognized prenatally because of a previous neonatal death. These reports describe variable success increasing survival beyond the neonatal period. To our knowledge, ours is the first report of attempt to treat an infant with documented prenatal manifestations. aEEG and laboratory findings in this case show that some of the pathology develops after delivery, progressing despite targeted therapy. It is our hope that additional investigation into pathophysiology behind this multi-organ failure in CPT II may lead to more successful treatments in the future.

405 AUTISM IN THE AMISH: EXOME SEQUENCING UNVEILS NOVEL CODING VARIANT

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10.1136/jim-2018-000939.402

Purpose of study To date, sequencing efforts to identify genetic determinants of autism spectrum disorder (ASD) have focused largely on *de novo* copy number variants and loss-of-function (LOF) variants in severely affected children. In this study, we evaluated exonic variants for association with quantitative measures of social impairment within the autism spectrum among adult subjects.
Methods used The Social Responsiveness Scale™, Second Edition (SRS-2), Adult Self-Report Form was administered to 357 generally healthy Amish adult research participants of the University of Maryland Amish Research Clinic. The SRS-2 is an objective measure of symptoms associated with ASD, with a higher Total T-score correlating with increased severity. The SRS-2 also generates scores for five treatment and two DSM-5-compatable subscales. Using exome sequencing data, an exome-wide association analysis (ExWAS) of each SRS-2 score was performed using the MMAP program, adjusting for age, sex, and relatedness. Results were limited to exonic variants in HWE ($p \geq 0.05$) with a MAC≥5.
Summary of results SRS-2 Total T-Score ranged from 36–75 with a mean of 48.9±6.4 (SD). A missense variant in *EvC ciliary complex subunit 1* (*EVC* p.D184N, rs41269549; MAF=0.7%) showed the strongest association with Total T-Score, reaching near exome-wide significance ($\beta=14.5$, $p=2.1x10–^{6}$). In addition, *EVC* p.D184N demonstrated exome-wide significant associations with scores for Repetitive and Restrictive Behaviors (RRB, $\beta=15.8$, $p=3.3x10–^{8}$) and Social Motivation (Mot, $\beta=16.3$, $p=7.7x10–^{7}$). Biallelic LOF variants in *EVC* are associated with Ellis-van Creveld Syndrome, in which ASD is not a feature; however the clinical significance of *EVC* p.D184N remains uncertain.
Conclusions We evaluated adults across the full spectrum of ASD-related behavioral traits, and through ExWAS, identified a germ-line variant in *EVC* associated with SRS-2 Total T-Score, as well as RRB and Mot scores. Possible explanations for this association include pleiotropy, incomplete dominance, and/or *EVC* p.D184N representing a gain-of-function mutation. These findings may provide insight into disease mechanisms and identify therapeutic targets.

406 FETAL NEURORADIOLOGIC PHENOTYPING MAY LEAD TO EARLIER DIAGNOSIS IN CONDITIONS IMPACTING THE MIDBRAIN-HINDBRAIN

R Gates, H Byers, C Guimaraes, H Dahmoush. *Stanford, Palo Alto, CA*

10.1136/jim-2018-000939.403

Purpose of study To emphasize the role of careful neuroimaging evaluation of mid- and hindbrain disorders to provide accurate information regarding diagnosis, prognosis and recurrence risk.
Methods used Two patients with complex hindbrain anomalies were identified through our Fetal and Pregnancy Health Program. Specific hindbrain findings were used to develop a differential and assess prognosis.
Summary of results Case 1 was referred at 12 w gestation for genetic counseling. Diagnostic testing was declined. Anatomic ultrasound at 17 w identified an appropriately-grown fetus with hypoplastic cerebellum, flat forehead, and possible club foot. Fetal MRI at 20 w identified a misshaped head and a small transverse cerebellar diameter with absence of cerebellar vermis, suggestive of rhombencephalosynapsis. Gomez-Lopez-Hernandez syndrome was suggested and counseling was provided. Postnatal exam by geneticist identified bitemporal narrowing with turribrachycephaly, patchy scalp alopecia, midface and brow retrusion and a depressed nasal bridge. Postnatal MRI confirmed rhombencephalosynapsis, aqueduct stenosis, hypoplastic corpus callosum and a dysplastic brainstem. The patient met clinical diagnostic criteria for Gomez-Lopez-Hernandez.

Case 2 was referred for fetal MRI for ultrasound finding of ventriculomegaly. Fetal MRI at 20 w noted asymmetric lateral ventriculomegaly, kinked hypoplastic brainstem, hypoplastic cerebellum, cleft lip/palate and bilateral club feet. Microarray on amniocytes was recommended. Neurology counseled the patient on outcomes in fetal brainstem anomalies. At 32 w, case was reviewed at multidisciplinary conference. Imaging findings were suggestive of a dystroglycanopathy. The fetus was born at term, had neonatal seizure, profound hypotonia, and creatine kinase >10 K U/L. Postnatal MRI noted cobblestone lissencephaly, hypoplastic kinked brainstem, vermian hypoplasia and aqueduct stenosis. Walker-Warburg syndrome was suggested. Molecular testing was sent, which identified pathogenic variant *POMT1* c.1432–2A>G (IVS14–2 A>G) and a LP variant *POMT1* c.89G>T (p.Arg30Leu). The infant died at 14 days age.
Conclusions Mid- and hind-brain anomalies may be complex and require specific phenotypic description for accurate diagnosis. Multidisciplinary consultation may aid in diagnosis and counseling.

407 NOVEL DE-NOVO PATHOGENIC VARIANT IN *PTEN*GENE CAUSES MALIGNANT MIXED CELL OVARIAN TERATOMA

[1]C Locke, [2]S Aradhya, [3]A Pawar, [1]S Shankar. *[1]UC Davis, Sacramento, CA; [2]Invitae, San Fransisco, CA; [3]University of California, Sacramento, CA*

10.1136/jim-2018-000939.404

Case report We report a 6-year-old Caucasian female who presented initially at 2.5 years of age with history of urinary urgency and abdominal pain for the preceding 5 months. An abdominal CT scan that revealed a soft tissue mass occupying the majority of the pelvis, AFP that was elevated to 3057.1 ng/mL, and beta-HCG at 2554 mIU/mL. She underwent gross total resection of the left adnexal mass along with a left salpingo-oophorectomy.Histology of the tumor was consistent with a malignant mixed cell ovarian germ cell tumor (OGCT). Later, at three years of age, a surveillance CT scan discovered a new mass that was resected. Histopathology revealed mature teratoma with predominantly intestinal or mucinous differentiation consistent with a diagnosis of growing teratoma syndrome. She was referred to genetics for determining underlying genetic etiology. On[AP1] [AP2] exam, she was noted to be macrocephalic (>2 SD above mean)and greater than the 95th percentile for height and weight. Scattered nevi, and a hypopigmented macule were also noted leading toward a diagnosis of possible overgrowth syndrome, including *PTEN*associated macrocephaly syndrome, Soto syndrome or Beckwith-Wiedemann Syndrome. An overgrowth panel sent to Invitae revealed a novel heterozygous

pathogenic variant c.685_686dupTC (p.Gly230Glnfs*27) in *PTEN*. *PTEN*is associated with the autosomal dominant *PTEN*hamartoma tumor syndrome (PHST). The variant was believed to be pathogenic as the two base pair duplication results in frame shift and a premature translational stop signal. It is expected to result in an absent or disrupted protein product. This variant has not been reported in the literature, however, it would create a nonfunctional protein and loss-of-function proteins have been found to be pathogenic in literature.[1 2] Targeted parental testing was negative for this variant. These results help in providing more directed care for our patient and helped provide family counseling about recurrence risk for parents and siblings. She is now being monitored based on *PTEN*Hamartoma syndrome associated screening guide lines.

REFERENCES
1. DOI: 10.1016/j.semcdb.2016.01.030
2. DOI: 10.1016/j.ajhg.2010.11.013

408 WILLIAM'S SYNDROME WITH EXTENSIVE INFILTRATIVE BASAL CELL CARCINOMA

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10.1136/jim-2018-000939.405

Case report William's Syndrome is a well-defined genetic disorder due to a microdeletion on chromosome 7. It is most commonly characterized by cardiovascular defects, electrolyte abnormalities, and abnormal facies. Cutaneous manifestations of this syndrome are uncommonly discussed in the literature, and its possible association w/various basal cell carcinoma syndromes is even less well established. Specifically, the hereditary basal cell carcinoma syndromes that have a well-established genetic basis—nevoid basal cell carcinoma syndrome, xeroderma pigmentosum, Bazex-Dupre-Christol syndrome, and Rombo syndrome—show no genetic correlation to William's Syndrome as none of them are due to any described mutations on chromosome 7. Herein, we present a review of the literature regarding the cutaneous manifestations of William's Syndrome and the various BCC syndromes, as well as a case report of an unspecified BCC syndrome comorbid in a patient with William's Syndrome and treated with Mohs micrographic surgery and vismodegib.

Neonatology General V
Concurrent Session
8:00 AM
Saturday, January 26, 2019

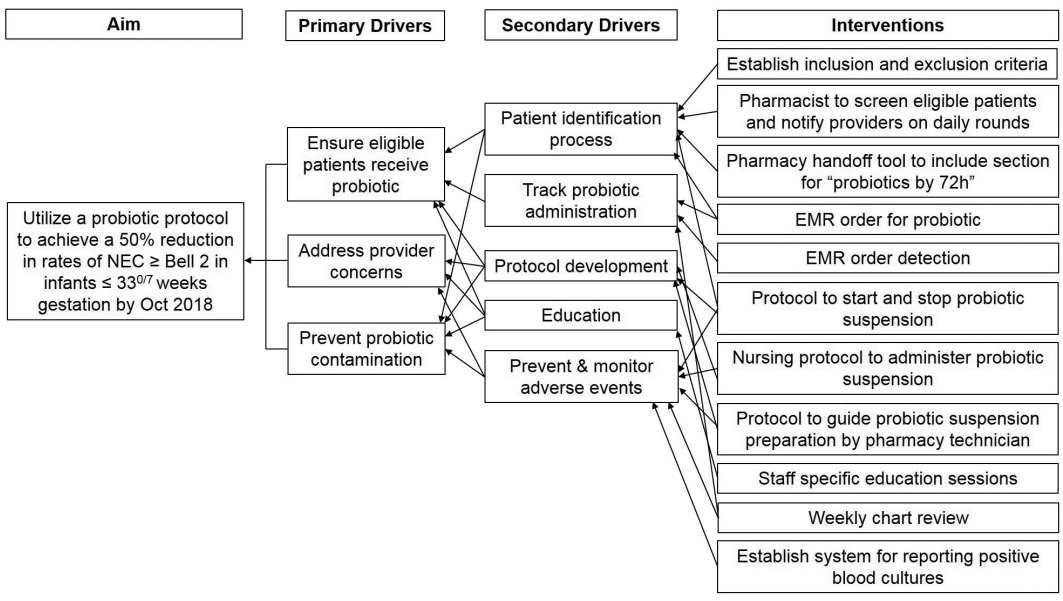
409 IMPLEMENTATION OF A PROBIOTIC PROTOCOL TO REDUCE NECROTIZING ENTEROCOLITIS

MK Sekhon, B Yoder. *University of Utah, Salt Lake City, UT*

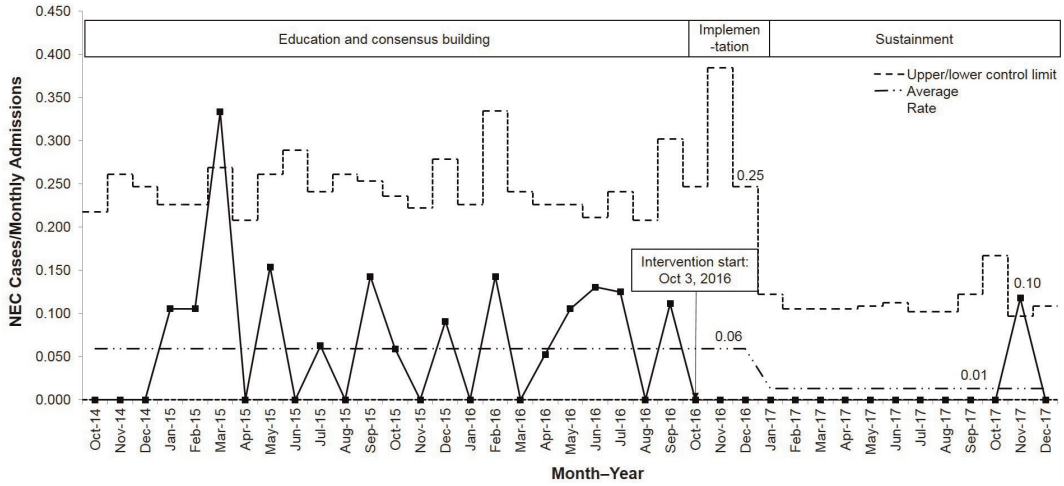
10.1136/jim-2018-000939.406

Purpose of study In the University of Utah NICU, rates of NEC Bell stage ≥2 in infants<30 weeks gestational age (GA) increased from 5% to 11% from 2014–2015, after a decline from 21% to 5% from 2010–2014. As probiotics in preterm infants reduces NEC risk, we implemented a quality improvement protocol to administer the probiotic, *Ultimate Flora*, to infants $<33^{0/7}$ weeks GA. Our aim was to reduce rates of NEC≥Bell 2 by 50% in infants $<33^{0/7}$ weeks GA by Oct 2018.

Methods used Drivers and interventions were identified (figure 1). Eligibility criteria were: $<33^{0/7}$ weeks GA or birth weight <1500 g, corrected GA of $24^{0/7}$ weeks, 72 hour of age, and feeding tolerance of 6 ml/d for 24 hour. We excluded infants with significant anomalies. The NICU pharmacist tracked eligibility. We had 3 PDSA cycles: education/intervention development, implementation, and sustainment. U-chart tracked monthly rates of NEC Bell stage ≥2. Compliance and probiotic sepsis were monitored.



Abstract 409 Figure 1



Abstract 409 Figure 2 NEC cases ≥bell stage 2 per monthly admissions U-chart

Summary of results 191 eligible infants received the probiotic from 10/3/2016–12/31/2017. 1 ineligible infant received the probiotic. 2 eligible infants were missed. There was a decrease in rates of NEC Bell stage ≥2 from 6% to 1% (figure 2). There was no probiotic sepsis.

Conclusions Implementation of a probiotic protocol was associated with decreased NEC Bell stage ≥2 in infants $<33^{0/7}$ weeks GA.

410 PROGRESS TOWARDS IMPROVING SYSTEM CAPACITY TO USE BUBBLE CONTINUOUS POSITIVE AIRWAY PRESSURE (BCPAP) TO TREAT NEONATES WITH RESPIRATORY DISTRESS IN NAKURU, KENYA

[1]N Switchenko, [2]J Mairura, [2]V Munene, [2]P Tsimbiri, [3]A Anderson-Berry, [1]B Fassl, [2]E Kibaru.
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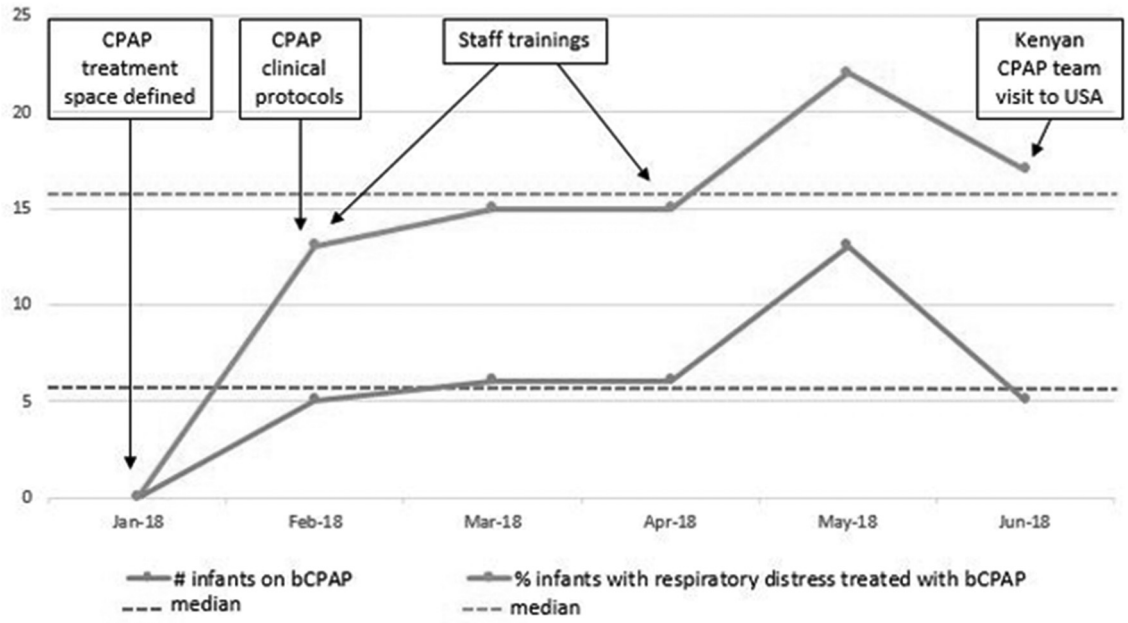
10.1136/jim-2018-000939.407

Purpose of study Respiratory distress (RD) contributes to the most common causes of neonatal mortality. bCPAP is a safe, low-cost therapy for RD that improves neonatal outcomes in low resource settings, however implementation of bCPAP programs is challenging. This quality improvement initiative aims to increase the percentage of neonates with RD treated with bCPAP from 0% to 25% by 01/19.

Methods used In the newborn unit (NBU) at the Provincial General Hospital (PGH) in Nakuru, Kenya a pre-intervention (pre) period (03/16 – 12/17) and a post-intervention (post) period (01/18 – 06/18) were defined. Tests of change included staff training, treatment protocols, and organization of infrastructure. Clinical and outcome data were abstracted from all available NBU medical records during pre and post periods. Unit admission and mortality books were used to compare mortality between periods.

Summary of results 405 infants were included in the pre group, with 0% bCPAP use. 513 infants were included in the post group, with 35 (7%) treated with bCPAP. bCPAP use



Abstract 410 Figure 1 bCPAP delivery in the PGH NBU

Abstract 411 Table 1

	2014 Compliance % (n)	2015 Compliance % (n)	2016 Compliance % (n)	2017 Compliance % (n)	2018 Compliance % (n)
Doctor present at delivery	28.57% (42)	50% (24)	15% (20)	37.5% (8)	84.62% (13)
Midwife present at delivery	2.04% (49)	0% (24)	0% (19)	12.5% (8)	53.85% (13)
Doctor caring for newborn at delivery	22.45% (49)	16.67% (24)	10% (20)	25% (8)	38.46% (13)
Midwife caring for newborn at delivery	0% (37)	0% (24)	0% (20)	12.5% (8)	38.46% (13)
Resuscitation equipment present	87.76% (49)	83.33% (24)	95% (20)	100% (8)	83.33% (12)
Resuscitation equipment checked	16.33% (49)	47.62% (21)	0% (20)	37.5% (8)	8.33% (12)
Meconium suctioned	13.16% (38)	20% (15)	40% (5)	33.33% (3)	50% (2)
Newborn dried thoroughly	95.92% (49)	100% (24)	100% (19)	100% (8)	100% (12)
Stimulation provided	66.67% (3)	100% (15)	100% (5)	100% (2)	100% (8)
Suctioning provided	100% (2)	73.33% (15)	80% (5)	50% (2)	50% (8)
Bag mask ventilation provided	100% (1)	0% (5)	0% (4)	0% (2)	0% (8)
Breastfed within 30 min of birth	0% (49)	8.7% (23)	0% (20)	12.5% (8)	10% (10)
Kept in kangaroo care after birth	2.38% (42)	4.17% (24)	0% (20)	0% (8)	0% (10)

increased during the post period (figure 1). Rates of RD (50% pre, 47% post, p=0.35) and mortality (30.9% pre, 30.4% post, p=0.84) were similar. In the post period, neonates treated with bCPAP had lower mean BW (2.1 kg pre, 2.6 kg pre, p=0.00) and higher risk of death (RR 1.9, 95% CI 1.3–2.7) compared to those not treated with bCPAP. No complications of bCPAP were seen.

Conclusions It is possible to build capacity for the use of bCPAP to treat neonates with RD in resource limited settings. Current capacity in the PGH NBU allows for application of bCPAP to smaller, likely, sicker neonates.

411 HELPING BABIES BREATHE – AN EVALUATION OF PROGRAM COMPLIANCE IN RURAL INDIA

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10.1136/jim-2018-000939.408

Purpose of study Neonatal deaths in India are on the decline but there are still 0.6 million neonatal deaths per year. In rural India, 23.1% of neonatal deaths are attributed to asphyxia. Helping Babies Breathe (HBB) was designed to help reduce asphyxia-related deaths through interventions that improve neonatal resuscitation. The purpose of this study was to evaluate compliance with HBB since it's implementation in rural India.

Methods used This study took place in the Mota Fofalia Pediatric Center in Gujarat, India between April 2014 and July 2018. All birth attendants completed standardized HBB training in April 2014 and subsequent refresher training annually. Trained observers measured HBB compliance using a standardized data collection form previously validated in rural India.

Summary of results A total of 114 deliveries were observed between 2014 and 2018. During this time, there was an increase in meconium suctioning and an extremely high compliance with providing stimulation and drying the newborn. There was also an increase in doctors and midwives assisting with deliveries and care for newborns after delivery. Ongoing challenges exist with regard to checking resuscitation equipment, performing resuscitation interventions when indicated, kangaroo care, and early breastfeeding (figure 1).

Conclusions Implementation of the HBB training program at Mota Fofalia has resulted in many important elements of the HBB protocol being put into practice. Further investigation into potential barriers to compliance and impact on overall neonatal survival is needed.

412 THE IMPACT OF A BABY FRIENDLY INITIATIVE ON NEONATAL HYPOGLYCEMIA

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10.1136/jim-2018-000939.409

Purpose of study The Baby Friendly Hospital Initiative (BFHI) is a global program implemented to support breastfeeding. Neonatal hypoglycemia is a disorder that may lead to neurologic injury. Supplemental feeding is the initial treatment; formula feeding is discouraged in BFHI. The objective of this project is to assess if the BFHI, followed by implementation of hypoglycemia guidelines, would affect the number of admissions to the Neonatal Intensive Care Unit (NICU) for the diagnosis of hypoglycemia. The hypoglycemia guidelines followed 2011 AAP recommendations.

Methods used Inborn, healthy infants greater than 36 0/7 weeks gestation transferred to NICU for isolated hypoglycemia were identified by chart review. Infants admitted for other pathologies were excluded. Outcomes of infants born from three different 18 month epochs [1=Before BFHI (1/1/2014 to 6/1/2015); 2=After BFHI (6/1/2014 to 1/1/2017); 3=After BFHI+Hypoglycemia Guidelines (1/1/2017 to 6/1/2018)] were compared; and were gestational age-weighted and adjusted for risk factors for hypoglycemia.

Summary of results There was a statistically significant increase in the number of infants admitted to the NICU for hypoglycemia in Epoch 2 (32/4395 in Epoch 2 versus 13/4681 in Epoch 1, p=0.002) that persisted in Epoch 3 (29/4064 in Epoch 3 versus 32/4395 in Epoch 2, p=0.94). Epoch 3 infants were more likely to have a risk factor for hypoglycemia (86% in Epoch 3 versus 69% in Epoch 2 versus 50% in

Abstract 413 Table 1

	Feb '14 Compliance % (n)	STAFF TRAINING INTERVENTIONS	Aug '14 Compliance % (n)	Feb '15 Compliance % (n)	May-Aug '15 Compliance % (n)	May 25-June 29 2016 Compliance % (n)	June 04-June 24 2018 Compliance % (n)
% of standard newborn records used	0% (138)	STAFF TRAINING INTERVENTIONS	NA (130)	NA (60)	98.07% (206)	100% (171)	100% (86)
% of newborns weighed during rounds	0% (31)	STAFF TRAINING INTERVENTIONS	88% (138)	83% (60)	59% (207)	95.9% (172)	95.3% (86)
% of newborns correctly identified as LBW	0% (31)	STAFF TRAINING INTERVENTIONS	64.5% (48)	23% (40)	31.3% (67)	15.4% (97)	69.4% (36)
% of newborns with HR documented	0% (2)	STAFF TRAINING INTERVENTIONS	NA (138)	NA (60)	88.7% (203)	80.8% (172)	56.9% (86)
% of newborns with temperature documented	0% (31)	STAFF TRAINING INTERVENTIONS	NA (138)	NA (60)	87.6% (202)	76.2% (172)	56.9% (86)
% of newborns with feeding intake documented	0% (138)	STAFF TRAINING INTERVENTIONS	30% (138)	100% (60)	75.6% (201)	78.3% (171)	36.5% (85)
% of LBW babies discharged after 5 days of care	0% (58)	STAFF TRAINING INTERVENTIONS	NA	10% (20)	11.3% (88)	16.7% (36)	25% (8)
% of babies with weight gain at discharge	0% (58)	STAFF TRAINING INTERVENTIONS	11.8% (17)	0% (9)	0% (8)	72.5% (91)	0% (4)
% LBW newborns with kangaroo care provided	0% (58)	STAFF TRAINING INTERVENTIONS	41.3% (58)	11.1% (27)	78.6% (14)	94.1% (68)	0% (32)
% LBW with daily RR recorded 2x daily	NA	STAFF TRAINING INTERVENTIONS	52.6% (78)	15.3% (59)	1.52% (66)	0% (97)	50% (4)
% LBW with feeding recorded 2x per day	0% (58)	STAFF TRAINING INTERVENTIONS	NA	NA	15.2% (66)	0% (97)	66% (3)

Epoch 2, p=0.009). Mean lowest bedside glucose was significantly lower in Epoch 3 with no statistically significant difference in serum glucose. This value persisted after controlling for risk factors (p=0.002).

Conclusions There were more admissions to the NICU for hypoglycemia after BFHI. This was unchanged after implementing the AAP recommended hypoglycemia guidelines. After implementation of a hypoglycemia guideline, 86% of NICU admissions for isolated hypoglycemia had at least one risk factor. Strategies to prevent hypoglycemia in at risk patients may be of benefit to decrease NICU admissions for isolated hypoglycemia.

413 ASSESSMENT OF QUALITY IMPROVEMENT INTERVENTIONS ON NEWBORN CARE DELIVERY IN RURAL INDIA

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10.1136/jim-2018-000939.410

Purpose of study 2.6 million newborns die worldwide each year. Birth asphyxia, infections and complications due to low-birth-weight (LBW <2500 g) are associated with 60%–80% of all neonatal deaths. These causes of death are largely preventable if health care workers are adequately trained to monitor at-risk infants and provide quality care. This study looked at the effects of a combined training and quality improvement intervention on newborn care delivery in a hospital setting in rural India.

Methods used The study took place in a rural hospital in Mota Fofalia, Gujarat where a neonatal care quality improvement program was implemented. From May of 2014 to June of 2018, medical students trained in data collection directly observed care delivery at the newborn unit and completed a standardized checklist of essential newborn care provided to infants. Elements of essential and evidence based newborn care were abstracted from World Health Organization recommendations. Data was collected using a standardized data collection tool. We report provider compliance and trends in the quality of care over time.

Summary of results A total of 723 care encounters during 6 distinct data collection periods were performed. At baseline compliance essential newborn care quality measures were low (0%). Following a combined training and quality improvement intervention for hospital staff, care quality increased for the majority of elements, but challenges about sustained compliance remain significant. See table 1.

Conclusions Although the staff has made improvements in neonatal care delivery after the initial training, the most recent data shows that many procedures are still not being fully implemented and further training may be needed.

414 GASTRIC RESIDUAL ALTERNATIVE MANAGEMENT QUALITY IMPROVEMENT STUDY: IMPACT OF ELIMINATION OF ROUTINE GASTRIC RESIDUAL EVALUATION ON FEEDING OUTCOMES AND INTERVENTIONS

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10.1136/jim-2018-000939.411

Purpose of study There is no evidence that routine evaluation of gastric residuals decreases complications of preterm infants.

Our Quality Improvement Team developed a gastric residual alternative management (GRAM) algorithm that eliminated routine gastric residual checks in preterm infants fed by gavage.

The objective of the GRAM quality improvement (QI) study was to decrease: 1) the 'nil per os' (NPO) time by a median of 2 days, 2) the time to full enteral feeds by a median of 1 day, and 3) the proportion of interventions associated with large gastric residuals by 25% in six months of intervention. Process measures were compliance with the protocol. Balancing measures were incidence of gavage tube malplacement, and length of stay (LOS). The incidence of necrotizing enterocolitis (NEC) was also monitored.

Methods used The study took place in a level IV NICU. The Nutrition QI Team developed the GRAM algorithm in January 2017 and used PDSA methodology to implement it then follow the process. After multidisciplinary team education, the project was implemented in March 2018. Compliance with the algorithm was monitored at least weekly. Data was collected on infants with birth weight <1800 g. Outcomes of infants born in the 6 months preceding this QI intervention were used as controls.

Summary of results There were 322 compliance audits performed in the first 5 months of intervention. Five-month preliminary results of the outcome metrics showed a median reduction of NPO-days of 4/1000 hospital days with the intervention. GRAM group reached full enteral feeds an average 2 days earlier than the control group. Combined screening exams such as radiographs and laboratory samples were reduced by 50% with the GRAM. Length of stay was reduced on average by 8 days with the proposed intervention. Malpositioned gavage tube-related adverse events were rare (0.006%), and none led to permanent harm or death. Incidence of NEC did not increase during this time period.

Conclusions Preliminary results with GRAM intervention supports improved feeding outcomes and reduced invasive interventions without significant adverse events captured by balancing measures.

415 NEWBORN INTERVENTION PROMOTING PRETERM INFANT EATING READINESS

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10.1136/jim-2018-000939.412

Purpose of study To increase nursing interventions that promote physiologic maturation necessary for successful feeding, improve skills of bedside nurses for recognition of signs of physiologic instability in relationship with feedings, limit negative and promote positive oral experiences in preterm infants, a bundled program titled 'NIPPER' (Newborn Intervention Promoting Preterm infant Eating Readiness) was developed. SMART aims of this quality improvement (QI) study were to, on average, shorten the time to first skin-to-skin (STS) contact, first oral feeding, and length of stay (LOS) each by 2 days, and to increase breastfeeding rates at discharge by 5% in one year of intervention.

Methods used This study used the Plan-Do-Study-Act quality improvement method. Six modules and algorithms that correspond to preterm infant's typical developmental progression with feeding were developed to assist caregivers in facilitating the development of infant feeding skills. Nurses were trained by study champions using didactic lessons and educational videos. NIPPER was implemented on January 23, 2018. Data were collected on infants less than 34 weeks gestation admitted to the NICU. Timeline for the study is 1 year. Outcomes of infants born the year preceding this QI intervention were used as controls.

Summary of results To date 1428 audits were performed and showed 93% nursing compliance with keeping the modules visible at the bedside and documenting daily interventions. The study groups were comparable with regard to baseline characteristics. Infants receving NIPPER intervention had their first STS contact 7 days earlier on average (DOL 2[1,3] in the NIPPER and DOL9[2,14] in the Control, p=0.02). First oral feeding occured 3 days earlier on average in the NIPPER group. Breastfeeding rates at discharge increased from 61% to 72% with the intervention (p=0.05). LOS was reduced on average by 4 days (39 days in NIPPER and 43 days in Control, p=0.29).

Conclusions All SMART aims of the study were accomplished in the first 7 months of intervention. NIPPER program appears to encourage and support physiologic maturation necessary for successful breastfeeding and oral feeding, in general, in preterm infants. There was a trend for shorter LOS with the intervention which did not reach statistical significance.

416 TIME TO ANTIBIOTIC ADMINISTRATION IN THE NEONATAL INTENSIVE CARE UNIT: IDENTIFICATION OF BARRIERS TO IMPROVE WORKFLOW

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10.1136/jim-2018-000939.413

Purpose of study Neonatal sepsis remains a leading cause of infant mortality. Multiple centers have explored utilization of an ideal, one-hour antibiotic administration time to reduce morbidity and mortality. A recent review examined hospital-acquired infections in neonates and found that optimizing antibiotic administration was a rather expansive effort. They found effective measures included reducing antibiotic delays through education, standardizing the evaluation of sepsis, and streamlining online ordering through electronic medical record. Based on these data we implemented an ongoing quality improvement (QI) program aimed at optimizing time to antibiotic administration.

Methods used Our chart review identified 622 infants who had received antibiotics following admission to the UC Davis NICU. 293 were excluded due to having the initial dose administered outside of the unit. 290 infants were reviewed from January 2017-December 2017, the highest average time to antibiotics was 6.82 hours (from initial order to medication administration) within a single month. We performed a root cause analysis, examining each step of the process, from pharmacy verification, drug delivery to the NICU, and administration in order to identify targets for improvement.

Summary of results In January 2018 we began a 2 month intervention period of nursing and resident education while continuing prospective data review, tracking time to antibiotic administration. As of June 2018, we observed an average time to medication administration of 2:30 with a

standard deviation of 47 min. We are currently in the process of collecting survey responses from the nursing staff to further identify other barriers to timely antibiotic administration.

Conclusions Our analysis suggested that antibiotic delay is a common yet preventable problem in the NICU. Our multi-system approach allowed us to target our deficiencies by improving education, optimizing time-sensitive antibiotic administration, and raising awareness of the importance of prompt treatment of sepsis in critically ill neonates. In this ongoing QI project, we plan to utilize staff survey data and continue staff education to further reduce our antibiotic administration times closer to the current best practice recommendations of under one hour.

Neonatology – Perinatal Biology II

Concurrent Session

8:00 AM

Saturday, January 26, 2019

417 HYPEROXIA INDUCES GOLGI STRESS IN RAT ALVEOLAR TYPE II CELLS

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10.1136/jim-2018-000939.414

Purpose of study The role of Golgi stress,an evolutionarily, highly conserved mechanism for cellular homeostasis in neonatal lung injury is not well defined. We hypothesize that exposure to hyperoxia, a well-established insult that results in neonatal lung damage, activates Golgi stress, and it can be modulated to prevent lung damage. Here, on exposure to hyperoxia, under both *in vitro* and *in vivo* conditions, we specifically evaluate the expression of markers of Golgi stress, i.e., Golgi-expressed genes, ADP-ribosylation factor (Arf4), GM130, and the transcription factor E3 (TFE-3).

Methods used One-day old Sprague-Dawley rat pups were exposed to either 21% (control) or 95% O_2 (hyperoxia) for 24 and 72 hour, and then sacrificed. Lungs samples were collected and analyzed for lung morphometry (radial alveolar count and mean linear intercept), apoptosis (Bcl-2 and Bax protein levels), and Golgi stress (Arf4, TFE-3, GM130 protein levels) by Western analysis and immunofluorescence. For *in vitro* studies, cultured RLE-6TN cells, alveolar type II rat cell line, were exposed to 21% or 95% O_2 for 24 hour, and similarly processed for markers of Golgi stress.

Summary of results Western blotting on lung extracts showed that 24 and 72 hour hyperoxia significantly induced ARF4, TFE3 and GM130 protein levels, and confirmed apoptosis induction (decreased ratio Bcl-2/Bax) and lung morphometric changes consistent with hyperoxic damage ($p<0.05$ for all vs. control). Similar data were obtained for *in vitro* studies. Furthermore, TFE-3 nuclear translocation (a marker of functional activation) was detected by immunofluorescence in RLE-6TN cells.

Conclusions Collectively, our data supports the induction of a Golgi stress response by hyperoxia exposure to rat lungs. Further experiments to examine the functional significance of this response and its modulation to block neonatal lung injury are in progress. ur We speculate that blocking Golgi stress may be an effective novel strategy to prevent hyperoxia-induced neonatal lung damage.

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418 DIFFERENTIAL ADIPOGENIC PROGRAMMING IN MALE AND FEMALE INTRAUTERINE GROWTH RESTRICTED RAT OFFSPRINGS

S Sreekantha, Y Wang, R Sakurai, J Liu, V Rehan. *Harbor-UCLA Medical Center, Torrance, CA*

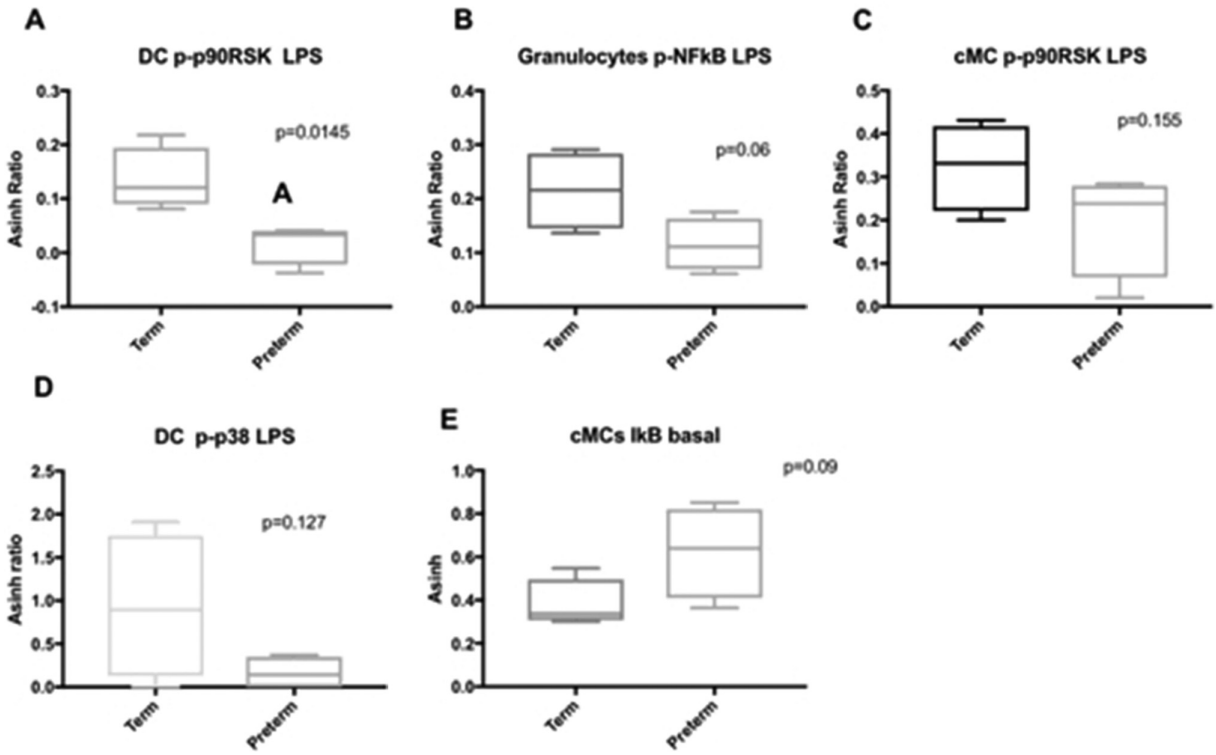
10.1136/jim-2018-000939.415

Purpose of study Intrauterine growth restriction (IUGR) results in offspring obesity. Bone marrow stem cells isolated from rat offspring born following maternal food restriction (MFR) show enhanced adipogenic programming; however, the effect of IUGR on white adipose tissue (WAT) progenitors and gender specific effects are not studied.

Methods used Established rat model of 50% global caloric restriction during the latter-half of pregnancy, with ad libitum diet postnatally, which results in an obese offspring with a metabolic phenotype was used. Using standard methods, WAT progenitors were isolated on postnatal day (PND) 1 and 21, and their adipogenic programming was determined by mRNA profiling.

Summary of results Preadipocyte phenotype was characterized by flow cytometry;>90% of cells were CD 31-, CD45-, CD 73+, and CD 90+. On PND1, key adipogenic programming genes, PPARγ and Pref-1 were downregulated in preadipocytes isolated from MFR males and females ($p<0.05$ vs controls); however, at PND21, preadipocytes from MFR females continued to show downregulation of PPARγ and Pref-1 expression, while male MFR preadipocytes showed upregulation in PPARγ and Pref-1 expression ($p<0.05$ vs. controls). Even after adipogenic induction, both male and female MFR adipocytes continued to show significantly lower PPARγ, ADRP, and adiponectin levels ($p<0.01$ vs controls), however, at PND21 although adipocytes from MFR females continued to show lower PPARγ, ADRP and adiponectin ($p<0.05$ vs controls) levels, in contrast, adipocytes from MFR males showed a trend towards increased expression of these adipogenic genes. These data were also corroborated by objective assessment of the adiogenic state of these cells by Oil Red O staining

Conclusions From these data, we conclude that IUGR programs WAT preadipocytes to an enhanced adipogenic potential, to a greater extent in males (vs. females). Some of these changes are detectable soon after birth (PND1), but these become more pronounced later (PND21), suggesting a role of



Abstract 419 Figure 1 Representative cells with decreased tone in the NFκB pathway. A-D) Response of cells to LPS. E) Basal IκB. IκB inhibits NFκB; elevated levels are associated with decreased NFκB activity.

postnatal nutrition in facilitating the adipogenic phenotype of IUGR offspring.

Grant Support HL127137, HD071731 (NIH); 23RT-0018 and 27IP-0050 (TRDRP)

419 DEEP PROFILING OF THE NEONATAL IMMUNE SYSTEM

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10.1136/jim-2018-000939.416

Purpose of study A comprehensive characterization of the neonatal immune system has yet to be accomplished due to limitations of traditional biologic techniques. High-dimensional mass cytometry (CyTOF) allows for simultaneous mapping of dozens of cell types and their signaling activity. We used CyTOF to examine the immune system in term vs preterm neonates.

Methods used Cord blood was collected. Samples were stimulated for 15 min with lipopolysaccharide (LPS), interferon alpha (IFNα), or interleukins 2, 4, and 6 (IL-2, IL-4, IL-6). Samples were stained with antibodies to 19 phenotypic markers and 15 phosphorylated signaling proteins and analyzed with CyTOF.

Summary of results 8 newborns have been analyzed: 4 preterm (mean gestational age 31.6 weeks, range 26.7–35.6) and 4 term (38.4 weeks, range 37.1–40.9 weeks). There were no demographic differences between groups. In innate immune cells, there was a trend towards a dampening of the pro-inflammatory NFkB signaling pathway (figure 1A-E). Given the small sample size, only the association with p90RSK in dendritic cells (DCs) reached statistical significance.

Conclusions This study is the first to utse CyTOF to profile the function of the immune system in neonates. Preliminary analysis demonstrates an altered NFkB pathway in preterm infants. A larger sample size is anticipated.

420 CHRONIC GLUCAGON INFUSION DOES NOT INCREASE INSULIN SECRETION IN LATE GESTATION FETAL LAMBS

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10.1136/jim-2018-000939.417

Purpose of study Pancreatic development and regulation of insulin secretion are critically important to fetal growth and metabolic programming, with effects that persist into adulthood. *In vivo* studies have demonstrated that chronic amino acid infusion increases serum glucagon concentrations and potentiates glucose-stimulated insulin secretion (GSIS) in late gestation fetal lambs. Based on these findings, we hypothesized that glucagon mediates this effect on insulin secretion via direct signaling to the beta cell, and therefore, increased exogenous glucagon would be sufficient to potentiate insulin secretion.

Methods used We investigated the impact of a chronic glucagon infusion on fetal growth and on *in vivo* insulin secretion and glucose concentrations. Late gestation singleton fetal sheep received a direct intravenous infusion of glucagon (5 ng/kg/min) or vehicle control for 8–10 days. Plasma glucose and insulin concentrations were measured throughout the study, and GSIS was measured in response to both acute (1 hour) and chronic (8–10 days) exposure to exogenous glucagon.

Summary of results Acutely, fetal plasma glucagon concentrations increased 1.7-fold to 98.9±7.3 pg/mL within one hour of infusion (control n=6, glucagon n=8). By study end, glucagon concentrations were 3.1-fold above baseline (185.2 ±15.0 pg/mL; control n=4, glucagon n=6). Despite elevated glucagon, glucose concentrations were not significantly different between vehicle- and glucagon-infused fetuses. Additionally, there were no significant differences in GSIS in response to acute or chronic exposure to elevated glucagon concentrations. However, there was a decrease in unstimulated plasma insulin concentrations in the glucagon fetuses (0.30±0.04 baseline vs. 0.10±0.02 end of study, $p<0.05$), with a nonsignificant trend toward lower insulin concentrations compared with controls. There were also nonsignificant trends toward lower body mass, in addition to lower normalized pancreas and liver weights in glucagon-exposed lambs.

Conclusions These findings demonstrate that exogenously infused glucagon does not stimulate *in vivo* insulin secretion or potentiate GSIS under either acute or chronic conditions but rather leads to suppressed insulin concentrations over time.

421 ACTIVITY OF SARCOLEMMAL SYSTEM A AND L AMINO ACID TRANSPORTERS AND SIGNALING PATHWAYS REGULATING MUSCLE PROTEIN SYNTHESIS IN GROWTH RESTRICTED FETAL SHEEP

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10.1136/jim-2018-000939.418

Purpose of study Fetuses with intrauterine growth restriction (IUGR) are born with reduced muscle mass, which cannot be fully compensated for postnatally. We previously demonstrated that *in vivo* skeletal muscle amino acid uptake rates, protein synthesis, and System A amino acid transporter gene expression are decreased the IUGR sheep fetus. The molecular mechanisms that underlie reduced skeletal muscle growth in IUGR fetuses are largely unknown. We hypothesize that IUGR hindlimb skeletal muscle has decreased activity of System A (Na +dependent) and L (Na +independent) amino acid transporters and inhibition of signaling pathways that promote protein synthesis and growth.

Methods used IUGR was induced in pregnant sheep by hyperthermia. Gastrocnemius muscle biopsies were obtained in late gestation from CON (n=12) and IUGR (n=12). Sarcolemma was isolated with differential centrifugation and recovery on a sucrose gradient. Membrane enrichment was determined using western blot analysis for Na +K + ATPase β, a plasma membrane marker. System A and L transporter activity was determined by measuring uptake of 14C-Histidine and 3H-Leucine respectively using rapid filtration techniques. Protein expression of total and phosphorylated AKT (Ser473), 4E-BP1 (Thr37/46 and Thr70), eIF2α (Ser51), and AMPKα (Thr172) was measured by western blot analysis.

Summary of results Sarcolemmal enrichment of Na +K + ATPase β was not different between the two groups. System A uptake by IUGR was similar to CON (CON 19.3±4.2, IUGR 17.0±3.1 pmol/mg x 300 s, $p=0.68$). System L uptake was not different between groups (CON 1.0±0.1, IUGR 0.9±0.1 pmol/mg x 300 s, $p=0.8501$). Expression of total and phosphorylated AKT (Ser473), 4E-BP1 (Thr37/46 and Thr70), eIF2α (Ser51), and AMPKα (Thr172) was similar between CON and IUGR.

Conclusions The activity of sarcolemmal System A and L amino acid transporters and signaling pathways regulating muscle protein synthesis is not significantly different in IUGR compared to control. The previously reported *in vivo* decreased skeletal muscle amino acid uptake and protein synthesis rates in IUGR sheep are therefore likely caused by other mechanisms such as decreased ATP synthesis or Na +K + ATPase activity.

422 EXPERIMENTALLY INCREASING FETAL INSULIN CONCENTRATIONS INCREASES PANCREATIC β-CELL AREA IN GROWTH RESTRICTED FETAL SHEEP

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10.1136/jim-2018-000939.419

Purpose of study Fetal insulin concentrations are critical for fetal growth, and while partly determined by the amount of pancreatic β-cells, may stimulate β-cell replication and increase β-cell mass. Intrauterine growth restricted (IUGR) fetuses are characterized by low insulin concentrations and fewer pancreatic β-cells. It is unknown if fewer β-cells are a result of low insulin concentrations. We hypothesized that an infusion of insulin for two weeks into the IUGR fetal sheep circulation would increase pancreatic β-cell area.

Methods used IUGR was induced by exposing pregnant sheep to elevated ambient temperatures. Fetal catheters placed in IUGR fetal sheep were infused with either 0.015 uU kg^{-1} hr^{-1} of insulin with glucose to maintain glucose concentrations (IUGR-I, n=5) or saline vehicle (IUGR-V, n=7), for 14 days. Normally growing fetuses received vehicle (CON-V, n=6). At the end of the infusion (85% of gestation), fetal pancreas was fixed in 4% paraformaldehyde. In four sections per fetus, percent area of pancreas was determined by positive stain for insulin. β-cell mass was calculated from percent area and pancreatic mass. Insulin and glucose concentrations were compared with a repeated measures ANOVA and pancreatic characteristics with a one way ANOVA.

Summary of results Gestational age at the end of the study was similar in all groups (126±0 IUGR-I, 126±0 IUGR-V, 125 ±1 days CON-V). IUGR fetuses weighed less than CON-V (1.8±0.3 IUGR-I, 1.6±0.2 IUGR-V, 2.5±0.2 kg CON-V; $p<0.05$). Insulin concentrations started lower in IUGR groups, and doubled in IUGR-I ($p<0.05$). Glucose concentrations were similar in IUGR groups. β-cell area was greater in IUGR-I than IUGR-V (3.47±0.07 vs. 2.53%±0.20%, $p<0.01$), and similar to CON-V (2.98%±0.20%). Pancreas weight was similar in all groups (1.81±0.24 IUGR-I, 1.97±0.19 IUGR-V, 2.52 ±0.33 gm CON-V). β-cell mass was almost 30% higher in IUGR-I vs. IUGR-V, but failed to be significant (63±9 IUGR-I, 49±5 IUGR-V, 78±17 mg CON-V).

Conclusions Increasing fetal insulin concentrations for two weeks in IUGR sheep results in greater pancreatic β-cell area. The results show that insulin may act as a fetal β-cell growth factor and low circulating fetal insulin concentrations may be partly responsible for decreased pancreatic β-cells in IUGR fetuses.

423 DIURNAL VARIATION IN MICROBIOME DYSBIOSIS AFFECTED BY DIET IN POSTNATAL INTRA-UTERINE GROWTH RESTRICTED RAT OFFSPRING

LV Maggiotto, B Shin, A Ganguly, V Lagishetty, S Ghosh, J Jacobs, SU Devaskar. *UCLA, Los Angeles, CA*

10.1136/jim-2018-000939.420

Purpose of study Intra-Uterine Growth Restriction (IUGR) is a risk factor for many adult-onset chronic diseases, such as diabetes and obesity. These diseases are associated with intestinal microbiome perturbations (dysbiosis). The establishment of an intestinal microbiome begins in utero and continues postnatally (PN). Western diet-induced dysbiosis is a major driver of childhood obesity, and it displays a circadian rhythm. The **objective** was to test the hypothesis that different postnatal diets superimposed on the IUGR offspring will diurnally alter the postnatal intestinal microbiome in a gender-specific manner.

Methods used We compared four groups: Control ad lib regular chow diet pre- and postnatally **(CON/CON),** IUGR induced by maternal caloric restriction prenatally followed postnatally by either *control diet* **(IUGR/CON)** *or High-Fat-high-fructose* **(IUGR/HFhf)** and lastly **HFhf ad lib (HFhf/HFhf)** group (table 1). The rat housing environment had lights on at zeitbeger (ZT) 0 and off at ZT12. At PN2 and 21 fecal samples were collected at ZT4 (AM) and ZT16 (PM) from male and female (n=5/group) offspring and subjected to microbiome analysis by 16S-based sequencing.

Summary of results Both prenatal calorie restriction and HFhf diet induced IUGR. At P2 IUGR pups were the smallest ($p<0.0001$). The microbiome composition at PN21 was different between all four groups ($p=0.04x10^{-10}$) and from that of PN2 ($p=0.02x10^{-17}$). PM Collection time (vs. AM) at night increased the Shannon diversity ($p=0.000001$) for both sexes. Diversity of the microbiome was significantly higher at PN21 in CON/CON and IUGR/CON groups each when compared to HFhf/HFhf and IUGR/HFhf. The microbiome of IUGR offspring displayed a diurnal variation where PM samples showed higher diversity ($p<0.05$).

Conclusions Maternal diet induced IUGR led to diurnal variation in the intestinal microbiome dysbiosis at PN21 but not at PN2. Postnatal HFhf diet reduced the microbiome diversity significantly with implications for subsequent health.

424 MECHANISM UNDERLYING INCREASED EXTRACELLULAR MATRIX DEPOSITION IN PERINATALLY NICOTINE EXPOSED OFFSPRING

A Ansari, T Chuang, R Sakurai, C Yu, J Liu, Y Wang, O Khorram, V Rehan. *LA BiMed Research Institute at Harbor UCLA Medical Center, Torrance, CA*

10.1136/jim-2018-000939.421

Purpose of study Perinatal nicotine exposure affects many organ systems including the developing lung and heart. Increased predisposition to cardiac fibrosis in perinatally nicotine exposed heart has been shown, but the underlying mechanisms are not completely understood. MiR-29 family is known to target mRNAs encoding extracellular matrix (ECM) proteins, particularly those involved in fibrosis. MIAT, a long non-coding RNA, has also been implicated in cardiac injury. In this study, we aimed to investigate the mechanisms behind the cardiac phenotype, i.e., increased ECM deposition in perinatally nicotine exposed offspring.

Methods used Pregnant Sprague-Dawley rat dams received either nicotine (1 mg/kg once daily sc) or diluent from embryonic day 6 until postnatal day (PND) 21. Pups delivered spontaneously and were breastfed ad lib. Hearts from pups were collected on PND21. For *in vitro* experiments, neonatal primary rat cardiac fibroblasts were isolated and treated with nicotine (10^{-9}M) for 96 hour–7 days. Additional experiments were performed by knocking down MIAT expression using siRNA. qRT-PCR, Western analysis, and immunostaining were performed to determine the expressions of MIAT, miR-29 family, and collagen types I and III.

Summary of results Perinatal nicotine exposure resulted in increased collagen types I and III expression ($p<0.05$; n=4), accompanied by a decrease in miR-29 family and increase in MIAT levels ($p<0.05$; n=8). Accompanying these *in vivo* data, nicotine treatment of cultured neonatal primary rat cardiac fibroblasts increased MIAT and collagen types I and III levels, while suppressing miR-29 expression ($p<0.05$); lastly, MIAT knockdown resulted in increased miR-29 expression, with a decrease in collagen types I and III expression ($p<0.05$).

Conclusions Perinatal nicotine exposure is associated with increased offspring cardiac MIAT levels, decreased miR-29 family levels, and increased ECM deposition. These data provide a mechanistic basis for increased ECM deposition in the

Abstract 423 Table 1 Study groups

Groups (n)	Sex (n) at DOL2	Sex (n) at DOL21	Diet during pregnancy	Maternal diet during suckling	Diurnal varation DOL21 (n=#samples)	Collection time (ZT)
CON/CON	females (n=7)	females (n=10)	regular chow	regular chow	AM(n=5)	AM- ZT4
	males (n=7)	males (n=10)			PM (n=5)	PM-ZT16
IUGR/CON	females (n=5)	females (n=10)	D10-D21: 50% calorie	regular chow	AM(n=5)	AM- ZT4
	males (n=5)	males (n=10)	restricted		PM (n=5)	PM-ZT16
IUGR/HFhf	females (n=5)	females (n=10)	D10-D21: 50% calorie	HFhf	AM(n=5)	AM- ZT4
	males (n=5)	males (n=10)	restricted		PM (n=5)	PM-ZT16
HFhf/HFhf	females (n=4)	females (n=10)	D10–21: HFhf and 25%	HFhf	AM(n=5)	AM- ZT4
	males (n=7)	males (n=10)	fructose water		PM (n=5)	PM-ZT16

Abstract 425 Table 1 Impact of LAS on HRQL after LTx

Part 1: Baseline Demographics				
	Overall (n = 250)	**Low LAS** (n = 129)	**High LAS** (n = 121)	**p-value**
Age	56 (±12.3)	56.1 (±13.2)	55.9 (±11.4)	0.89
LAS	57.4 (±21.5)	39.7 (±5.2)	76.3 (±15.4)	<0.0001
FVC (L)	2.0 (±0.8)	2.2 (±0.8)	1.9 (±0.8)	0.01
6-MWD (meters)	260.1 (±139.2)	301.7 (±122.2)	214.3 (±142.8)	<0.0001
Female, n %	109, 43.6%	54, 41.9%	75, 58.1%	0.57
SF-12 PCS (MCID=5)	23.7 (±8.4)	25.0 (±8.1)	22.1 (±8.5)	0.01
SF-12 MCS (MCID=5)	48.9 (±10.5)	50.5 (±10.0)	47.1 (±10.7)	0.01
AQ20R (MCID=1.75)	6.85 (±3.73)	6.91 (±3.98)	6.79 (±3.44)	0.8
EQ5D (MCID=0.06)	0.65 (±0.21)	0.72 (±0.16)	0.58 (±0.23)	<0.0001
Data presented by mean (±SD). FVC = forced vital capacity, 6-MWD = 6-minute walk distance, LAS = lung allocation score: high > 50, low ≤ 50. MCID = minimally clinically important difference. For HRQL measures, higher scores denote better HRQL. SF12 PCS range 0-100, SF12 MCS range 0-100, AQ20R range 0-20, HRQL; EQ5D range 0-1.				
Part 2: Effects of changes in HRQL before and through 6-months after LTx				
	Low LAS	**High LAS**	**Difference**	
SF-12 PCS (MCID=5)	18.9 (16.8 to 21)	20.6 (18.5 to 22.7)	1.7 (-1.2 to 4.7)	
SF-12 MCS (MCID=5)	3.8 (2.0 to 5.6)	6.8 (4.9 to 8.6)	2.9 (0.4 to 5.5)*	
AQ20-R (MCID=1.75)	8.69 (7.93 to 9.46)	8.71 (7.92 to 9.50)	0.02 (-1.08 to 1.12)	
EQ5D (MCID=0.06)	0.13 (0.10 to 0.16)	0.25 (0.20 to 0.27)	0.11 (0.06 to 0.16)*	
Effect estimates (95% confidence interval) reflects the change in HRQL from before to 6 months after transplant by linear mixed effects models adjusted for age, sex, diagnosis, pre-transplant FVC and 6MWD.**Denotes p<0.05 and stastical significance*				

perinatally nicotine exposed offspring heart, and provide multiple novel therapeutic targets.

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Pulmonary and Critical Care II

Concurrent Session

8:00 AM

Saturday, January 26, 2019

425 HIGH LUNG ALLOCATION SCORES DO NOT PRECLUDE IMPROVEMENT IN HEALTH-RELATED QUALITY OF LIFE AFTER LUNG TRANSPLANTATION

AA Perez, Hays S, Y Gao, A Soong, M Kleinhenz, A Venado-Estrada, L Leard, R Shah, J Kukreja, J Golden, J Greenland, P Blanc, JP Singer. *UCSF, San Francisco, CA*

10.1136/jim-2018-000939.422

Purpose of study High lung allocation listing scores (LAS) are associated with higher mortality after lung transplantation (LTx). Whether high LAS is associated with attenuated improvements in health-related quality of life (HRQL) is unknown.

Methods used In a single-center prospective cohort study from 2010–2017, we assessed HRQL before and through 6 months after LTx. HRQL was assessed by the Medical Outcomes Study Short Form Physical and Mental Component Summary scales (SF12-PCS and -MCS), the Airway Questionnaire 20-Revised (AQ20R), and the Euroqol 5D (EQ5D) (table 1 includes measure ranges and minimally clinically important differences). High LAS (range 0–100) was defined as >50. We used t-test and chi-square tests to compare clinical characteristics. We compared change in HRQL from before through 6 months after LTx between the high and low LAS groups by linear mixed effects models adjusting for age, sex, diagnosis, pre-transplant forced vital capacity, and 6 min walk distance.

Summary of results Two-hundred fifty subjects underwent LTx. Median LAS was 50. The high LAS group generally had worse HRQL before LTx than the low group (table 1, part 1). In adjusted models, the high LAS group had similar improvements in HRQL after LTx compared to the low LAS group (table, part 2) except for the SF12-MCS and EQ5D in which their improvements were greater (SF12-MCS difference 2.94 points, 95% CI: 0.36, 5.51; EQ5D difference 0.11 points, 95% CI 0.06, 0.16).

Conclusions LTx recipients with high LAS at the time of transplant have similar or greater improvements in HRQL after LTx compared to recipients with low LAS. Despite their increased risk of mortality, subjects with high LAS can be reassured that the improvements in HRQL provided by LTx are large and similar to those with lower scores.

426 RECURRENT EPISODES OF DIFFUSE ALVEOLAR HEMORRHAGE IN SYSTEMIC SCLEROSIS 30 DAYS APART

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10.1136/jim-2018-000939.423

Case report A 46-year-old female with systemic sclerosis with features of dermatomyositis, presented to the ED complaining of right-sided chest pain. Initially, her EKG and chest x-ray were unremarkable. However, she progressively decompensated into acute respiratory failure with PaO2 of 69 on 15L of oxygen, resulting in intubation. Repeat CXR and CT showed diffuse bilateral alveolar infiltrates suggesting DAH and pleural effusions. Video bronchoscopy with BAL showed numerous RBCs, neutrophils, macrophages, and respiratory epithelial cells consistent with acute DAH. She was started on IV pulse-dosing Solu-Medrol 1 gm daily for five days. After improvement, patient was extubated and discharged to be followed up by rheumatology. One month later, patient returned with intractable nausea and vomiting. Again, she went into acute respiratory distress with a PaO2 of 59 while on a 10L non-rebreather mask. CXR revealed development of alveolar infiltrates in the right lung suggesting another episode of DAH. Bronchoscopy with BAL showed bilateral infiltrates with hemosiderin-laden macrophages with numerous RBCs and

neutrophils, thus confirming her second episode of DAH. Patient improved after IV pulse-dosing Solu-Medrol 1 gm daily for five days, was discharged after stabalization with a Rheumatology follow-up and has not had any other similar episodes for the past 12 month.

DAH is a rare phenomenon in systemic sclerosis. A recurrence of such episodes in a single patient within a short period of time is even rarer. Its life-threatening nature makes a systemic approach and aggressive treatment crucial to decreasing morbidity and mortality – making it a diagnosis that should not be overlooked, especially in patients with nonspecific symptoms.

427 FRAILTY IS ASSOCIATED WITH GREATER IMPAIRMENTS IN HEALTH-RELATED QUALITY OF LIFE AFTER LUNG TRANSPLANTATION THEN BEFORE

N Kolaitis, A Soong, Y Gao, J Greenland, R Shah, A Venado-Estrada, J Kukreja, Hays S, M Kleinhenz, J Golden, P Katz, P Blanc, JP Singer. *UCSF, San Francisco, CA*

10.1136/jim-2018-000939.424

Purpose of study Frailty is associated with impaired health-related quality of life (HRQL) in non-lung transplant populations. We tested the association of frailty and HRQL both before and after lung transplantation in the same individuals.
Methods used In a single-center prospective cohort from 2010–2016, we assessed frailty and HRQL before and 6 months after lung transplantation. Frailty was quantified by the Short Physical Performance Battery (SPPB; range 0–12). HRQL was quantified by the generic SF12-Physical Component Score (SF12PCS; range 0–100), the respiratory-specific Airway Questionnaire 20-Revised (AQ20R; range 0–20), and the health-utility instrument Euroqol 5D (EQ5D; range −1.11–1). Higher scores denote better HRQL. We tested the association of frailty and HRQL using multivariate linear regression adjusting for age, sex, race, and FEV_1. We compared regression coefficients at baseline and 6 months using a 'seemingly unrelated' estimation.
Summary of results 232 enrolled subjects underwent lung transplantation. At baseline, worse frailty was associated with worse HRQL by SF12PCS and EQ5D (both $p<0.02$). There was no statistical association between frailty and HRQL as quantified by AQ20R. At post-transplant follow-up, worse frailty was associated with worse HRQL by all measures (SF12PCS, AQ20R, and EQ5D, [all $p<0.005$]). The magnitude of the association between frailty and HRQL was greater at 6 months after transplant than at baseline for SF12PCS and AQ20R (both $p<0.001$), but not EQ5D.

Abstract 427 Table 1

Instrument	Instrument Type	Range	Baseline	6 months post transplant	p-value
SF12PCS	Generic-Physical	0–100	−0.51 (95% CI: −0.93 to −0.10)	−2.04 (95% CI: −3.01 to −1.07)	<0.001
AQ20R	Respiratory-Specific	0–20	−0.01 (95% CI: −0.18 to 0.18)	−0.59 (95% CI: −0.94 to −0.24)	<0.001
EQ5D	Health-Utility	−1.11–1	−0.02 (95% CI: −0.04 to −0.02)	−0.02 (95% CI: −0.04 to −0.01)	0.58

Linear regression coefficients of frailty and HRQL (95% confidence interval). P-value denotes difference between coefficients pre- and post-transplant.

Conclusions The association of frailty with impairment in HRQL is stronger post-lung transplant than in candidates pre-transplant. Nonetheless, lung transplant patients should undergo screening for frailty both as candidates and after transplantation given that frailty is potentially modifiable.

428 A META-ANALYSIS OF BIOMARKERS IN ASTHMA-COPD OVERLAP

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10.1136/jim-2018-000939.425

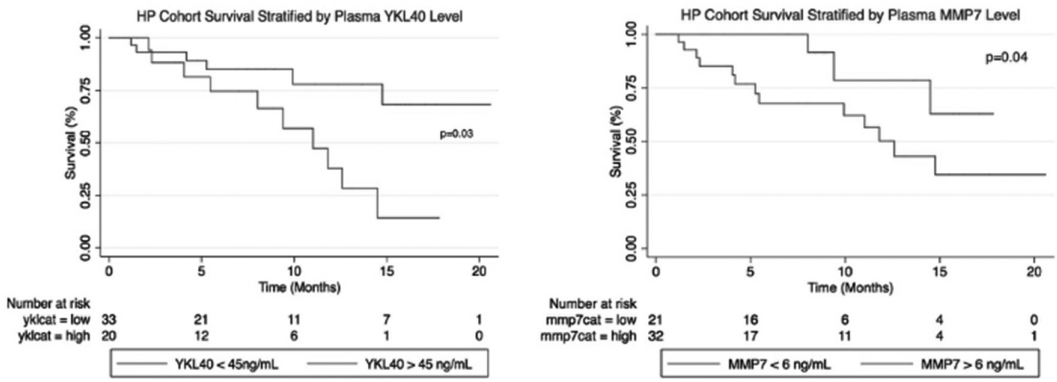
Purpose of study There is no universally accepted definition of asthma-COPD overlap (ACO). ACO is associated with more severe symptoms and higher exacerbation rates. GINA published guidelines to help identify ACO based on clinical features but not specific biomarkers. We hypothesize ACO patients have higher type 2 inflammation and thus more disease severity. Biomarkers may be useful in ACO diagnosis.
Methods used We performed a literature search using PubMed, EMBASE, CINAHL, and Cochrane (from inception through August 21, 2017). Two reviewers selected studies that included data for ACO and COPD and/or asthma patients. We examined FEV1% and type 2 inflammation biomarkers (IgE, serum absolute eosinophil counts, sputum percent eosinophils, and the fraction of exhaled nitric oxide). Meta-analyses examining pooled mean differences between ACO and asthma and COPD cohorts were performed. These were converted to z-statistics with value >1.96 or <-1.96 representing significant differences.
Summary of results After review of 230 studies, 23 studies were included in the analysis due to use of GINA description of ACO in their patient cohorts. There was a statistically significant mean pooled difference in FEV1% of 15.8% between asthma and ACO cohorts, with higher FEV1% in asthma (95% CI [6.8 to 24.7], z-statistic 3.4). We found that ACO patients had a trend of higher FeNO as compared to COPD with mean pooled difference of 12.5 ppb (95% CI [−27 to 2], z-statistic 1.7). No significant differences were found between ACO and asthma or ACO and COPD with respect to serum IgE, serum absolute eosinophil counts, or sputum percent eosinophils.
Conclusions Results show that ACO patients have decreased lung function compared to asthma patients. A trend in elevated FeNO in ACO compared to COPD may help in clinical practice. Assessment of other biomarkers was limited due to lack of studies that identified patients using GINA and lack of routine measurement of the aforementioned biomarkers. Future studies should include the measurement and reporting of FeNO, IgE, serum eosinophils, and sputum eosinophils to identify patterns of inflammation in ACO.

429 PLASMA BIOMARKERS OF SURVIVAL IN PATIENTS WITH INTERSTITIAL LUNG DISEASE

S Alqalyoobi, A Linderholm, R Harper, B Morrissey, J Oldham. *University of California-Davis Medical Center, Sacramento, CA*

10.1136/jim-2018-000939.426

Purpose of study The interstitial lung diseases (ILD) are a group of heterogeneous diseases that are differentiated based on specific clinical, pathologic and radiological features.



Abstract 429 Figure 1

Recognition of specific ILD biomarkers may provide a clinically useful tool to identify patients at risk of death and disease progression. The objective of this study was to determine whether circulating proteins associated with IPF mortality are associated with survival in patients with chronic hypersensitivity pneumonitis (CHP), connective tissue disease-associated ILD (CTD-ILD) and unclassifiable ILD (U-ILD).

Methods used Plasma samples were obtained from patients attending UC Davis ILD clinic from May 2016 to March 2018. Samples were collected at the first ILD clinic visit, stored and processed together. We measured plasma biomarkers for CA125, CXCL13, MMP7, SPDD, YKL40, MMP1, Osteopontin and VCAM1 using a Luminex multiplex assay. Pertinent clinical data were extracted from the electronic medical record. Survival was compared using an unadjusted log rank and plotted using the Kaplan-Meier estimator. Multivariable Cox regression was also performed to test protein levels for mortality association.

Summary of results 249 patients were included in the analysis, including 82 with IPF, 69 with CTD-ILD, 54 with CHP, and 44 with U-ILD. Differential levels of SP-D and MMP7 were observed between ILD subtypes, with the highest levels observed in patients with CHP and IPF and lowest observed in patients with CTD-ILD. Among patients with CHP, increased YKL-40 and MMP-7 levels were associated with increased mortality risk (figure 1). Increased VCAM1 level was associated with increased mortality risk in patients with CTD-ILD while increased CXCL13 level was associated with increased mortality risk in patients with U-ILD.

Conclusions YKL-40 and MMP-7 are promising prognostic markers in CHP patients. VCAM1 and CXCL 13 are associated with increased CTD-ILD and U-ILD respectively.

Case Reports II

Concurrent Session

10:15 AM

Saturday, January 26, 2019

430 STREPTOCOCCUS AGINOSUS INFECTIVE ENDOCARDITIS DECADES AFTER ROSS PROCEDURE

A Heidari, F Joolhar, R Boyer. *Kern Medical, Bakersfield, CA*

10.1136/jim-2018-000939.427

Case report Ross procedure or pulmonary autograft is indicated to correct various aortic valve disease. The patient's pulmonary valve replaces the diseased aortic valve while a cadaveric pulmonary allograft supplants the native valve. Infective endocarditis following Ross procedure may occur decades after surgery.

A 39 year old female presented to the emergency department with 4 days of fever and non-radiating right-sided back pain. She underwent aortic balloon valvuloplasty followed by Ross procedure for a bicuspid aortic valve at age 17.

Clinical examination revealed fever of 102.9 F, heart rate of 101/min, high blood pressure of 174/103 mmHg, 20 respirations/min and an oxygen saturation of 97 on room air. A 3/6 systolic ejection murmur was noted in both pulmonic and aortic areas. The electrocardiogram showed sinus rhythm with rate 85/min. Chest X-ray indicated mild cardiomegaly and previous sternotomy. Cardiac CT revealed right ventricular outflow tract narrowing up to 5 mm in the proximal main pulmonary artery with pulmonary annulus narrowing measuring 25 × 12 mm. Transesophageal echocardiogram reported left ventricular ejection fraction of 60%, pulmonary artery max velocity 4.7 m/s, maximum gradient of 88 mmHg and a mean gradient of 47 mmHg. Blood culture grew Streptococcus aginosus sensitive to ceftriaxone. The patient was treated with 6 weeks intravenous antibiotics followed by pulmonary valve replacement.

Compared with a prosthetic replacement, Ross procedure is a favorable alternative without the need for lifelong anticoagulation. However, it often implies certain risk of reoperation during the patient's life and potential infection. Infection of the pulmonary homograft is rarely reported decades after Ross procedure. We present a case of pulmonary homograft Streptococcus aginosus endocarditis 22 years after Ross procedure in a 39 year old woman successfully treated surgically with pulmonary valve replacement and intravenous antibiotics.

431 REACTIVE INFECTIOUS MUCOCUTANEOUS/MUCOSAL-PREODMINANT ERUPTION: A CASE STUDY ON A NEWLY RECLASSIFIED MUCOCUTANEOUS SYNDROME

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10.1136/jim-2018-000939.428

Case report Reactive infectious mucocutaneous/mucosal-predominant eruption (RIME) is a recently characterized syndrome that is distinct from the more commonly understood

mucocutaneous eruptions of erythema multiforme (EM), Stevens-Johnson Syndrome (SJS), and Toxic Epidermal Necrolysis (TEN). Unlike SJS and TEN, RIME is a syndrome triggered by infection with a microbial agent, and unlike EM, it is limited to mainly the oral, orbital, and urogenital mucosa, rather than being a widespread infection with extensive mucosal, cutaneous, and systemic symptoms. This distinction is important for managing the clinical implications of the syndrome as well as guiding patient treatment and prognosis. Herein, we present a review of the literature regarding the mucocutaneous manifestations and distinguishing features of RIME, EM, SJS, and TEN, as well as a case report of a 19 y.o. M patient with a misdiagnosed RIME syndrome masquerading as SJS. A concise review of the distinguishing characteristics, similarities, and differences of each of the aforementioned dermatologic eruptions will be discussed and then applied to our patient to correctly identify and diagnose his lesions and better guide management.

432 STEROID-INDUCED HYPERTROPHIC CARDIOMYOPATHY IN A TERM INFANT WITH SHOCK

M Ringle, L Peterson, K Ryan, K Van Meurs, N Yamada, S Bhombal. *Stanford University LPCH, Palo Alto, CA*

10.1136/jim-2018-000939.429

Case report A male infant was born at 37 weeks via c/s for non-reassuring fetal heart tones, decreased fetal movement, and polyhydramnios to a G3P2 mother with obesity, alcohol use during pregnancy, and poorly controlled gestational diabetes (HbA1C 8.5%). Apgar scores were 1/5/7. Arterial cord gas showed pH 6.93, CO2 115, and base deficit −11. Sarnat exam was consistent with moderate encephalopathy and therapeutic hypothermia was initiated. He was placed on high frequency oscillatory ventilation, inhaled nitric oxide (iNO), dopamine, and hydrocortisone shortly after admission. Echo on day of life (DOL) 1 showed mild left ventricular (LV) hypertrophy and a moderately hypertrophic and dilated right ventricle with depressed function. Hydrocortisone and iNO were unable to be weaned for more than two weeks due to cardiovascular instability. Echo on DOL 8 showed severe right ventricular hypertrophy and a flat, thickened intraventricular septum. Serial echoes over the following week showed progression of septal hypertrophy with evolving LV hypertrophy and left ventricular outflow tract obstruction with peak gradient of 90 mmHg. The infant also developed sinus tachycardia >200 bpm with worsened dynamic outflow tract obstruction and hypotension that improved with esmolol. Due to the rapidly progressive nature of his ventricular hypertrophy, a metabolic and genetic work-up was initiated; ultimately negative for common heritable causes of hypertrophic cardiomyopathy (HCM). Hydrocortisone was weaned off DOL 16, and serial echoes on DOL 18–23 revealed significant and rapid improvement suggestive of steroid-induced HCM complicating mild HCM in an infant of a diabetic mother (IDM).

Discussion Steroid-induced HCM is well described in premature infants, particularly among very low birthweight infants treated for the prevention of bronchopulmonary dysplasia. However, to our knowledge there are no reports of term infants of diabetic mothers with hypertrophy developing worsening HCM secondary to hydrocortisone use. This may be an under-appreciated side effect of hydrocortisone in the IDM population and should be considered in cases of prolonged cardiovascular instability.

433 A RARE CASE OF CRYPTOCOCCUS GATTII MENINGITIS AND SAGITTAL THROMBOSIS IN AN HIV HOST REFRACTORY TO TREATMENT

[1]A Targovnik, [1]A Heidari, [1]N Khan, [2]B Andruszko, [2]J Okudo, [1]R Johnson. *[1]UCLA-Kern Medical, Bakersfield, CA; [2]Kern Medical, Bakersfield, CA*

10.1136/jim-2018-000939.430

Introduction Cryptococcus gattii is a relatively new species known to affect immunocompetent and immunocompromised hosts. It commonly presents as pneumonia or subacute meningitis. In North America C. gattii is found primarily in the Pacific Northwest and British Columbia. Immunocompetent hosts may acquire C. gattii and experience a period of dormancy prior to reactivation during immunosuppression.We are reporting a rare case of persistent and refractory infection with Cryptococcus gattii in an AIDS host.

Case presentation Patient is a 45-year-old Caucasian male who presented to our hospital with severe headache and nausea. He was diagnosed with AIDS (CD4 count of 38). Lumbar puncture revealed increased opening pressure and CSF was positive for a Cryptococcus Ag (CrAg) titer of >1:4096. His imaging showed a single pulmonary and several intracranial cryptococcomas. Following a 2 week induction course of AmBisome and Flucytosine, consolidation therapy with Fluconazole was started. Antiretrovirals were started 8 weeks later to avoid reconstitution syndrome. Fungal speciation of CSF showed C.gatti. Further history revealed that he lived and worked in Washington state in 1991.

After nearly 11 weeks on Fluconazole, patient was readmitted with fever, worsening headache, and increased CSF CrAg titers. AmBisome and Flucytosine were restarted and continued for 9 weeks, at which point he was transitioned to Voriconazole. After 18 weeks on Voriconazole and persistent sub-therapeutic levels, he was readmitted for headaches and increased CSF CrAg titers. AmBisome was given for 6 weeks with Voriconazole after. He then returned with headache, and was found to have superior sagittal thrombosis due to chronic inflammation. Therapeutic anticoagulation was initiated. AmBisome was restarted for 8 weeks. He has since been started on Isavoconazonium without recurrence of symptoms.

Conclusion Clinicians should have high level of suspicion for reactivation of fungal infections in immunocompromised hosts based on exposure to endemic fungal infections. More studies are needed to determine how to treat refractory cases of Cryptococcus gattii.

434 NECROTIZING RHIZOPUS OF THE ABDOMINAL WALL IN AN EXTREMELY LOW BIRTH WEIGHT NEONATE

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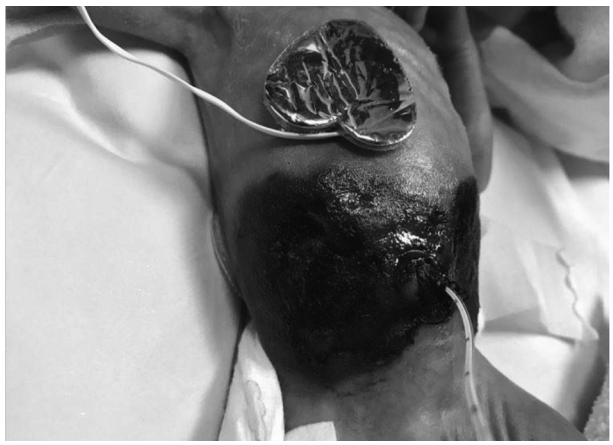
10.1136/jim-2018-000939.431

Introduction Zygomycoses are fungal infections predominantly seen in the immunocompromised host. *Rhizopus* is one of the



Abstract 434 Figure 1

most common causative organisms in this group and one of clinical importance to humans. They may contaminate adhesive bandages and sites of previous intravascular catheters. Though rare, these fungal infections have a high risk of mortality, especially in premature neonates.

Case summary A 4 day old female born 25 weeks gestation via cesarean section for preterm labor presented in the neonatal intensive care unit with abdominal wall erythema adjacent to the umbilicus. Antibiotics were previously discontinued after 48 hours for negative sepsis workup initiated at birth. She was intubated and had umbilical lines for parenteral nutrition and medication. From the time the erythema was first noted, the rash rapidly darkened and spread over the entire abdomen over the next 24 hours. Amphotericin and caspofungin were initiated for suspicion of fungal infection. Tissue culture confirmed Rhizopus spp. The patient underwent surgical debridement of necrotic tissue with concurrent medical therapy. Despite maximal therapy, there was continued tissue necrosis in this extremely low birth weight neonate and a joint decision was made for redirection of care.

Conclusion This is a rare case of rapid and fatal Rhizopus infection of the abdomen in an extremely premature neonate. Given that this population is immunocompromised and placed in environmental conditions that support fungal growth, this case highlights the importance of high index of suspicion, recognition, and prompt treatment to prevent fatal dissemination.

435 PULMONARY COCCIDIOIDOMYCOSIS WITH INTRAPARENCHYMAL, OSSEOUS, AND CUTANEOUS DISSEMINATION

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Introduction Coccidioidomycosis (cocci) can disseminate to the central nervous system (CNS), bones, joints, and skin. Intraparenchymal cocci is a rare form of disseminated CNS infection.

Case report A 27-year-old Hispanic male with no past medical history presented with subjective fevers, rigors, night sweats, unintentional weight loss, decreased appetite, nausea, vomiting, photophobia, and constant diffuse headaches of three months duration. Coccidioides (cocci) serology of the cerebrospinal fluid (CSF) showed positive immunodiffusion (ID) IgG and complement fixation (CF) of 1:8. Serum cocci serology demonstrated positive ID IgG, ID IgM, and CF of 1:256. Patient also presented with cutaneous skin lesions along the right lower lip and scalp, excisional biopsy showed Coccidioides spherules with endosporulation. Whole body bone scan was negative for osseous cocci. Patient was discharged on oral fluconazole 1000 mg daily. Consequently, patient returned approximately three months later, complaining of right knee and buttock pain, as well as short-term memory loss. Neuroimaging revealed Intraparenchymal lesions suggestive of parenchymal cocci. Computed tomography (CT) demonstrated a right middle lobe infiltrate, and a complex multiloculated fluid collection in the right gluteus with sacroiliitis status post drainage of right gluteal abscess with a pigtail catheter left in place. Cultures of the pelvic fluid grew C. immitis. CT findings are consistent with presumptive disseminated cocci to the soft tissue, right posterior iliacus muscle, right flank, spleen, suprahilar, retroperitoneal, and mesenteric lymph nodes. CT also revealed disseminated osseous cocci to L1 vertebra, right hemisacrum, and right iliac bone despite negative bone scan. Treatment plan entailed lifelong fluconazole 1000 mg daily for his meningitis plus liposomal amphotericin B infusions for 12–24 weeks depending on his serological and clinical response.

Conclusion When host is immunogentically disadvantaged, there is no limit for degree of dissemination of coccidioidomycosis. Optimal choice and duration of treatment in intraparenchymal dissemination is not clear.

436 NECROTIZING ENTEROCOLITIS AFTER INTRAVENOUS CONTRAST IN A TERM NEWBORN

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10.1136/jim-2018-000939.433

Introduction Necrotizing enterocolitis is associated with prematurity, but term infants with diminished mesenteric perfusion are also at risk, per Robert et al (2013). This case describes NEC developing in a term infant with no identifiable risk factors after injection with intravenous contrast for chest computed tomography. It is thought that the hypertonic contrast agent decreased perfusion to the gut, causing NEC. At the time of this writing, a literary search turned up no similar cases.

Case description A term baby weighing 2.6 kg was admitted to the neonatal intensive care unit for respiratory distress. The child went on to develop recurrent tension pneumothoraces requiring emergent needle thoracostomies. In the 2nd week of life, 5 mL of iopamidol 61% was injected for chest computed tomography, which suggested congenital pulmonary airway malformation. In the 24 hours after imaging, there was progressive lethargy with poor feeding and then frank rectal bleeding. The abdominal X-ray showed pneumatosis intestinalis. Oral feedings ceased and IV fluids, ampicillin, gentamicin and metronidazole commenced. An orogastric tube was set to suction. The overall NEC course was mild. An echocardiogram showed no gross abnormalities; creatinine of 0.3 mg/dL before discharge confirmed normal renal function; and a repeat chest CT without contrast showed resolution of the pneumothorax. The baby was discharged home at three weeks of life.

Discussion Term neonates with poor mesenteric perfusion, possibly by contrast agent, are at increased risk of NEC. Cooke et al postulated that contrast can cause bowel ischemia through two possible mechanisms: 1. The contrast is hyperosmolar with a diuretic effect, which is compounded by dehydration. 2. The contrast may cause direct vasospasm. When contrast is indicated in a neonate, it is thought that IV hydration prior to contrast injection may provide an enteroprotective effect by enhancing perfusion to the gut.

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Health Care Research III

Concurrent Session

10:15 AM

Saturday, January 26, 2019

437 DESCRIPTION OF THE 22Q11.2 DELETION SYNDROME PATIENT POPULATION IN BRITISH COLUMBIA AND CHARACTERIZATION OF THEIR CARE NEEDS

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10.1136/jim-2018-000939.434

Purpose of study 22q11.2DS is the second most common genetic cause of developmental delay and congenital heart disease. With advances in pediatric diagnostics and surgical care, survival into older adulthood is expected. Health care planners must consider the care needs of this multi-system complex population. Currently, there is a paucity of information describing the coordination of requisite health and transition services for 22q11.2DS patients in BC. Study of this population is challenging, given the lack of data integration amongst the diverse specialty services utilized across major healthcare centers. This study aims to describe this population and characterize their care needs, use of specialty services, and transition requirements.

Methods used This was an 18 year retrospective review of patients diagnosed with 22q11.2DS receiving specialty services at our pediatric provincial health service BC Children's and Sunny Hill Hospitals. A combined cohort of 22q11.2DS patients was created using both hospital and subspecialty clinic databases. A variety of data, including demographics, subspecialty service visits, and follow up, was collected to help quantify and characterize this population.

Summary of results The study cohort comprised of 293 patients (57% female). The median age at genetic diagnosis was 3 years old. A rising trend in 22q11.2DS diagnoses was noted after introduction of chromosomal microarray, with nearly half diagnosed before 1 years old. On average, 13 new patients a year were admitted, consistent with birth prevalence worldwide, and were followed for an average of 7 years. There was an average of 16 visits per patient, per year. Greater than 50% of the patient cohort visited more than three specialty clinics, with an average of five clinics per patient. Cardiology, Developmental Pediatrics, Cleft Palate/Craniofacial Program, Otolaryngology, and Endocrinology served the majority of our cohort.

Conclusions The information gained from this study provides concrete data on the current care of patients with 22q11.2DS in BC and will guide the development of transitional and adult care services for this population. Future directions include the establishment of a 22q11.2DS BC multidisciplinary care model and a 22q11.2DS international registry.

438 POOR UNDERSTANDING OF PREGNANCY ASSOCIATED HEALTH RISKS BY PREGNANT WOMEN

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10.1136/jim-2018-000939.435

Purpose of study Evaluate health literacy among pregnant women to highlight potential gaps in maternal health knowledge.

Methods used This study was conducted in a prenatal clinic at a public teaching hospital and was approved by the John F. Wolfe Human Subjects Committee and the Research Committee of the Los Angeles BioMedical Research Institute at Harbor-UCLA Medical Center on an exempt basis. Potential subjects were provided a consent statement outlining the study goals, the voluntary nature of their participation, and a pledge to maintain their anonymity. Participants were asked a series of questions in English or Spanish on a one-to-one basis in private areas designed to assess the participant's knowledge of seven well recognized health risks (blood clots, diabetes, gallstones, hemorrhoids, high blood pressure, kidney infection, and anemia) associated with pregnancy. Statistical significance was identified using Chi Square tests with $p<0.05$.

Summary of results 163 pregnant women were interviewed in the study; of which 85% were English speaking, 82.2% had at least some college education, and 65% had at least one prior pregnancy. When asked about seven known health risks associated with pregnancy 5.0% of the 162 women who responded to the questions were able to identify that all seven medical problems increased with pregnancy. Focusing just on the three most serious risk conditions (hypertension, gestational diabetes, and venous thromboembolism), 30.6% of women recognized that the risks for these conditions increased during pregnancy. Higher education was the only variable that correlated with knowledge, but only 48.7% of those with college education gave correct answers to the three risks.

Conclusions Health literacy about pregnancy is dangerously low, even among a pregnant population. Public health campaigns are needed to educate reproductive age women about the health risks of pregnancy. From a clinical perspective, awareness of pregnancy health risks might motivate women to seek preconception care earlier in order to maximize the chances of better outcomes of both mom and child.

439 THE IMPACT OF OBESITY ON 30-DAY HOSPITAL READMISSION RISK FACTORS AMONG ASTHMATIC ADULTS

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10.1136/jim-2018-000939.436

Purpose of study This study investigated the impact obesity has on 30 day hospital readmission for asthmatic adults. Limited research existed on the association between obesity and asthma readmission. We evaluated readmission risk factors to further explore the link between asthma and obesity.
Methods used Data was obtained from the 2012–2014 National Readmission Database and analyzed via Surveyfreq and Surveylogistics analysis in the SAS Software. Patients included were >18 years, had a primary diagnosis of asthma, discharged alive, and had a non-elective readmission. Obese asthmatic patients were compared to non-obese asthmatic patients in regards to risk of readmission. Factors included: emergency department (ED) utilization, length of stay (LOS), risk of mortality and severity of illness (minor, moderate, major, or extreme), income quartile, and insurance.
Summary of results Of 29,350,055 asthma-related hospitalizations the overall readmission rate was 12.4%. Increased likelihood of readmission within 30 days of discharge was associated with: obesity, being female, having Medicare, and having moderate risk of mortality. Obese asthmatic patients had a significantly higher risk of mortality (6.1% vs 5.1%), higher severity of illness (7.4% vs 6.2%), longer LOS (median 4 vs 3 days), and higher ED utilization (82.6% vs 78.4%). Median total charges for obese patients were $29 353 compared to $23 848 for non-obese patients (p-value<0.0001). Moreover, obese patients with asthma were also more likely to be female (61.6% vs 56.3%), reside in the lowest income quartile (32.2% vs 29.7%), and have private insurance (25% vs 23.1%).
Conclusions Findings suggest social factors such as income status are associated with higher readmission rates for obese asthmatic patients. Analysis showed having private insurance did not reduce readmission in obese asthmatic patients. Identification of criteria associated with higher readmission in this subset is important as obese asthmatic patients had a higher risk of mortality, illness severity, and ED utilization, which has implications for readmission and disease management costs.

440 SURGERY AND SOCIETY: EMERGING TRENDS IN THE SOCIAL DETERMINANTS OF HEALTH AND ADVERSE CHILDHOOD EXPERIENCES AMONG THE PEDIATRIC PATIENT POPULATION IN BRITISH COLUMBIA

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10.1136/jim-2018-000939.437

Purpose of study Social determinants of health (SDoH) contribute significantly to one's overall well-being, and children from lower socioeconomic backgrounds are at a higher risk of poor physical and mental health. While much of the research examining the effects of SDoH is in primary care, there is limited data on its impact in pediatric specialties such as surgery and complex multidisciplinary care. This study aims to gain a broader perspective of the SDoH of pediatric patients requiring surgical and other sub-specialty care in British Columbia (BC), and thereby identify resources to address those needs.
Methods used Parents of pediatric patients from nine different subspecialty clinics at BC Children's Hospital were invited to voluntarily complete a confidential questionnaire during their ambulatory visit. The questionnaire was comprised of items adapted from earlier studies examining the effects of SDoH and adverse childhood experiences (ACEs). A target recruitment goal was set at 25 patients from each clinic. Data collection commenced in January 2018 and is ongoing.
Summary of results 204 patients completed the questionnaire, of which 94.5% said that they have a primary healthcare provider (PHCP). However, almost one-quarter felt that they cannot easily turn to their PHCP for assistance (e.g. housing, disability supports, etc). Over 25% of the families live below the BC poverty line, which is twice the current BC poverty rate. Nearly 50% indicated that they 'sometimes' or 'always' have difficulty making ends meet, and over one-third of families are socially isolated. On the optional section about ACEs, 13.2% of the parents who responded said that their child has an ACE score of 4 or more.
Conclusions This study provides early evidence for pediatric specialists and key child health stakeholders that a significant proportion of pediatric patients receiving care in specialty settings face a multitude of social and financial adversity. Strategies to mitigate these challenges and dismantle barriers to care need to be explored. Future work is directed at examining what effects do the SDoH have on health outcomes, particularly in patients with complex needs.

441 CARDIOVASCULAR DISEASE RISK ASSESSMENT IN TRANSGENDER PATIENTS WITH EPIC

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10.1136/jim-2018-000939.438

Purpose of study It has been suggested that transgender patients, particularly transfemales receiving hormone therapy, are at an increased risk of cardiovascular disease (CVD) relative to similarly-aged non-transgender patients. This study looks at the viabilty of using EPIC, the electronic medical records system, to analyze the CVD risk in transgender patients.
Methods used Transgender patients in the University of Utah Health system were identified by author SL. CVD risk factors were abstracted from the Epic electronic medical record sections of patient history, notes, and discrete, queryable fields for clinical data where available. We compared the prevalence of CVD risk factors for female-to-male (FTM) and male-to-female (MTF) patients. Descriptive statistics for known CVD risk factors were compared for FTM and MTF patients using tests of mean, median, and proportions.
Summary of results Our search strategy identified 129 transgender patients. A majority of CVD risk factors were located in discrete, queryable data fields, although notable exceptions required abstraction from patient history and notes (lipid screening results, mental health screening results, alcohol use, and tobacco use). FTM patients, both on or off hormone therapy, had higher GAD-7 scores

(11.22) than MTF patients (6.46). Self-identified smoking (defined as 'current every day smoker') was higher for FTM patients (21%) compared with MTF patients (7%). FTM patients were more likely to be obese (defined as a BMI of 30.0 kg/m^2 or higher) than MTF patients 39% vs 27%, respectively.
Conclusions Retrospective analysis of CVD risk in transgender patients is possible using electronic medical records, although some fields require abstraction from text. We identified higher prevalence of tobacco use, anxiety, and obesity in FTM relative to MTF patients.

442 ENDOMETRIOSIS AND NEGATIVE PERCEPTION OF THE MEDICAL PROFESSION

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10.1136/jim-2018-000939.439

Purpose of study Endometriosis is a gynecological condition affecting 10% of reproductive-aged females and commonly leads to pelvic pain and poor quality of life. Delay in diagnosis may result in inadequate or inappropriate treatments that may lead to patients' negative perceptions of the medical profession. This study aims to identify factors independently associated with negative impressions of the medical profession in females with endometriosis.
Methods used Cross-sectional analysis of a prospective data registry at a tertiary referral centre for pelvic pain and endometriosis. The main outcome variable is negative feelings about the medical profession, measured with the 4-item subscale of the Endometriosis Health Profile-30 and divided into 3 groups: no (0), some (1–8), and many (9–16) negative impressions.
Inclusion criteria completion of baseline questionnaire between December 2013 to June 2017 and surgically-staged diagnosis of endometriosis. Exclusion criteria: postmenopausal and incomplete data. Bivariate analyses determined significant associations with the main outcome. Variables with significant association ($p<0.05$) were put into ordinal logistic regression with sequential backwards elimination.
Summary of results Presence of irritable bowel syndrome and/or painful bladder syndrome (OR 3.00, 95% CI 1.72–5.24, $p<0.0005$), previous visits to a complementary healthcare provider (OR 2.38, 95% CI 1.44–3.94, $p=0.001$), previous surgery that did not help symptoms (OR 2.29, 95% CI 1.30–4.03, $p=0.004$), presence of multiple severe pain types (deep dyspareunia, dysmenorrhea, and/or chronic pelvic pain) (OR 1.86, 95% CI 1.13–3.06, $p=0.015$), and presentation to an emergency room in the past 3 months (OR 1.78, 95% CI 1.03–3.08, $p=0.039$) were independently associated with more negative impressions of the medical profession.
Conclusions In chronic pain conditions, patient-physician relationships can be lifelong and the quality of these relationships have been found to affect patient outcomes. Thus, the factors identified here may be important indicators/predictors of negative impressions of the medical profession that should be addressed as part of effective treatment for females with endometriosis.

443 ENROLLMENT IN WIC IS ASSOCIATED WITH POSITIVE GROWTH AND DEVELOPMENTAL OUTCOMES IN PRETERM INFANTS AT A SAFETY NET HOSPITAL AFTER DISCHARGE

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10.1136/jim-2018-000939.440

Purpose of study Little is known about the impact of enrollment in the Special Supplemental Nutrition Program for Women, Infants and Children (WIC) and the Supplemental Nutrition Assistance Program (SNAP) on infant somatic growth and neurodevelopmetal outcomes in preterm infants.
Methods used We surveyed families with preterm infants in a high-risk infant follow-up clinic at a safety net hospital. Primary outcomes were: (1) somatic growth represented by z scores and (2) neurodevelopmental outcomes represented by composite cognitive and motor scores on the Bayley Scales of Infant and Toddler Development-Third Edition (Bayley-III) and composite communication scores on the Vineland Adaptive/Behavior Scale (VABS-II).
Summary of results After adjusting for confounders, children who were enrolled in WIC or WIC/SNAP had weight z scores U (95% CI) that were 1.32 (0.42, 2.21) or 1.19 (0.16, 2.23) higher than those of children who were not; enrollment in WIC/SNAP was associated with length z scores U (95% CI) that were 1.42 (0.19, 2.65) higher than those of children who were not. We found that enrollment in WIC or WIC/SNAP was associated with a change weight z score U (95% CI) from birth to current by 1.15 (95% CI: 0.10, 2.20 or 1.20 (0.13, 2.28) independent of other risk factors. Enrollment in WIC or WIC/SNAP was associated with a higher score on the Bayley-III cognitive scale and the VABS-II composite scale.
Conclusions Enrollment in food assistance programs is associated with positive somatic growth and neurodevelopmental outcomes. These findings support increased advocacy for participation in WIC or WIC/SNAP for families with high-risk infants.

Hematology and Oncology III

Concurrent Session

10:15 AM

Saturday, January 26, 2019

444 VIRUS-LIKE PARTICLE DISPLAY ENHANCES THE IMMUNOGENICITY OF A CANDIDATE VACCINE FOR GLIOBLASTOMA

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10.1136/jim-2018-000939.441

Purpose of study Glioblastoma (GBM) is the most common malignant brain tumor in adults but is stubbornly resistant to treatment and uniformly lethal. A subset of GBM patients

(~30%) express EGFRviii, a truncated, constitutively active form of epidermal growth factor receptor that is associated with worse outcomes. A vaccine targeting a unique epitope in EGFRviii progressed to a phase 3 trial but was unsuccessful partially due to the kinetics of the antibody response. As an alternative, we developed a vaccine targeting EGRFviii using virus-like particles (VLPs) to improve immune responses.

Methods used VLP-EGFRviii was generated using a unique 16-residue peptide from EGFRviii region conjugated to a bacteriophage (Qb) VLP. Mice were given a single IM dose of 5 µg VLP-EGFRviii and sera were collected at 1, 2, and 3 weeks. As a comparison, mice were immunized with 15 or 25 µg CDX-110 (rindopepimut), obtained from Celldex, or control unconjugated Qb VLPs. Antibody responses to the EGFRviii peptide were evaluated by ELISA. Data was analyzed using Prizm v7 with unpaired t-tests to compare CDX-110 and VLP-EGFRviii.

Summary of results Mean IgG titers after 1 week were 27.5 and 390 for 25 ug CDX-110 and 5 ug VLP-EGFRviii, respectively ($p<0.00001$). Mean IgG titers after 2 weeks were 90 and 2640 ($p<0.01$) with titers after 3 weeks of 410 and 5120 ($p<0.001$). All Qb control mice were non-responsive through 3 weeks. At weeks 1 through 3, 100% of VLP-EGFRviii mice were responders. For 15 ug CDX-110 mice, 30% were responders at week 1, with 60% at week 2% and 80% at week 3. For 25 ug mice, 50% were responders in weeks 1 and 2, with 90% responding by week 3.

Conclusions In the rindopepimut phase 3 trial, a small data set showed potential improved outcomes for those GBM patients that were rapid humoral responders. Here we demonstrated a new VLP vaccine with improved kinetics, achieving 100% response in 1 week compared to 50% response in rindopepimut. In addition, the average IgG antibody titer was significantly higher at every time point tested, indicating more robust IgG production. Taken together, our data suggests that the VLP-EGFRviii vaccine produces a more rapid and robust response than rindopepimut, which previous studies suggest is a substantial factor for overall survival in GBM patients.

445 DECISION-MAKING ABOUT GENETIC TESTING BY WOMEN WITH A PERSONAL AND FAMILY HISTORY OF BREAST CANCER

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10.1136/jim-2018-000939.442

Purpose of study Despite increasing availability of genetic testing for hereditary cancer risk, little is known about testing use and decision-making. We conducted a survey-based study of these topics.

Methods used A survey was administered online by a patient advocacy group for hereditary cancer, Facing Our Risk of Cancer Empowered (FORCE), from 10/2017 to 03/2018. The survey was distributed to subscribers of the FORCE mailing list and other cancer advocacy groups. Descriptive statistics are reported.

Summary of results Of 1377 respondents, 83% were non-Hispanic White, 7% Ashkenazi Jewish and 46% were diagnosed with breast cancer before age 45. Nearly all (97%) had a first-degree relative with cancer. Of 1100 respondents (80%) who reported genetic testing, 55% reported a pathogenic variant in a cancer susceptibility gene (BRCA1/2 or other). Most (87%) tested respondents were very satisfied with their testing decision, versus 32% of untested respondents: about half (57%) of untested respondents would consider testing in the future. Factors reported in favor of testing included relatives' cancer risk (75%), clinicians' recommendations (68%) and implications for treatment decision-making (66%). Factors reported in opposition to testing included concerns about insurance coverage (14%), cost (14%), and discrimination (9%); approximately one-third (38%) of respondents recalled being told by a clinician that genetic discrimination is illegal. Respondents often recalled a clinician informing them about genetic inheritance patterns (66%) and other cancer risks with a pathogenic variant (65%), but less often that results have implications for clinical trial eligibility (38%) and targeted therapies (14%).

Conclusions Among breast cancer patients with high risk of pathogenic variant carriage, fewer than half recalled being informed by a clinician that genetic discrimination is illegal or that their test results might make them eligible for clinical trials or targeted therapy. Clinicians are influential in patients' decisions about genetic testing and should address concerns including testing access and treatment implications.

446 CRISPR-CAS9-BASED EPIGENOME EDITING TO UPREGULATE THE P14ARF TUMOR SUPPRESSOR FOR SKIN CANCER INHIBITION

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10.1136/jim-2018-000939.443

Purpose of study The $p14^{ARF}$tumor suppressor induces cell cycle arrest in response to oncogenic stimuli and plays a key role in tumor surveillance. $p14^{ARF}$ is frequently inactivated in skin cancers due to promoter hypermethylation, whereas the $p14^{ARF}$ gene remains intact. Thus, $p14^{ARF}$ expression can be restored by reducing DNA methylation at the $p14^{ARF}$ promoter. We aim to develop epigenome editing tools to demethylate DNA at specific genomic loci in order to upregulate tumor suppressor genes and inhibit skin cancer.

Methods used We modified the CRISPR-Cas9 system for targeted DNA demethylation. Specifically, deactivated Cas9 (dCas9) was fused to the catalytic domain (CD) of ten-eleven translocation methylcytosine dioxygenase 1 (TET1), which induces DNA demethylation. Human skin cancer cell line A-431 was transduced with a lentiviral vector that expressed doxycycline-inducible dCas9-TET1CD, and stable cell clones were established. These clones were subsequently transduced with another lentiviral vector that expressed a guide RNA (gRNA) to direct dCas9-TET1CD to the $p14^{ARF}$ promoter, which is hypermethylated in A-431. RNA expression levels of dCas9-TET1CD, gRNA, $p14^{ARF}$, and unrelated gene β-actin were determined by RT-qPCR.

Summary of results We optimized doses and incubation periods of doxycycline treatment to maximize dCas9-TET1CD

expression; 4 μg/ml doxycycline for 2 days induced the highest level of dCas9-TET1CD expression. gRNA was constitutively expressed in A-431 cells transduced with dCas9-TET1CD and gRNA lentiviral vectors. Compared to untreated cells, doxycycline-treated cells showed upregulation of $p14^{ARF}$ (2-fold increase), not affecting β-actin expression, implying its selective effect on the targeted gene. In contrast, untransduced A-431 cells treated with 5-aza-2'-deoxycytidine, a global DNA methylation inhibitor, showed upregulation of both $p14^{ARF}$ and β-actin, suggesting its genome-wide effects on gene expression.

Conclusions Our epigenome editing system for targeted DNA demethylation is specific and inducible, allowing us to selectively upregulate a gene of interest and assess its effects on cellular phenotypes. Further studies will determine whether DNA demethylation at the $p14^{ARF}$ promoter inhibits proliferation and migration of skin cancer.

447 FACTORS AFFECTING TIME FROM DIAGNOSIS TO TIME TO TREATMENT IN LUNG CANCER PATIENTS AT THE UNIVERSITY OF WASHINGTON MEDICAL CENTER

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10.1136/jim-2018-000939.444

Purpose of Study The purpose of this retrospective chart review is to analyze factors affecting the time from diagnosis and the time to treatment in lung cancer patients.

Methods used Patient charts were queried from 1/10/1995 to 6/16/2017 for malignant neoplasms of the lung. The exclusion criteria were as follows: patients with stage IV disease, patients receiving neoadjuvant surgical resection, patients first seen by an oncologist or diagnosed before 1/1/2000, and patients treated with palliative intent. 318 patients were included in the final analysis. Univariate and multivariate regression of time from diagnosis to first treatment assessed the variables Age at Radiation Therapy, Gender, Race (White, Black, Asian, or Other), Previous Malignancy (Yes or No), First Treatment (Chemotherapy, Radiation Therapy, or Both), Histology (Non-Small Cell or Small Cell), ECOG (0, 1, or 2/3), and Previous Radiation Therapy. Outcomes were determined based on Recurrence and Vital status (deceased or alive).

Summary of results Based on the multivariate linear regression analysis, statistically significant ($p<0.0001$) increased time from diagnosis to treatment was observed in patients receiving radiation as opposed to chemotherapy. Significantly decreased time from diagnosis to treatment was observed in patients with small cell as opposed to non-small cell lung cancer ($p<0.0001$). All other variables did not show significant differences in time from diagnosis to treatment.

Conclusions The time from diagnosis to the time to treatment is significantly lower in patients with small cell lung cancer most likely due to the neoplasm's rapid progression as well as its chemotherapy responsiveness. The significantly increased time from diagnosis to treatment in patients receiving radiation may be due to limited availability and logistical scheduling restraints of radiation treatment compared to chemotherapy. Despite the lack of significant differences in time of diagnosis to treatment based on gender, race, and previous malignancy, future studies should investigate these variables in a larger sample size.

448 UTILIZING PROSTATE ORGANOIDS AS A MODEL TO EVALUATE REGULATORS OF BASAL STEM/PROGENITOR SELF-RENEWAL AND DIFFERENTIATION

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10.1136/jim-2018-000939.445

Purpose of study Prostate cancer is a leading cause of cancer and cancer-related deaths worldwide. Factors contributing to disease initiation are poorly understood, due to a lack of knowledge about key regulators of the cells-of-origin for prostate cancer. Using the prostate organoid system as a model of prostate regeneration and differentiation, we employed small molecule inhibitors to identify key regulators of prostate progenitor self-renewal and differentiation.

Methods used Mouse prostate basal epithelial cells marked with cell surface antibodies are isolated via Fluorescence Activated Cell Sorting and cultured under well-defined organoid growth conditions in the presence or absence of small molecule inhibitors. Two-tailed unpaired t-tests were used to compare percent organoid formation in control vs inhibitor-treated organoids. Western blot was used to measure protein expression of lineage specific markers.

Summary of results Percent organoid formation is lower in primary basal-derived cells treated with one particular small molecule inhibitor. This difference becomes more drastic in secondary organoids never exposed to inhibitor relative to those treated with inhibitor in both primary and secondary culture. Protein expression of luminal specific markers were decreased in inhibitor-treated primary basal-derived organoids. This effect however was slightly reversible in secondary organoids treated with inhibitor in primary but not secondary culture.

Conclusions We demonstrated in a 3D organoid culture model that the short-term and long-term effect of inhibiting a particular enzyme causes basal derived cells to lose progenitor activity. Cells exposed to inhibitor fail to retain the same progenitor activity as untreated cells. Furthermore, we have shown that this inhibition impairs basal-to-luminal differentiation that is partially reversible with removal of the inhibitor in secondary culture. These inhibitor-based effects suggest that self-renewal and differentiation of basal cells may be susceptible to disturbances in this pathway. Future research is necessary to determine the role of this pathway in prostate cancer initiation, progression and treatment-resistance.

449 TESTICULAR CANCER PATIENT INFORMATION: AN EVALUATION OF THE QUALITY OF INFORMATION RESOURCES AVALIBLE

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10.1136/jim-2018-000939.446

Purpose of study The continuous growth of the internet has allowed increasing amounts of information to be available to the public, including medical information. Testicular cancer is the most common solid malignancy diagnosed in young men aged 15–29. This population is also the age group that searches most actively for health information online. Despite patients increasingly using the internet as an important resource, little is known about the quality of testicular cancer information online. This study looks to systematically evaluate the quality of websites available to patients with testicular cancer.
Methods used The search term 'testicular cancer' was inputted into the search engine Google and metasearch engine Dogpile and Yippy. The top 100 websites intended for the purpose patient education were compiled. A previously validated structural rating tool was used to evaluate the websites with respect to attribution, currency, disclosure, interactivity, readability and content.
Summary of results Of the top 100 websites, less than half (44) disclosed authorship. 61 websites provided a last modified date, and of those websites 46 were updated in the last 2 years. The average readability level was 11.01 using the Flesh Kincaid grade level system. The most accurately covered topics were etiology/risk factors and treatment. The least accurate topics were prognosis and prevention, as a majority of websites simply did not cover these topics or were missing essential information.
Conclusions These results show that authorship and currency are lacking in many online testicular resources. Missing information such as this can make it difficult for patients to validate the reliability of information they find online. The high average readability of testicular cancer websites may make it difficult for patients to comprehend the information available. An average target readability grade level of 6 is recommended by the AMA and NIH. However only 1 of the websites evaluated was written at an FK grade level of 6. Additionally, topics such as prognosis were infrequently covered although represent an area for which patients often seek more information. The results of this study can be used to counsel patients on the strength and weaknesses of online testicular cancer resources.

450 ARCTIGENIN AS A NOVEL ANTI-INFLAMMATORY AGENT FOR METASTATIC COLON CANCER TREATMENT

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10.1136/jim-2018-000939.447

Purpose of study In an effort to develop a novel therapy for colorectal cancer, we investigated the therapeutic potential and mechanisms of the natural compound Arctigenin.
Methods used *MTS Assay For Arctigenin IC50 Value*
BCA Assay
Western Blot Analysis
MTS Assay For Combination Treatment
Apoptosis Array
Cell Sorting
Summary of results *Arctigenin inhibits HCT-116 and DLD-1 cell proliferation at low concentrations*
Arctigenin shows no toxicity towards normal colon cell lines CCD-841 and CCD-18CO
Arctigenin reduces STAT3 phosphorylation in HCT-116 and DLD-1 cell lines
Arctigenin in combination with 5-Fluoro Uracil did not exhibit strong effects
Arctigenin treated CRC cell lines show a decrease in CD-51 and CD-133 expression
Arctigenin induces multiple apoptotic pathways in HCT-116 and DLD-1
Conclusions Based on the data obtained from the above stated experiments Arctigenin is proving to be a potent compound against Colorectal Cancer. In order to further understand the mechanisms of action of this compound further experiemtns need to be conducted. Combination treatment of Arctigenin with other potent anticancer compounds like Cisplatin and Oxaloplatin need to be conducted in the near future.

Immunology and Rheumatology II

Concurrent Session

10:15 AM

Saturday, January 26, 2019

451 PLATELET S100A8/A9 IS UPREGULATED IN PATIENTS WITH GRANULOMATOSIS WITH POLYANGIITIS AND REGULATES VASCULAR INFLAMMATION

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10.1136/jim-2018-000939.448

Purpose of study Granulomatosis with Polyangiitis (GPA) is a systemic vasculitis characterized by granulomatous inflammation and thrombosis of small blood vessels of the sinuses, lungs, and kidneys. Cellular mechanisms driving this thromboinflammation remain incompletely understood. We hypothesized that altered platelet gene expression drives thromboinflammation in GPA patients.
Methods used Patients with GPA (n=42) and matched healthy controls (n=25) were recruited with informed consent. Platelet reactivity was assessed by flow cytometry. Platelet transcriptomes were profiled via RNA-seq followed by validation of differentially expressed genes by qRT-PCR and immunoblot. Pro-inflammatory cytokines were measured by ELISA. Platelet mRNA expression changes and cytokine levels were correlated with clinical indices in GPA patients. For functional studies, activated platelets were incubated with human umbilical vein endothelial cells (HUVECs), and ICAM-1 expression (a vascular inflammation surrogate) measured by ICC with and without an S100A8/A9 blocking antibody.
Summary of results GPA patient platelets were hyperactive (e.g. increased integrin activation) compared to healthy controls ($p<0.001$). RNA-seq revealed that the top differentially expressed genes in GPA patient platelets were S100A8 and S100A9, which form a heterodimer that promotes thrombosis and inflammation. qRT-PCR and immunoblot confirmed increased platelet S100A8 and S100A9 in GPA (~3 fold mRNA increase, $p<0.05$). Plasma S100A8/A9 was also increased in GPA patients vs. controls (1793 ng/mL vs.

937 ng/mL, $p<0.05$), and correlated with inflammatory markers (e.g. CRP, $r=0.621$, $p<0.05$) and disease activity (e.g. Birmingham Vasculitis Activity Score, $p<0.05$). Platelet S100A8/A9 mRNA also correlated with pro-inflammatory plasma cytokines, including the chemokine CCL5/RANTES, which is implicated in vascular inflammation. S100A8/A9 blocking partially rescued platelet adhesion to HUVECs and ICAM-1 expression.

Conclusions The thrombo-inflammatory genes S100 A8 and A9 are upregulated in platelets of GPA patients. Expression of these platelet genes correlates with clinical disease markers and may contribute to the vascular inflammation characteristic of GPA, thus representing a potential diagnostic or therapeutic target.

452 PLACENTAL HTRA1 CLEAVES ALPHA-1-ANTITRYPSIN AND GENERATES A NET-INHIBITORY PEPTIDE

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10.1136/jim-2018-000939.449

Purpose of study Neutrophils (PMNs) release neutrophil extracellular traps (NETs) to trap and kill microbes. Dysregulated NET formation, however, contributes to inflammatory tissue damage. We identified a novel NET-inhibitory peptide (NIP), neonatal NET-Inhibitory Factor (nNIF), present in the fetal circulation. nNIF is a cleavage fragment of alpha-1 antitrypsin (AAT), a circulating protease inhibitor in humans and mice. How nNIF is generated in fetal blood remains unknown. The placenta expresses high temperature requirement A 1 (HTRA1) which inhibits AAT. We hypothesized that placental HTRA1, a serine protease, regulates the formation of NIPs through cleavage of AAT.

Methods used We determined placental and serum HTRA1 and AAT levels using proteomic techniques in neonates and adults. We incubated recombinant or placental HTRA1 with AAT and assessed NIP generation using proteomic techniques. We assessed NET formation by PMNs using live cell imaging and high throughput NET assays. We assessed NIP effects on PMN nuclear decondensation, ROS generation, chemotaxis, phagocytosis, and bacterial killing using standard assays. We also assessed NET formation by murine PMNs from WT or $HTRA1^{-/-}$ pups at 1–3, 4–6, and 7–10 days after birth.

Summary of results Placentas express HTRA1, and neonatal plasma has higher levels of HTRA1 than adult plasma. HTRA1 generates a 4 kD NIP when incubated with AAT. NIP preincubation with PMNs inhibits NET formation, but does not alter PMN ROS generation, chemotaxis, or phagocytosis following LPS stimulation. NIP preincubation does reduce NET-associated bacterial killing and nuclear decondensation by stimulated PMNs, suggesting it inhibits PAD4 activation. Neonatal murine plasma contains a 4 kD NIP which inhibits NET formation by murine PMNs, indicating that NIP generation is conserved in mice. Neonatal PMNs stimulated with LPS exhibit delayed NET formation following birth. However, PMNs from $HTRA1^{-/-}$ pups generate more NETs between day 4–6 of life compared to WT controls.

Conclusions Placental HTRA1 cleaves AAT to generate a NIP similar to nNIF. We conclude that placental HTRA1 generates NIPs in fetal circulation, and speculate that NIPs participate in the immune tolerance required during transition to extrauterine life.

453 TARGETED LIPOSOMAL DELIVERY OF TYROSINASE-RELATED PROTEIN-2 PEPTIDE IMMUNOTHERAPY TREATMENT FOR MELANOMA IN MICE

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10.1136/jim-2018-000939.450

Purpose of study Melanoma is the deadliest form of skin cancer. Vaccination with Tyrosinase-related protein-2 (TRP-2) peptide $_{(180–188)}$ has been shown to reduce the growth of melanoma in mice. Our lab developed liposomes conjugated to complement C3 (C3-liposomes), allowing for antigen targeted immune stimulation of Antigen Presenting Cells (APCs). We hypothesize TRP-2 antigen delivery to APCs using C3-liposomes will heighten immune response and further reduce tumor growth in mice.

Methods used 20 C57BL/6 mice were divided into 5 groups of 4 equally distributed by sex and inoculated with 7.5×10^5 B16F10 melanoma cells in the left flank. On days 3 and 10, each were injected with 200 µL in the right flank containing 50 µg of poly I:C and their respective treatments of PBS, 9.5 µg TRP-2, 100 µg TRP-2, TRP-2 filled C3-liposomes, or TRP-2 filled C3-liposomes with increased level of C3 group. The 9.5 µg TRP-2 group matched the amount of TRP-2 in both liposomes. Blood and tumor immune cells were measured with flow cytometry, T cell IFN-γ response to TRP-2 antigen in spleen cells was measured by Elispot, and tumor growth rate was tracked every 2 days with calipers. Volumes were recorded as mm^3 using [(4/3)p(length*width*minimum)/8]. A one-way ANOVA tested the null hypothesis that all groups have equal means.

Summary of results All TRP-2 treated groups had reduced tumor size, increased B cell count, and fewer immunosuppressive Myeloid Derived Suppressor Cells (MDSCs) compared to the PBS group ($p<0.05$). No statistical differences were seen in CD4 or CD8 T cell count in tumor or blood samples between groups. Elispot showed stronger T-cell response in both C3-liposome groups versus low TRP-2, PBS and Naïve control. Vitiligo appeared first in both C3-liposome groups followed by high free TRP-2 and low TRP-2.

Conclusions Vitiligo is an autoimmune response where T cells attack melanocytes. Vitiligo and Elispot data show a higher T cell response in C3-liposomes proving the first part of our hypothesis, but this failed to show better tumor reduction compared to free TRP-2. This suggests immunosuppression by another mechanism, like Tregs or PD-L1 on tumor cells. More study is needed to find this mechanism to improve our C3 targeted approach.

454 THIOREDOXIN-1 IS AN INFLAMMATORY MARKER FOR MACROPHAGES

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10.1136/jim-2018-000939.451

Purpose of study Monocyte-derived macrophages (MDM) are immune cells derived from hematopoietic progenitors. They interact with a variety of stimuli and carry out a diverse array of functions, from phagocytosis to wound healing. Macrophages have traditionally been classified as M1 (pro-inflammatory) or M2 (anti-inflammatory) based on their mode of activation. Previously, we sought to distinguish human MDM differentiated by granulocyte-monocyte colony stimulating factor (GMCSF) or monocyte colony stimulating factor (MCSF), which are known to respectively produce pro-inflammatory and anti-inflammatory macrophages. Using canonical surface markers, we found quantitative but not qualitative differences between these two states. However, these macrophages are functionally diverse and context dependent by stimulus and cytokine production. From this data, we hypothesized that there was an altered transcriptional program underlying these distinct phenotypic states.

Methods used To test this hypothesis, GMCSF and MCSF differentiated human MDM were analyzed by single cell RNA sequencing (scRNAseq). This allowed an unbiased interrogation of cellular state while accounting for potential cell-to-cell heterogeneity. We assessed the increased protein expression of the gene by western blot or by flow cytometry. In addition, we hypothesized that the marker found in GMCSF macrophages would be applicable to inflammatory macrophages broadly. To test this hypothesis, we generated classical 'M1' macrophages using LPS and IFNg or 'M2' macrophages using IL-4 and probed for this distinguishable marker.

Summary of results Thioredoxin-1, CD44, and CD52 were highly expressed genes distinguishing GMCSF differentiated macrophages from MCSF differentiated macrophage by scRNAseq. We validated the increased protein expression of thioredoxin-1 (TRX1) in GMCSF macrophages by western blot; however, surface levels of CD44 and CD52 did not distinguish the two macrophage subsets. We also found that M1 macrophages also had higher expression of TRX1 as compared to M-CSF or M2 macrophages.

Conclusions This indicates that high TRX1 expression is a conserved feature of inflammatory macrophage state and potentially plays a role in modulating macrophage function.

455 COMBINATORIAL IMMUNOTHERAPY WITH ADJUNCTIVE OMALIZUMAB FOR PEANUT ALLERGY

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10.1136/jim-2018-000939.452

Purpose of study Without an FDA-approved treatment, dietary avoidance remains the standard of care for Peanut Allergy (PA). Oral immunotherapy (OIT) for PA shows promise, but is limited in efficacy and safety: long-term tolerability is rarely assessed, and adverse reactions can be fatal. The aim of this study was to investigate how omalizumab (OML) might hasten treatment time and mitigate adverse reactions in combination with OIT.

Methods used We consulted databases like Cochrane, PubMed and Clinical Trials. Only studies pretreating and co-administering OML were included. Multi-allergen OML studies were included if peanut data were separated. Nine of 51 relevant studies used OML, and 5 of 9 sufficed our inclusion criteria (see table 1 below).

Summary of results Threshold tolerance at initial oral food challenge (OFC) screenings was <100 mg. OML pretreatment was given every 2–4 weeks, for 8–16 weeks, and was co-administered for 4–8 weeks into OIT. OIT began with rapid desensitizations under close supervision. After updosing, subjects continued maintenance doses of 2000–4000 mg peanut. After discontinuing OML, subjects underwent exit OFCs. Median exit OFC tolerances ranged from 2000 to 8000 mg (200–400x screening doses). Tolerance to 2000 mg peanut was seen up to 62 months after discontinuing OML in one study. Severe side effects were rare, with mild-moderate effects occuring in <10% of doses given. Though most studies

Abstract 455 Table 1

	N Subjects; Age Range (years) †	Desensitization top dose (mg)	Length of OML pretreatment; and co-administration (wks)	Escalation top dose/duration	Maintenance dose (mg)	N (%) tolerance at Exit OFC	Side Effects
Schneider L, 2013	13; 7–14	500	12; 8	4 g over 8 wks (range, 7–12)	4000	12 (92%) passed 8000 mg 30–32 wks after stopping OML	72 (2%) of doses
Bégin P, 2014	25; 4–15	250	8; 8	4 g over 18 wks (range, 7–36)	4000	22 (88%) passed 4000 mg 18 wks after stopping OM	all mild; 11 (11%) of doses in escalation and 3 (3%) in maintenance‡
MacGinnitie A, 2016 †	29; 7–19 (OML) 8; 6–17 (placebo)	250 (OML) 22.5 (placebo)	12; 7	2 g over 20 wks	2000	22 (76%) of OML and 1 (12.5%) placebo passed 4000 mg 12 wks after stopping OML	Eosinophilic esophagitis in 2 (OML) and 1 (placebo)
Henson M, 2012	6;≥12	300	16; 4	4 g, duration not stated	4000	not stated	6 (9.5%) of doses associated with mild side effects
Andorf S, 2017	26; 4.6–16.7 ¶	500	12; 8	4 g over 8 wks (range, 7–12)	2000 (high dose) 300 (low dose)	26 (100%) passed 2000 mg 62 months after stopping OML	No major

†Placebo-controlled. ‡1 subject given epinephrine at 16 g. ¶LTFU from Bégin. 26/34 subjects were allergic to peanut alone or alongside another food.

reported peanut-specific IgE, no conclusion was made on this metric's reliability to indicate therapeutic success.
Conclusions Our review suggests OML may expedite therapy duration and prolong tolerance in peanut-allergic patients. While side effects were minimal, all but one study lacked a control arm. Larger prospective randomized controlled trials with and without OML are needed to better evaluate the safety and efficacy of OML in OIT.

456 RELAPSING POLYCHONDRITIS PRESENTING AS OPTIC NEURITIS AND ASPECTIC MENINGITIS

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10.1136/jim-2018-000939.453

Background Relapsing polychondritis is a rare disorder affecting 3.5 per 1 million people per year. It is characterized as immune mediated inflammation of predominantly cartilaginous structures including the ears, nose, eyes, and laryngealtracheobronchial tree. Most commonly presenting as unilateral or bilateral external ear inflammation. The diagnosis is often missed or unrecognized for month to years because of intermittent manifestations of symptoms.
Case Highlighted is a case of relapsing polychondritis (RP) in a 23 year old Hispanic female who is a student at local university uniquely presenting as sudden onset headache accompanied with blurry vision. Upon her admission, she was urgently evaluated by ophthalmology which revealed severely decreased visual acuity (20/200 right eye and 20/100 left eye), pre-papilledema, central scotoma with deferential diagnosis of central serous chorioretinopathy. She was immediately referred to the emergency department and was admitted. Lumbar puncture (LP) showed lymphocytic predominant aseptic meningitis picture with 340 WBC and normal glucose and slightly elevated protein. All infectious work up was unrevealing. MRI brain showed abnormal meningeal enhancement primarily in the cerebellar vermis region in a sugar coating or zuckerguss pattern common in leptomeningeal carcinomatosis. She further suffered vertigo, hyperacusis and thinning of the pinna without redness. Due to the acute and worsening visual acuity high dose pulse steroids were initiated where her vision and headache improved. A rheumatologic history revealed that the patient herself had been evaluated for polyarthralgia at the age of 11 and mother with rheumatoid arthritis and spondyloarthropathy. Her follow up LP and MRI brain revealed resolution of pleocytosis and leptomeningeal enhancement.
Conclusion The elusive diagnosis of RP was masked by multiple differentials including aseptic meningitis, central serous chorioretinopathy and leptomeningeal carcinomatosis. This case is further unique due to only 19 cases in literature reporting an associated aseptic meningitis in RP patients.

457 FIRST REPORTED CASE OF MALIGNANT OTITIS EXTERNAL SECONDARY TO TREATMENT WITH SECUKINUMAB

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10.1136/jim-2018-000939.454

Purpose of study Secukinumab is a fully humanized monoclonal antibody that selectively inhibits interleukin (IL) 17A, and has been approved for the treatment of autoimmune disorders that arise from dysregulation of this IL such as psoriasis. However, inhibition of IL17A is associated with increased incidents of nasopharyngitis, upper respiratory and mucocutaneous infections (28.7% vs. 18.9% placebo). We are presenting a case of malignant otitis external associated with the use of Secukinumab.
Methods used Retrospective case report
Summary of results A 38-year-old non-diabetic male with cutaneous and psoriatic arthritis suppressed with Secukinumab presented with a five-day history of unilateral ear pain, discharge, swelling and numbness of cheek and hearing loss. Outpatient oral and otic ciprofloxacin did not improved his symptoms. Upon admission, he had no fever but was found to have periauricular and postauricular erythema and tenderness consistent with malignant otitis picture. On otoscopy, a ruptured right tympanic membrane and whitish discharge were visualized. His WBC was 12.4 u/L without a left shift. CT scan showed opacification of the middle ear cavity, external auditory canal with superficial soft tissue component and involvement of mastoids. ENT did not agree with the presence of mastoiditis and no interventions recommended. He was placed on broad-spectrum antibiotics with vancomycin and piperacillin/tazobactam, and otic ciprofloxacin, to cover pathogens associated with malignant otitis external. Gram stain from the ear canal was consistent with gram positives and gram negatives. Subsequently, the culture grew *Streptococcus agalactiae* and *Pseudomonas aeruginosa*. His symptoms started to improve with resolution of the pain, swelling, discharge and hearing loss. His antibiotics were de-escalated to levofloxacin 750 mg daily based on sensitivities, and he later was discharged home to finish a 14 day course of treatment. He was instructed to hold Secukinumab. Secukinumab was resumed six months later at patient's insistence, and he subsequently suffered from a perirectal cellulitis.
Conclusion Clinicians should be aware of the balance between suppression of autoimmune disorders and increase risk of serious infections using Secukinumab or other biosimilar agents.

Neonatology General VI

Concurrent Session

10:15 AM

Saturday, January 26, 2019

458 ACUTE BILIRUBIN ENCEPHALOPATHY: A REGISTRY AND DATABASE INCLUDING NEXT GENERATION SEQUENCING OF POTENTIAL GENETIC ASSOCIATIONS

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10.1136/jim-2018-000939.455

Purpose of study One of the most devastating adverse outcomes of hemolytic anemia in neonates is Acute Bilirubin

Encephalopathy (ABE). In theory, this tragic problem should be completely preventable, yet it still occurs in one per 50 000 to 1 00 000 births in the United States. We herein describe our new National Acute Bilirubin Encephalopathy Registry. This mechanism will enable a prospective root-cause analysis of ABE cases, including a next generation sequencing panel of 28 genes involved in hyperbilirubinemia. In a previous kernicterus registry a clear explanation for the hyperbilirubinemia was found in only 45% (Bhutani and Johnson, *J Perinatol*, 2009). A Utah registry from 2009 to 2018 utilized our 28-gene panel and revealed a clear explanation for the jaundice in each of seven cases (Christensen et al, *Blood Cells Molecules Dis*, 2018). We now propose to greatly expand our Utah registry to a national registry. This will permit discovery of genetic associations using a nationwide population of ABE cases, and will constitute a needed step toward focusing new efforts on early detection of 'at risk' neonates and devising strategies to prevent future cases.

Methods used We have organized a nationwide, voluntary, central IRB approved, web-based, REDCap registry for neonates≤14 days old with a total serum bilirubin ≥28 mg/dL and moderate to severe ABE (BIND score ≥4). A 1 mL blood sample is obtained from each neonate and sequenced for disease-causing variants in 28-genes involved in hyperbilirubinemia free of charge. Enrollment will begin in January 2019.

Summary of results Many cases of ABE previously thought to be idiopathic have an identifiable genetic cause. Over the next three years we anticipate enrolling >100 neonates with ABE and identifying genetic associations.

Conclusions Future advances in preventing ABE must be guided by accurate information about the true causes. The National Acute Bilirubin Encephalopathy Registry plans to discover these in a large nationwide voluntary registry.

459 HOSPITAL READMISSION AND LONG-TERM MORBIDITIES OF NEONATES WITH CONGENITAL DIAPHRAGMATIC HERNIA TREATED IN CHILDREN'S HOSPITALS

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10.1136/jim-2018-000939.456

Purpose of study To describe the patient characteristics of and examine the rate and risk of readmission for morbidities in congenital diaphragmatic hernia (CDH) neonates who were readmitted after their index hospital visit.

Methods used Data were obtained from the Pediatric Healthcare Information System database. Univariate and multinomial regression analyses were used.

Summary of results 4637 neonates with CDH were admitted to a children's hospital between January 1st, 2004 and June 31 st, 2016 nationwide. 26.2% received ECMO support and 31.9% had at least one readmission. Patients who received ECMO had a mean of 4 readmissions with a mean length of stay (LOS) of 7 days, whereas those who did not had a mean of 3 readmissions with a mean LOS of 8 days. Non-Hispanic babies were less likely to be admitted (p-value 0.008). There were regional differences in the likelihood of readmission (p-

Abstract 459 Table 1

	Readmission frequency				
	1 (n=616)	2 (n=285)	3 (n=176)	4 (n=401)	p-value
Gender					
Male	Ref				0.007
Female	0.84 (0.66 - 1.08)	0.84 (0.60 - 1.18)	0.59 (0.38 - 0.92)	0.56 (0.40 - 0.80)	
Ethnicity					
Hispanic	Ref				0.008
Non-Hispanic	0.63 (0.45 - 0.88)	0.71 (0.43 - 1.15)	0.60 (0.33 - 1.07)	0.55 (0.35 - 0.86)	
Race					
White	Ref				0.35
Black	1.15 (0.76 - 1.72)	0.67 (0.37 - 1.21)	1.61 (0.84 - 3.09)	1.18 (0.70 - 2.00)	
Asian/Pacific Islander	0.41 (0.16 - 1.06)	1.23 (0.50 - 3.02)	1.15 (0.38 - 3.48)	0.48 (0.14 - 1.64)	
Other	0.84 (0.59 - 1.21)	0.72 (0.42 - 1.21)	0.87 (0.47 - 1.59)	0.77 (0.47 - 1.25)	
Primary source of payment					
Private insurance	Ref				0.71
Government insurance	0.86 (0.65 - 1.13)	1.15 (0.77 - 1.71)	0.65 (0.41 - 1.05)	0.90 (0.61 - 1.34)	
Other	0.72 (0.36 - 1.43)	1.11 (0.44 - 2.79)	0.71 (0.23 - 2.18)	0.82 (0.32 - 2.10)	
Region					
West	Ref				0.02
Midwest	1.09 (0.76 - 1.54)	1.82 (1.10 - 3.01)	0.53 (0.28 - 1.00)	0.65 (0.40 - 1.06)	
Northeast	0.84 (0.56 - 1.27)	1.43 (0.80 - 2.57)	0.89 (0.46 - 1.72)	0.93 (0.55 - 1.57)	
South	0.84 (0.59 - 1.18)	1.08 (0.65 - 1.78)	0.62 (0.35 - 1.09)	0.54 (0.35 - 0.86)	
Complex chronic conditions (CCCs)					
Cardiovascular	0.95 (0.74 - 1.23)	1.24 (0.88 - 1.74)	1.91 (1.23 - 2.97)	1.36 (0.97 - 1.92)	0.02
Gastrointestinal	1.31 (0.97 - 1.79)	1.60 (1.09 - 2.36)	1.97 (1.22 - 3.18)	2.32 (1.60 - 3.38)	<0.001
Renal	1.00 (0.70 - 1.44)	1.22 (0.77 - 1.91)	1.01 (0.57 - 1.79)	1.40 (0.92 - 2.12)	0.56
Respiratory	0.81 (0.62 - 1.06)	0.72 (0.50 - 1.04)	0.76 (0.48 - 1.20)	0.74 (0.51 - 1.07)	0.17
Mechanical ventilation	0.67 (0.42 - 1.08)	0.86 (0.38 - 1.94)	0.65 (0.25 - 1.69)	0.52 (0.25 - 1.09)	0.26
ECMO	0.52 (0.38 - 0.72)	0.75 (0.50 - 1.12)	0.60 (0.36 - 1.00)	0.60 (0.40 - 0.91)	<0.001

value 0.02). Infants with complex chronic cardiovascular and gastrointestinal conditions were significantly more likely to be admitted (p-values 0.02 and <0.001).
Conclusions CDH neonates who received ECMO had more readmissions, longer LOS at readmissions and were more likely to develop other morbidities. Infants with chronic cardiovascular and gastrointestinal conditions were more likely to be readmitted.

460 OUTCOMES OF NEONATES EVALUATED BY A NEONATAL NEUROCRITICAL CARE SERVICE

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10.1136/jim-2018-000939.457

Purpose of study To examine the outcomes of neonates cared for by a neonatal neocritical care service (NNCS), at UCSF.
Methods used Neonates seen by the NNCS and followed by the High Risk Infant Program between 6/2008 and 7/2018 were included. The outcome of each neonate was considered normal, mild, moderate or severe based on the most recent evaluation using Bayley Scales of Infant and Toddler Development III (BSID-III) and the Gross Motor Function Classification System (GMFCS). Scores from the Behavior Assessment System for Children, 3rd Edition Preschool (BASC-3), administrated beginning in 2015, and the Toddler Sensory Profile, administered beginning in 2010, were also analyzed.
Summary of results Clinical characteristics of the 326 neonates are summarized in table 1. Overall, 40 (15%) had mild neurodevelopmental impairment, 27 (8%) moderate, and 11 (3%) severe (1 child could not be classified). The remaining 237 (73%) had normal outcomes. BASC-3 was administered in 27; 20 (74%) were abnormal. Sensory Profile was administered in 33; 16 (50%) were abnormal (table 2).
Conclusions Approximately 3/4 of neonates had *normal* neurodevelopmental outcome as classified by cognitive BSID-III and GMFCS scores. However, there was a high rate of clinically significant behavior and sensory issues among children without cerebral palsy or low cognitive scores. This implies that children who are considered neurodevelopmentally normal may have clinically significant impairments that suggest high risk for behavior and sensory processing disorders. Infant follow-up programs should consider implementing screening tools to identify children that may benefit from early intervention.

Abstract 460 Table 1

Study Population	n=326
Preterm (	103 (32%)
Neurologic Diagnosis:	
- HIE	176 (54%)
- Seizures (EEG or clinical)	98 (30%)
- Parenchymal hemorrhage	46 (14%)
- Ischemic Stroke	32 (10%)
- Intraventricular hemorrhage (I, II, III)	29 (9%)
Patients with >1 neurologic diagnosis	152 (47%)

Data presented as n(%)

Abstract 460 Table 2

Developmental Outcome	Abnormal BASC-3 n=27	Developmental Outcome	Abnormal Sensory Profile
Normal and mild, n=23	17 (79%)	**Normal and mild, n=29**	45 (41%)
Moderate and severe, n=4	3 (75%)	**Moderate and severe, n=4**	3 (75%)

Results presented as (n, row%)

461 NEURODEVELOPMENTAL OUTCOMES IN EXTREMELY LOW BIRTH WEIGHT INFANTS EXPOSED TO GRADED OXYGEN SATURATION TARGETS

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10.1136/jim-2018-000939.458

Purpose of study The use of unrestricted oxygen in the NICU has been linked to long-term morbidities such as ROP and BPD. A graded oxygen saturation target protocol was developed to limit the oxygen that extremely low birth weight infants were exposed to and combat these long-term morbidities. Few studies have evaluated the long-term neurodevelopmental outcomes in these infants at later follow-up between 1 to 3 years of age. The primary objective of this study is to evaluate the prevalence of major disability in extremely low birth weight infants exposed to graded oxygen saturation targets.
Methods used This is a retrospective chart review. The infants included had a birthweight of <1,000 g and were between 24^{0}–^{7}-$27^{6/7}$ week gestation at birth and who subsequently followed-up in the high risk infant follow-up clinic between 12–18 months corrected age. Exclusion criteria includes death prior to discharge or prior to administration of developmental testing, birth weight >1,000 g, congenital anomalies, and genetic disorders associated with developmental delay. Follow-up variables under consideration include scores on neurodevelopmental testing using the Bayley Scales of Infant and Toddler, third edition. Major disability is defined as scores of <85 in the language and cognitive domains.
Summary of results Neurodevelopmental testing was administered at 12–18 months corrected gestational age using the Bayley Scales of Infant and Toddler Developmental, third edition. The average gestational age of the infants in this cohort was 25.8 weeks with an average birth weight of 728.5 grams. 47% of the infants were male, 20% had grade III or higher intraventricular hemorrhage, with an average time on supplemental oxygen of 83.3 days. In regards to the developmental testing, the average scores were 86.9, 80.4, 83.6, and 95.4 in the cognitive, language, motor, and social-emotional domains, respectively.
Conclusions In the preliminary data accumulated, the average infant who participated in neurodevelopmental testing at 12–18 months had scores that reflect major disability, as reflected in the language domain average score. The next phase of this research will evaluate and compare the neurodevelopmental outcomes of those infants who were exposed to graded

oxygen saturations and those who were not, as well as follow-up test scores at 36 months.

462 GROWTH TRAJECTORIES IN INFANTS WITH GASTROINTESTINAL ANOMALIES FOR THE FIRST TWO YEARS OF LIFE

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10.1136/jim-2018-000939.459

Purpose of study Infants born with gastrointestinal (GI) anomalies are at risk for prolonged hospitalization secondary to surgery, sepsis and necrotizing enterocolitis (NEC). These complications lead to growth delays that may have far-reaching consequences. This study's aim was to investigate long-term growth among neonates with GI anomalies and gastroschisis.

Methods used This single site study used a retrospective and prospective approach. Inclusion criteria: neonates with congenital GI defects (gastroschisis, omphalocele, esophageal/bowel atresia, etc) born between 2010–2017. Weight, length and head circumference (HC) z-scores were collected for the first 27 mos.

Summary of results Mean (±SD) gestational age of this cohort (n=61) was 36±3 weeks; 66% were male, 39% were small for gestational age, and 35% were gastroschisis. 10% developed NEC; 13% developed late-onset sepsis. Infants with GI anomalies and gastroschisis had weight, length and HC z-scores less than zero from birth through 13 mos ($p<0.01$, tables 1 and 2). From birth to 13 mos, only HC z-score increased over time (slope 0.08 per mo, $p<0.001$). In contrast, in the gastroschisis cohort, HC, weight and length z-scores increased over time (slopes 0.1, 0.08, 0.07 per mo $p<0.05$). At 27 months using a z-score change of ±0.25, z-scores for all measurements comparing birth to 27 months were not equivalent (95% CI HC −0.8, 1.5; weight −0.8, 0.7; and length −1.1, 0.2). Similar results were found in the gastroschisis cohort (95% CI weight −0.2, 1.5 and length −0.2, 0.7).

Conclusions In this cohort, GI anomalies were associated with early growth failure. All infants, but particularly gastroschisis infants, appeared to 'catch-up.' It remains to be determined how this growth pattern affects neurodevelopment.

Abstract 462 Table 1 Mean (±SD) growth measurements all GI anomalies

	Birth (n=61)	30 days since birth (n=83)	4 mo (n=73)	13 mo (n=36)	18 mo (n=27)	27 mo (n=18)
Weight z-score	-0.3±1.2	-1.1±1.1	-1.7±1.2	-0.7±1.2	-0.7±1.1	-0.4±0.8
Length z-score	-0.5±1.3	-1.3±1.3	-1.6±1.5	-1.0±1.1	-1.1±1.2	-1.1±1.8
Head Circumference z-score	-0.6±1.2	-1.0±1.2	-1.2±1.1	0.2±1.3	-0.1±1.5	1.4±0.4

Abstract 462 Table 2 Mean (±SD) growth measurements gastroschisis

	Birth (n=24)	30 days since birth (n=32)	4 mo (n=31)	13 mo (n=12)	18 mo (n=8)	27 mo (n=3)
Weight z-score	-0.8±0.7	-1.6±1.0	-1.4±1.0	-0.4±0.8	-0.3±0.3	-0.1±0.2
Length z-score	-0.8±1.3	-1.9±1.4	-1.8±1.4	-0.6±1.1	-0.7±0.4	0.3±0.4
Head Circumference z-score	-1.1±0.7	-1.2±1.1	-1.1±0.9	1.0±1.0	-0.2±1.2	0.4±0.9

463 NEURODEVELOPMENTAL OUTCOMES OF PRETERM INFANTS WITH CEREBELLAR HEMORRHAGE

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Purpose of study CBH in preterm infants has the potential to negatively impact cognition, learning, behavior, and language functions. The purpose of this study is to investigate the neurodevelopmental outcomes of preterm infants with CBH and to determine if outcomes are different between mild and moderate to severe CBH.

Methods used Retrospective cohort study of preterm neonates born less than 1250 grams at birth admitted to the neonatal intensive care unit (NICU) at LAC+USC Medical Center between January 1, 2009 to October 31, 2013 with a diagnosis of CBH. Bayley Scales of Infant and Toddler Development 3rd Edition was used at 6 months and 18 months corrected age for neurodevelopmental outcome assessment. Social emotional composite score was self-reported by the parents.

Summary of results There were 157 preterm infants included in this study. A diagnosis of CBH was confirmed by magnetic resonance imaging (MRI). Infants with CBH had lower mean BW (672±200 vs. 839±185, $p\leq0.00001$) and lower mean GA (25.1±2 vs. 27.5±2.5, $p\leq0.00001$) compared to infants without CBH. There were 57 infants without CBH (control) and 24 with CBH who had completed neurodevelopmental assessment. At 6 months corrected age, only cognitive composite score in infants with CBH was significantly lower compared to controls; 95 (IQR:12.5) vs. 100 (IQR:15) p value=0.04. At 18 months corrected age, social emotional composite score was significantly lower in infants with moderate to severe CBH. All infants tested had composite scores above 70 on all categories. (table 1)

Abstract 463 Table 1

18 months corrected age	Cerebellar Hemorrhage n=24	No Cerebellar Hemorrhage n=57	P-Value	Mild Cerebellar Hemorrhage n=10	Moderate to Severe Cerebellar Hemorrhage n=10	P-Value
Cognitive*	82.5 (20)	85 (15)	0.14	87.5 (15)	77.5 (20)	0.27
Language*	75.5 (12)	81 (18.5)	0.07	77 (12)	72.5 (12)	0.16
Motor*	88 (15)	94 (19.5)	0.26	89.5 (9)	82 (18)	0.24
Social*	85 (12.5)	100 (15)	0.04	95 (25)	85 (5)	0.04

* Median (IQR)

Abstract 464 Table 1 Additional Adjusted Length of Stay and Hospital Costs for Neonates with EA/TEF and CCC[a]

Complex Chronic Conditions[b]	Length of Stay (95% CI)	p-value	Hospital Costs[c] (95% CI)	p-value
Malignancy	79.7 days (50, 109.3)	<0.001	$271,112 (169122, 373102)	<0.001
Respiratory	41.5 days (36.2, 46.8)	<0.001	$151,655 (133360, 166950)	<0.001
Metabolic	23.9 days (14.3, 33.5)	<0.001	$83,886 (50908, 116864)	<0.001
Neuromuscular	18.1 days (11.3, 24.8)	<0.001	$56,733 (33492, 79975)	<0.001
Cardiovascular	17.5 days (12.7, 22.4)	<0.001	$74,093 (57405, 90781)	<0.001
Hematology/immunodeficiency	11.1 days (-1.2, 23.4)	0.08	$70,682 (28416, 112948)	0.001
Congenital/genetic disorder	7 days (2.2, 11.8)	0.004	$24,441 (7990, 40892)	0.004
Renal	4.1 days (-1.2, 9.3)	0.13	$12,733 (-5342, 30808)	0.17
Gastrointestinal	2 days (-39.7, 43.8)	0.92	$21,453 (-122166, 165073)	0.77

[a]Mean (SD) LOS per survivor 54 days (62) with hospital costs of $162,097 ($197,497). Additional LOS in table is relative to having the specified CCC compared to those who did not.
[b]Diagnoses based on ICD-9-CM code groupings.
[c]Total hospital costs are in 2015 U.S. dollars.

Conclusions Despite lower BW and GA of infants with CBH, cognitive, language and motor composite scores were not significantly different with controls at 18 months corrected age. Infants with moderate to severe CBH did not have scores correlated with severe delay in any of the domains evaluated. Further studies including large number of preterm infants are needed to determine the impact of moderate to severe CBH on neurodevelopmental outcomes.

464 LENGTH OF STAY AND HOSPITAL COSTS IN NEONATES WITH ESOPHAGEAL ATRESIA 2005–2015

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Purpose of study Esophageal atresia with or without tracheoesophageal fistula (EA/TEF) has an incidence of 2–4 cases per 10 000 births. These infants require surgical repair and intensive care, and the majority will also have complex chronic conditions (CCC). We assessed predictors of length of stay (LOS) and hospital costs in this population.
Methods used Retrospective cohort analysis of survivors and non-survivors (n=3724) in the Pediatric Healthcare Information System (PHIS) database from 2005–2015 using ICD-9-CM codes to identify admissions within 30 days of life. A multivariate linear regression model adjusting for patient characteristics was used to identify predictors of LOS and costs.
Summary of results The mean (SD) adjusted LOS per survivor was 54 days (62) with hospital costs of $1 62 097 ($197,497). Neonates with EA/TEF and malignancy had the greatest increased LOS (95% CI), 79.7 days (50, 109.3), followed by respiratory, 41.5 days (36.2, 46.8), and metabolic, 23.9 days (14.3, 33.5). These CCC were also associated with higher costs (table 1). After adjusting for CCC, neonates who required mechanical ventilation, ECMO, and TPN were associated with increased costs.
Conclusions Neonates with EA/TEF and concomitant diagnoses of CCC were associated with increased LOS and costs compared to those who did not.

Neonatology – Perinatal Biology III

Concurrent Session

10:15 AM

Saturday, January 26, 2019

465 ASSESSMENT OF THE NUMBER OF NEURONAL PROGENITOR CELLS IN THE BRAIN OF FORMER PRETERM LAMBS

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10.1136/jim-2018-000939.462

Purpose of study Although brain injury happens in chronically ventilated preterm infants, pathogenic mechanisms remain to be identified in part because brain tissue is not

typically part of clinical material for study. We showed that preterm lambs supported by mechanical ventilation (MV) have more apoptosis, and less proliferation, of neurons and glial subtypes compared to non-invasive support (NIS). These results suggest that cell survival may be decreased in the brain of preterm lambs that are managed by MV. Disruption might lead to shift to more progenitor cells as a compensatory response. Neural stem cells give rise to neuronal progenitor cells, which are identifiable by doublecortin. We hypothesized that decreased neuron survival during MV may increase the number of neuronal progenitor cells in the brain.

Methods used Preterm lambs, treated with antenatal steroids and postnatal surfactant, were managed by MV or non-invasive support for either 3d or 21d (n=4/group). We use non-invasive support (NIS, by high-frequency nasal support) as the positive gold-standard for alveolar formation in the lung. At the end of 3d or 21d of respiratory support, cortical brain tissue from the temporal lobe was fixed. We used immunohistochemistry to localize doublecortin-positive neuronal progenitor cells. We used stereology to quantify numerical density of doublecortin-positive neurons in Layer II, using systematic, uniform, random sampling.

Summary of results We found no difference in numerical density of doublecortin-positive neuronal progenitor cells in cortical Layer II of the temporal lobe at 3d (PT MV 2.4 $\pm$0.3 10^5 µm and PT NIS 2.9$\pm$0.5$\times10^5$ µm, respectively) or 21d (PT MV 2.1$\pm$0.2 10^5 µm and PT NIS 2.7$\pm$0.5 10^5 µm, respectively) between the two modes of respiratory support.

Conclusions We conclude that MV of preterm lambs for 3d or 21d does not alter the number of neuronal progenitor cells in layer II of the temporal lobe of the brain. Current analyses are quantifying doublecortin-positive neuronal progenitor cells in white matter and in the periventricular zone. Supported by R01 HL110002 and Division of Neonatology

466 MATERNAL DHA ALTERS FATP2 AND FABP4 MRNA IN THE IGUR RAT PLACENTA

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10.1136/jim-2018-000939.463

Purpose of study Uteroplacental insufficiency (UPI) and subsequent intrauterine growth restriction program sex-divergent disease in offspring. Programming events are often characterized by inappropriate fetal acquisition of fatty acids, such as docosahexaenoic acid (DHA). Fetal acquisition of DHA is regulated by placental transport and binding proteins, including FATP2 and FABP4. We previously demonstrated that UPI alters placental chromatin structure and subsequent expression of transport and binding proteins in a sex-divergent manner. However, the combined effects of IUGR and maternal DHA supplementation on mRNA expression of FATP2 and FABP4 are unknown.

We hypothesize that IUGR and maternal DHA supplementation cause sex-divergent changes in mRNA expression of FATP2 and FABP4 in the rat placenta.

Methods used Term placenta were collected from control and UPI (induced by bilateral uterine artery ligation) Sprague Dawley rats fed either a control diet, or a diet supplemented with 0.01% DHA from mid-gestation to term. Placenta supporting male fetuses (male placenta) and placenta supporting female fetuses (female placenta) were treated as separate groups, n=5–6 per group from different litters. Real-time RT-PCR was used to measure mRNA transcript levels of FATP2 and FABP4 in placental homogenate.

Summary of results Results are UPI as% sex-matched control $\pm$SD (*p=0.05). In male placenta, UPI increased FATP2 mRNA expression (552%$\pm$190%*), which was normalized to control levels with DNA (288%$\pm$152%). In contrast, in female placenta, FATP2 mRNA was not effected by UPI (152%$\pm$56%), however, DHA increased FATP2 mRNA (345% $\pm$38%*). In male placenta, UPI decreased FABP4 expression (36%$\pm$8%*), which was normalized to control levels with DHA (74%$\pm$31%). In female placenta, UPI also decreased FABP4 mRNA, however, DHA did not correct FABP4 mRNA levels (56%$\pm$20%).

Conclusions We conclude that UPI and DHA supplementation have sex-divergent effects on placental expression of FATP2 and FABP4. We speculate that maternal DHA supplementation has sex-divergent effects on chromatin structure, independently of IUGR, in rat placenta. Ongoing studies are evaluating the effect of maternal DHA supplementation on the epigenetic regulation of placental FATP2 and FABP4 genes.

467 THE PPARGAMMA AGONIST ROSIGLITAZONE DOWN REGULATES THE ANGIOTENSIN 2 RECEPTOR IN THE NORMAL NEWBORN LAMB

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10.1136/jim-2018-000939.464

Purpose of study The normal newborn has a hyperfunctioning renin angiotensin system (RAS) that maintains its blood pressure (BP). The literature shows an angiotensin 2 blocker lowered MBP by 10 mm Hg in the normal newborn lamb. The PPARgamma agonist Rosiglitazone, a member of the nuclear hormone receptor superfamily of ligand -dependent transcription factors, has been shown to act on the vasculature and BP through the RAS. We hypothesize that Rosiglitazone can lower BP, angiotensin 2, and aldosterone through its actions on the angiotensin 2 receptor.

Methods used One set of six newborn lambs received 4 mg/kg of Rosiglitazone for 10 days, and the control lambs a placebo for 10 days. MBP was measured on days 1, 3, 5, 8, and 10 via the carotid catheter for 4 hours, and the blood samples collected for plasma renin, aldosterone, sodium, and potassium. Necropsy tissue samples of the aorta, renal artery, and kidney cortex were collected for AT1 and AT2 mRNA and Western Blot.

Summary of results MBP, plasma aldosterone, and plasma angiotensin 2 decreased maximally by day 5 and remained steady. The MBP decreased from 98.16 mm Hg $\pm$3.76 (S.E. M.) to 92$\pm$4.17 ($p<0.002$). Plasma aldosterone decreased from 75.08 ng/dl $\pm$15.88 to 45$\pm$15.88 ($p<0.05$). Plasma angiotensin 2 decreased from 272 pg/ml$\pm$60.57 to 212.66 $\pm$44.87 ($p<0.05$). There was no change in plasma sodium (Na) or potassium (K). The AT1 and AT2 receptor protein was suppressed in the aorta, renal artery, and kidney cortex in the treated newborn lamb.

Conclusions Rosiglitazone suppressed blood pressure, angiotensin 2, and aldosterone in the lamb. Rosiglitazone down regulates the angiotensin AT1 and AT2 receptor protein in the aorta, renal artery, and kidney cortex.

468 LONG TERM HYPOXIA NEGATIVELY INFLUENCES CA^{2+} SIGNALING IN BASILAR ARTERIAL MYOCYTES OF FETAL AND ADULT SHEEP

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Purpose of study Ca^{2+} sparks and waves have been shown to play a major role in the regulation of vascular tone. Without the spark's activation of BK channels, vasculature will constrict, and without waves, total cell calcium decreases and diminishes the ability of Ca^{2+} to do work and therefore dilates. In this study we aimed to observe any impact that long term hypoxia and ontogeny may have on this signaling in basilar arterial myocytes.
Methods used Calcium oscillations were recorded using Fluo-4 loaded basilar arterial myocytes from full-term fetal, or adult sheep. Recordings were made at room temperature in HEPES buffered saline and kept in a normoxic atmosphere. Analysis of sparks was performed using SparkLab 4.3.1, a program allowing us to observe fluorescence spikes at 529 frames per second. We measured wave activity with, LCpro, an automatic program that detects and then analyzes individual regions of interest. Quantification of the Ca^{2+} event's temporal and spatial properties was performed using Prism. Regions of interest that did not have calcium oscillatory activity were excluded from the final dataset by visual analysis of the automated output.
Summary of results In adult animals, LTH decreased spark frequency where fetal LTH animals showed only an increase in spark amplitude. LTH decreases total intracellular calcium from waves independent of age due to a faster decay in the Ca^{2+} signal, decreasing vasoconstriction and increasing cerebral blood flow. Along with producing smaller events, we found that LTH inhibits the cell's ability to respond to depolarization in fetal and adult sheep resulting in basal levels of calcium upon stimulation. LTH and Ontogeny play interconnected roles in signaling as LTH is shown to inhibit distant communication in fetal sheep where, in adult sheep, it stimulates both local and temporally similar Ca^{2+} waves.
Conclusions Overall, the data shows that hypoxia has a negative influence on Ca^{2+} waves, and ontogeny increases depolarization responses for both sparks and waves. These observations illustrate that both altitude and maturation influence Ca^{2+} signaling which play a role in arterial contractility and other mechanisms of cerebral blood flow.

469 POSTNATAL GROWTH RESTRICTION INDUCES PULMONARY HYPERTENSION IN NEONATAL RATS VIA INTESTINAL DYSBIOSIS AND ELEVATED TRIMETHYLAMINE N-OXIDE

K Halloran, S Wedgwood, S Lakshminrusimha, M Underwood. *UC Davis School of Medicine, Sacramento, CA*

10.1136/jim-2018-000939.466

Abstract 469 Table 1 Results

	Normal growth, air (control)	Normal growth, air+TMAO	PNGR +Hyperoxia	PNGR +Hyperoxia +DMB
TMAO, fold	1		1.76±0.22	
l-carnitine, fold	1		0.80±0.02	
Phosphatidylcholines, fold	1		0.91±0.03	
PAT:ET	0.30±0.01		0.21±0.01	0.28±0.03
Fulton's index	0.21±0.01	0.27±0.01	0.37±0.02	0.33±0.02

Purpose of study Pulmonary hypertension (PH) is associated with serious morbidity and mortality in premature infants. Those with fetal or post-natal growth restriction (PNGR) are at highest risk of developing PH. We have previously shown that PNGR augments hyperoxia-induced PH in an established neonatal rat model, and causes intestinal dysbiosis with increased proportion of Enterobacteriaceae. These bacteria create a precursor to trimethylamine N-oxide (TMAO, a metabolite linked with adverse cardiovascular events) via dietary choline and carnitine. We hypothesize that inhibition of bacterial TMAO generation reduces PH in PNGR +hyperoxia rats, while TMAO induces PH in control rats.
Methods used Newborn pups were assigned to litter size of 17 (PNGR) or 10 (normal growth) and exposed to room air or 75% oxygen for 14 days. Some PNGR +hyperoxia pups were treated with DMB (an inhibitor of bacterial TMAO precursor generation) from birth. Some control pups were given TMAO by subcutaneous injection from birth. Echocardiograms were performed to determine the ratio of pulmonary acceleration time (PAT) to pulmonary ejection time (ET), a decreased ratio indicating PH. Right ventricular hypertrophy (RVH) was quantified via Fulton's index, an increased value indicating PH. Plasma levels of l-carnitine, phosphatidylcholine and TMAO were measured via metabolomics.
Summary of results TMAO induced RVH in control pups. Inhibiting bacterial production of the TMAO precursor attenuated PH and RVH in PNGR +hyperoxia pups (table 1).
Conclusions In pups exposed to PNGR +hyperoxia, competition in the gut for nutrients between host and microbes results in decreased plasma phosphatidylcholines and carnitine, and increased TMAO. These molecules may represent biomarkers of PNGR-induced PH in premature infants. Targeting gut microbes with inhibitors to decrease circulating TMAO may improve the outcomes in patients with PH.

470 TOLL-LIKE RECEPTOR 4 ACTIVATION IN POSTNATAL GROWTH RESTRICTION RELATED PULMONARY HYPERTENSION

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10.1136/jim-2018-000939.467

Purpose of study Pulmonary hypertension (PH) is one of the major causes of morbidity and mortality in premature neonates. In very premature infants, postnatal growth

Abstract 470 Table 1

	Normal growth, air	PNGR+Hyperoxia	PNGR+Hyperoxia+TAK-242
PAT:ET	0.30±0.01	0.21±0.01	0.25±0.01
Fulton's index	0.21±0.01	0.37±0.02	0.27±0.02
Lung IκB, fold	1	0.33±0.03	0.81±0.30

restriction (PNGR) is common and increases the risk of developing PH. The mechanisms by which PNGR induces PH are poorly understood. We have shown previously that PNGR augments hyperoxia-induced PH in neonatal rats, and causes intestinal dysbiosis including decreased lactobacilli and increased Enterobacteriaceae. Probiotic *Lactobacillus reuteri* attenuates PH in PNGR +hyperoxia pups indicating a causal relationship between dysbiosis and PH. Enterobacteriaceae activate intestinal toll-like receptor 4 (TLR4) signaling in necrotizing enterocolitis triggering pro-inflammatory pathways. We hypothesize that inhibiting TLR4 pathway in PNGR +hyperoxia reduces lung inflammation and subsequent PH.

Methods used Newborn rats were assigned to a litter size of 17 (PNGR) or 10 (normal growth) and exposed to room air or 75% oxygen for 14 days. Some PNGR +hyperoxia pups were treated with the TLR4 inhibitor TAK-242 by subcutaneous injection. Echocardiograms were performed on day 14 to determine the ratio of pulmonary acceleration time (PAT) to pulmonary ejection time (ET), and decreased PAT:ET indicates PH. Pups were then euthanized and lung tissues harvested. Fulton's index (RV weight divided by LV weight +septum wt) was quantified to identify RV hypertrophy. Lung expression of the NFκB inhibitory protein IκB was analyzed by Western blotting as a marker of inflammation.

Summary of results PNGR +hyperoxia decreased PAT:ET and increased Fulton's index indicating increased PH and reduced lung IkB suggesting increased lung inflammation. Treatment with TLR4 inhibitor reduced PH and lung inflammation (table 1).

Conclusions PNGR +hyperoxia induces intestinal dysbiosis, PH, RVH and lung inflammation. Attenuation of PH, RVH and lung inflammation by inhibition of TLR4 support the hypothesis that activation of intestinal TLR4 by Enterobacteriaceae disrupts the developing gut-lung axis. Treatments to normalize this axis may be clinically relevant in the prevention of PH.

471 AEROSOLIZED PPARγ AGONIST PIOGLITAZONE AND SYNTHETIC SURFACTANT PROTEIN B MIMIC B-YL PREVENTS HYPEROXIA-INDUCED LUNG INJURY IN ADULT MICE

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Purpose of study Acute lung injury (ALI) and its severe form, Acute Respiratory Distress Syndrome (ARDS) are serious conditions and often life threatening. ALI and ARDS are characterized by acute alveolar injury, disrupted epithelial-mesenchymal signaling, oxidative stress, and surfactant dysfunction. Using a rat model, we have recently demonstrated that aerosolized Pioglitazone (PGZ) and synthetic surfactant protein B (SP-B) mimic B-YL prevents hyperoxia-induced neonatal lung injury. However, whether this approach is effective in adult lung injury as well is unknown. We hypothesize that by stabilizing alveolar homeostasis, combined PPARγ agonist PGZ and oxidant resistant synthetic surfactant B-YL blocks hyperoxia-induced adult lung injury.

Methods used 4 to 6 weeks old C57BL/6 adult mice lungs were harvested. Lung explants were placed in 10% FBS/Waymouth medium and exposed *ex-vivo* to 21% or 95% O_2 for 24 or 72 hour. Treatment groups included:1) untreated control 2) B-YL (100 mg/kg) only; 3) PGZ (1 mg/kg) only; and 4) PGZ (1 mg/kg)+B YL (100 mg/kg). Markers of alveolar homeostasis [PPARγ, C/EBPα, SP-C, and cholinephosphate cytidylyltransferase (CCT-α)] and injury (LEF-1 and fibronectin), and apoptosis (Bcl-2 and BAX) were determined by Western analysis. Inflammatory cytokines (IL6, IL1β, TNFα, and MCP1) were measured by qRT-PCR.

Summary of results In normoxia, PGZ only and PGZ +B YL treated groups showed significant increases in PPARγ, SP-C, and CCT-α protein levels ($p<0.05$ vs control). Hyperoxia exposure resulted in significant increases in lung injury markers LEF-1, fibronectin, apoptosis and reduction in lung homeostatic markers PPARγ and C/EBPα ($p<0.05$ vs. 21% O_2). However, PGZ only and PGZ +B YL treated groups showed significant amelioration of hyperoxia-induced alterations in the homeostatic and injury markers (vs. 95% O_2). Similarly, hyperoxia-induced increases in IL6, IL1β, TNFα, and MCP1 were blocked in B-YL alone and PGZ +B YL treated groups.

Conclusions Effectiveness of combined PGZ+B YL in blocking hyperoxia-induced adult lung injury *ex-vivo* sets the stage to test this novel therapeutic approach for adult lung injury *in vivo*.

Neuroscience III

Concurrent Session

10:15 AM

Saturday, January 26, 2019

472 IDENTIFYING THE BRAINSTEM REGION WITH THE HIGHEST DENSITY OF MOTOR NEURON PROGENITOR CELLS AS POTENTIAL CANDIDATE CELLS FOR SPINAL CORD INJURY REPAIR

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10.1136/jim-2018-000939.469

Purpose of study The corticospinal tract connects the primary motor cortex in the brain to the motor neurons in the ventral horn of the spinal cord and ventral interneurons to control voluntary movements. A spinal cord Injury that involves the corticospinal tract reduces or completely eliminates voluntary motor function at that level and the levels below it. The brainstem acts as a relay between the brain and the rest of the body, therefore motor neuron progenitor cells located at

the brainstem have a great potential to serve as relay neurons to connect the severed corticospinal tract with spinal cord ventral interneurons and motor neurons to restore voluntary movements if used for stem cell therapy. For this reason, it is crucial to identify the brainstem region that has the highest density of motor neuron progenitor cells to be used in spinal cord Injury grafts.
Methods used We dissected the brainstem and cervical spinal cord of E14 Fischer rat embryos and used immunostaining to locate PAX6 and NKX6.1 markers to label the dorsal and ventral neural progenitor cells, respectively.
Summary of results The medulla had the highest density of NKX6.1-expressing cells indicating that it has the highest density of motor neuron progenitor cells compared to the midbrain, pons, and cervical spinal cord.
Conclusions These findings indicate that the medulla could be the best candidate to be used in spinal cord Injury grafts to connect severed corticospinal tract and restore motor function.

473 REGULATION OF LYSOSOMES THROUGH MANIPULATION OF LYSINE RESIDUES IN P18

E Chiang, W Lin, J Sun, X Hao, B Diep, M Baudry, X Bi. *Western University of Health Sciences, Pomona, CA*

10.1136/jim-2018-000939.470

Purpose of study Acylation of p18, also known as LAMTOR1, is essential for anchoring the Ragulator complex to endosomal/lysosomal membranes, which has been shown to play critical roles in activation of the mechanistic target of rapamycin complex 1 (mTORC1). Our laboratory has previously reported that UBE3A–mediated p18 ubiquitination and degradation regulate mTORC1 activity, which might have significant implications for the pathology of Angelman Syndrome. Recent studies have shown that the Ragulator complex directly binds BORC and inhibits lysosome centrifugal trafficking in an mTORC1-independent manner. This project seeks to characterize which lysine residues are responsible for UBE3A-mediated p18 ubiquitination and investigates whether p18 ubiquitination is also involved in regulation of lysosomal trafficking and positioning.
Methods used We first engineered p18 proteins with individual lysine to arginine substitutions (K20R, K31R, K60R, K103/104R, and K151R, respectively) via site-directed mutagenesis. Cultured HeLa cells were transfected with GFP-tagged plasmid constructs of the various proteins for 20 hour. Cell images were obtained using a Zeiss LSM 880 confocal laser-scanning microscope at 60x. Quantification was obtained using ZEN software. Images were obtained and analyzed using identical acquisition parameters for all groups.
Summary of results Our preliminary results suggested a significant increased fluorescence intensity of p18-immunopositive puncta with K to R substitution at positions 103/104, as compared to wild-type controls. All the other mutations had little effects on p18 levels.
Conclusions Previous data obtained with His-ubiquitin pull-down assays showed a decrease in p18 ubiquitination with the introduction of a K103/104R mutant. Together, these results suggest that lysine residues 103 and 104 are more likely to be ubiquitinated by UBE3A, resulting in increased p18 levels of the K103/104R mutant. Further investigation will be performed to evaluate the effects of these mutations on lysosomal function.

474 ELUCIDATING THE FUNCTION AND ROLE OF P18 IN LYSOSOMAL POSITIONING

B Diep, J Sun, W Lin, X Hao, E Chiang, M Baudry, X Bi. *Western University of Health Sciences, Pomona, CA*

10.1136/jim-2018-000939.471

Purpose of study mTORC1, also known as mechanistic target of rapamycin complex 1, is involved in protein synthesis and plays a critical role in cellular homeostasis. p18, also known as LAMTOR1, is one of five components of the Ragulator complex and is responsible for anchoring mTORC1 to the lysosomal surface through Rag proteins (RagA,B,C,D). Our laboratory has previously reported that UBE3A, an E3 ligase, is responsible for p18 ubiquitination, resulting in its degradation, thus attenuating mTORC1 activation. We also found that UBE3A deletion (such as found in a mouse model of Angelman syndrome (AS)) resulted in elevated p18 levels. In this study, we focused on understanding the role of p18 in lysosomal localization in AS and wild-type (WT) mice.
Methods used Adult (2~4 month-old) AS and WT mice were used for characterization of p18 localization and lysosome positioning. We first performed double-staining with LAMP2, a lysosomal marker, and p18 or RagA, in brain sections from both AS and WT mice. To determine whether p18 played any roles in lysosome localization, we performed *in vivo* AAV-shRNA p18 knockdown. Stereotaxic AAV injection in the CA1 region of the hippocampus was done in 8-week-old mice. Mice were allocated into experimental or control group in a randomized manner. AAV p18 shRNA or AAV scrambled shRNA constructs were injected bilaterally in CA1. Brains were harvested 4–8 weeks later for immunostaining with LAMP2 and p18. Images were acquired using a Zeiss LSM 880 with Airyscan confocal laser-scanning microscope with a 60X objective. Images for all groups were obtained using identical acquisition parameters and analyzed using ImageJ software (NIH).
Summary of results We found that there was an increase in colocalization of both p18 and RagA with LAMP2 in AS mice, as compared to WT mice. We also found that there was an increase in hippocampal lysosomal content following shRNA AAV-induced p18 knockdown, particularly in the soma and proximal dendrites.
Conclusions These findings suggest that p18 may play a role in lysosome trafficking and/or lysosomal biogenesis. More experiments must be done to more fully understand the role and function of p18 in lysosomal functions.

475 VAGUS NERVE STIMULATION MAY ENHANCE MOTOR LEARNING THROUGH MODULATION OF CHOLINERGIC BASAL FOREBRAIN

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10.1136/jim-2018-000939.472

Purpose of study Vagus nerve stimulation (VNS) is currently used to treat drug-resistant epilepsy and depression. There

are results indicating that VNS may also be useful in treating a wide range of autoimmune, metabolic, and neurological disorders. Preclinical studies show that VNS can induce cortical plasticity and improve rehabilitation after stroke or SCI. Albeit showing tremendous potential, the underlying mechanism of VNS remains ambiguous. We aim to tease apart the specific circuitry that underlies VNS-induced cortical plasticity in a healthy mouse model. Identifying these specific anatomic pathways will help guide future research on the use of VNS in patients with motor deficits and may illuminate the mechanisms of other therapeutic benefits.

Methods used We used immunohistochemistry staining of an immediate early gene, cFos, to identify neuronal activation in key neuromodulatory centers such as the cholinergic basal forebrain and noradrenergic locus coeruleus. We then performed electrophysiological recordings in the basal forebrain during VNS and confirmed neural activity driven by vagal stimulation. To ensure that these changes reflected the state of a brain with increased cortical plasticity, we paired these experiments with behavioral investigations of a motor learning task.

Summary of results Our behavioral findings confirm that VNS, when paired to successful trials, increases learning of a skilled motor forelimb reach task in a healthy mouse model. Immunohistochemically, we see that following vagal stimulation there is increased activity in neuromodulatory regions, which is further solidified by our electrophysical findings that indicating that VNS affects the local field potential and firing rate in cholinergic basal forebrain.

Conclusions These results indicate that the enhancement of motor learning may be mediated by the excitation of basal forebrain, a neuromodulatory nuclei that widely projects to cortex. The projections from vagus nerve to the basal forebrain are still not fully defined, and may be mediated through locus coeruleus. To further dissect this, we will employ tracing experiments using a retrograde tracer in basal forebrain and an anterograde tracer in the Nucleus of Solitary Tract, where vagal afferents terminate.

476 SPINE MORPHOLOGY IN ADULT MOUSE HIPPOCAMPUS WITH CALPAIN-1 OR CALPAIN-2 DELETION

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10.1136/jim-2018-000939.473

Purpose of study Our laboratory recently discovered that calpain-1 knockout (C1-KO) mice have impaired learning while a selective calpain-2 inhibitor enhanced learning. The present study was therefore directed at testing the hypothesis that alterations in learning and memory in C1-KO and calpain-2 conditional knockout (C2-CKO) genotypes could be due to alterations in spine morphology in neurons of the hippocampus, the brain structure critically involved in the initial stages of memory formation.

Methods used 3-month-old male mice for wild type (WT), C1-KO, and C2-CKO genotypes were anesthetized using isoflurane. Following decapitation, brains were quickly removed, and Golgi impregnation was performed according to FD Rapid Golgi Stain Kit instructions (FD Neurotechnologies). 100 µm coronal sections were sliced and mounted on gelatin coated slides (75 × 25 mm, FD Neurotechnologies). 8 slices for each genotype were obtained. Dendritic branches of hippocampal CA1 pyramidal neurons were visualized using a Zeiss light microscope with both a 20X and 60X objective. Using representative light micrograph images, Image J software was used for quantification of filipodia-like and mature mushroom-like dendritic spines. Average dendritic spine density was calculated as the number of spines divided by the length of the dendrite (spines/µm).

Summary of results C1-KO mice exhibit a significantly increased density in filopodia-like spines and a decreased density in mature mushroom spines in basal and apical dendrites of CA1 pyramidal neurons, as compared to WT mice. Conversely, C2-CKO mice exhibit a significant increase in mushroom-like spines and a decrease in filopodia spines in basal and apical CA1 dendrites, as compared to WT mice. The overall spine density remains the same in the 3 genotypes.

Conclusions These results indicate that both calpain-1 and calpain-2 regulate the morphology of dendritic spines, with calpain-1 activity being required for the maturation of dendritic spines. On the other hand, calpain-2 might be needed to limit activity-dependent maturation of dendritic spines.

477 STABILITY STUDIES OF VARIOUS SELECTIVE CALPAIN-2 INHIBITORS IN MOUSE PLASMA AND LIVER HOMOGENATES

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10.1136/jim-2018-000939.474

Purpose of study The overall goal of our studies is to further define the characteristics of various selective calpain-2 inhibitors, as these molecules could be used to elucidate the roles of calpain-2 in TBI-induced neuronal damage and cognitive and motor impairment. Results from these studies will provide further support for their future development for the treatment of a variety of disorders associated with acute neurodegeneration and learning impairment

Methods used Various selective calpain-2 inhibitors (2 mM) were diluted 10 times with mouse liver homogenates or plasma, and incubated at 37°C for various periods of times (0, 0.5, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, and 24 hours). At each indicated time point, 1 µl of the mixture was added to 99 µl of a calpain assay solution containing 5 mM Ca^{2+}, 200 µM Suc-Leu-Tyr-AMC substrate and 100 nM recombinant human calpain-2. Calpain-2 activity was determined by the hydrolysis of the Suc-Leu-Tyr-AMC substrate, and was measured on a plate reader. As a control, 1 µl of plasma alone was subjected to calpain assay and its hydrolysis rate was set as 100% of calpain activity. Residual calpain-2 activity at each time-point reflected the rate of degradation of the inhibitor in plasma or liver homogenates.

Summary of results We found that compound 15 (NA115) dissolved in CAPTISOL, a solvent-free cyclodextrin, was more stable than NA115 dissolved in DMSO in liver (half-life 8.9 hour vs. 9.7 hour) and in plasma homogenates (half-life 4 hour vs. 8.6 hour). Compound 17 (NA117) was also more stable than the original calpain-2 inhibitor (NA101). Half-life of NA117 in plasma was 13.4 hour and 28 hour in liver homogenates. On the other hand, half-life of NA101 in plasma was 7.6 hour and 9.9 hour in liver homogenates.

Conclusions These results indicate that NA117 is more stable than NA115 and NA101. They also indicate that NA115 is less stable than NA101, and that CAPTISOL is a better formulation than DMSO in terms of metabolic stability. Further studies are needed to determine the potential clinical use of these various inhibitors for the treatment of different disorders associated with neuronal damage and/or cognitive impairment.

478 CHARACTERIZING PURKINJE CELL ENCODING OF PAW POSITION

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10.1136/jim-2018-000939.475

Purpose of study Cerebellar dysfunction is a common presentation in children and adults and is a major cause of movement disorders. While the anatomy and physiology of the cerebellum is well described, how the cerebellar circuit contributes to ongoing movement and what role it plays in generating motor dysfunction is unclear. The principle cell of the cerebellar cortex– the Purkinje cell– is thought to integrate motor commands and sensory feedback to encode the body's past and future movements; However, a mechanistic understanding of how Purkinje cell firing encodes movement is lacking. In this project we sought to understand how Purkinje cell simple spike firing patterns the encode movement across the sequence of a reach.

Methods used We used a motion capture system to track mouse paw position during a skilled reaching movement while recording Purkinje cells *in vivo*. Electrophysiological recordings were amplified, digitized at 50 kHz, and streamed into Spike2 software where spike times were extracted and smoothed into a continuous firing rate using a 20 ms Gaussian convolution. Firing rate was then regressed against position, P, velocity, V, and acceleration, A, of the paw:

$$FR(t+\tau)=B_1 + B_2P_{xyz}(t) + B_3V_{xyz}(t) + B_4A_{xyz}(t)$$

Where $FR(t+\tau)$ is firing rate at time t, offset by a value τ ranging from −2000 ms to +2000 ms. The peak R^2 was used to determine the value of τ where FR was most closely related to kinematics.

Summary of results Recordings show Purkinje cells that both increase and decrease their firing rates during reach. When these firing rates and coincident kinematic data were regressed, consistent peaks in the fit of the regression were observed at a τ of roughly −70 ms (R^2 peak values>0.5 for individual reaches). To date, no Purkinje cells have showed a peak R^2 value that occurs at a positive τ.

Conclusions Despite the relatively different profile of bursting and pausing Purkinje cells, their regressions consistently showed negative τ in the regression. This indicates that Purkinje cell simple spikes have a primarily predictive encoding of paw position. Individual regression coefficient values in the regression differ widely between cells, potentially indicating a mechanism of enhancing the dimensionality of Purkinje cell predictive encoding.

NOT PRESENTED – PUBLISHED ONLY

479 NICOTINE-MEDIATED MUTAGENIC EFFECTS AND UNIQUE CYTOKERATIN EXPRESSION IN AFRICAN-AMERICAN TRIPLE NEGATIVE BREAST CANCER CELLS

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10.1136/jim-2018-000939.476

Purpose of study The genetic and epigenetic factors influencing breast cancer heterogeneity are still not widely understood despite it affecting one in eight women in the United States. There are many risk factors that attribute to its incidence, including nicotine. This paper seeks to examine nicotine-mediated mutagenesis of normal mammary epithelial cells and whether antioxidant *n*-acetylcysteine (NAC) can downregulate key players that promote aggressive properties in African-American TNBC cells. Lastly, we further examined unique cell surface proteins that are expressed in African-American (AA) triple negative (TN) breast tumors.

Methods used MCF10-A cells were treated with nicotine and qPCR was performed to determine gene expression of embryonic and cancer stem cell population. MDA-MB 468 cells were treated with increasing concentrations of *n*-acetylcysteine and immunoblot analysis was used to determine if there were changes in expression in cancer-like properties. Various ER +and ER- breast cancer cell lines were used to perform immunoblot analysis for cytokines and epithelial-to-mesenchymal transition (EMT) markers.

Summary of results This study found MCF-10A cells had above a 10-fold increase in level of expression of embryonic stem cell markers and cancer stem cell markers. Although there was no apparent EMT signature, some cytokines were exclusively expressed in AA TNBC. Also, as the concentration of *n*-acetylcysteine increased in the treatment of MDA-MB 468 cells, there was a decrease in embryonic and cancer stem cell markers.

Conclusions Nicotine exposure could increase the risk of developing cancer. *N*-acetylcysteine does show potential to reduce AA TNBC and could be added as a supplement to treatment.

480 A CASE OF A PERSISTENT, PERMEATING, PANCREATIC PSEUDOCYST

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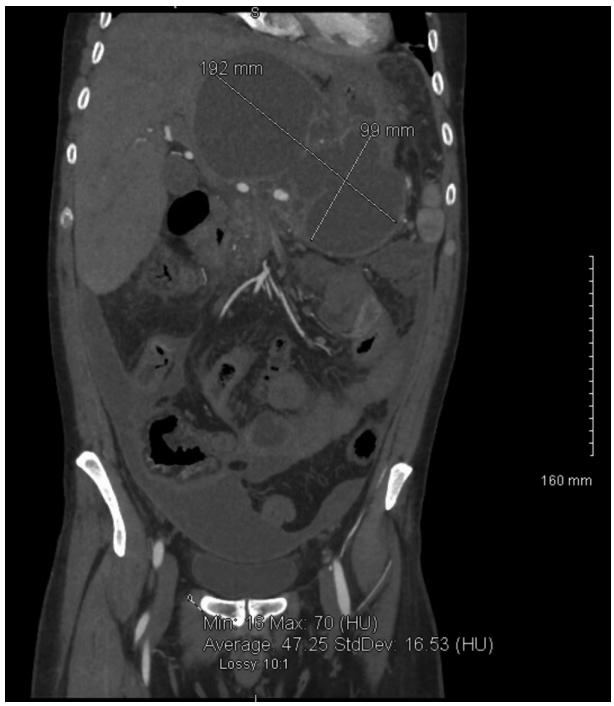
10.1136/jim-2018-000939.477

Case report Pancreatic pseudocyst is a common complication associated with acute and chronic pancreatitis that may be managed medically or surgically. It is imperative to take a multidisciplinary approach in optimizing the patient's clinical status while the pseudocyst fully matures. A 44-year-old Caucasian male with past medical history of alcoholic pancreatitis presented with complaint of abdominal pain associated with nausea, vomiting, and decreased appetite



Abstract 480 Figure 1

for 3 weeks. On physical exam the patient appeared fatigued, abdomen had hyperactive bowel sounds and was diffusely tender to palpation. Combining history and physical examination yield a suspicion of acute-on-chronic pancreatic pseudocyst secondary to alcohol abuse. Laboratory data was significant for leukocytosis, macrocytic anemia, hyponatremia, hypokalemia, and elevated lipase. CT revealed several thinly walled pancreatic pseudocysts. The largest was 19.2 × 9.9×10.5 cm and exerted profound mass effect on surrounding structure. The case was thoroughly discussed with general surgery and interventional radiology to determine the best course of action. This treatment plan included the unconventional approach to perform percutaneous drainage of the largest, thin walled pseudocyst and associated pelvic abscesses in order to provide symptomatic relief and decrease risk of pseudocyst rupture. After the procedure, patient endorsed symptomatic relief including tolerating oral intake and being able to ambulate more comfortably for the duration of the hospital course.

481 OCULOPHARYNGEAL MUSCULAR DYSTROPHY: A RARE GENETIC DISORDER

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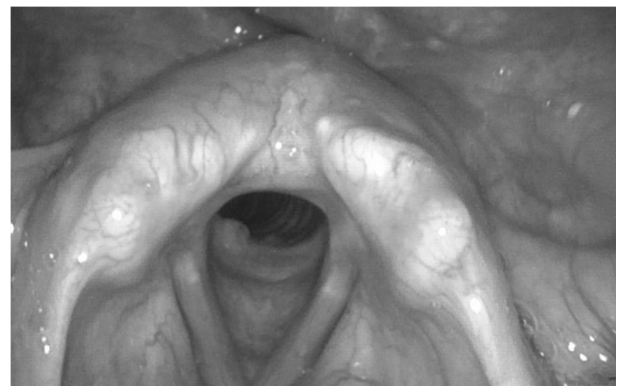
10.1136/jim-2018-000939.478

Case report

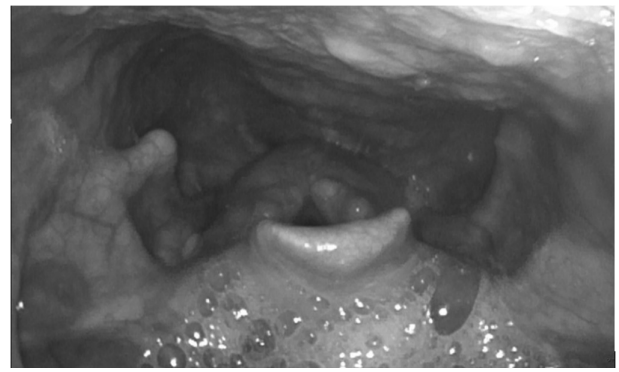
Objective To discuss a unique case of oculopharyngeal muscular dystrophy (OPMD) presenting with ptosis and dysphagia.

Study design A case report with review of literature.

Methods A 64 year old male presenting to the neurology department with bilateral ptosis, dysphagia with both solid and liquids, dysarthria, and extremity weakness and



Abstract 481 Figure 1



Abstract 481 Figure 2

incoordination. Patient was referred to the department of Head and Neck Surgery for dysphagia management. Patient's father has 4 brothers, two of which are affected with OPMD

Results Genetic testing revealed 8 GCG repeats suggestive of an expanded allele in the PABP2 gene, consistent with OPMD.

Conclusion OPMD is a genetic disorder caused by an expanded allele of GCG repeats in the PABP2 gene. Muscular dystrophies with a clear genetic origin should be included in the differential diagnosis of patients with dysphagia and trouble swallowing as it is one of the hallmarks for OPMD.

482 PHYSICAL EXAMINATION IN THE DIAGNOSIS OF PSORIATIC ARTHRITIS

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10.1136/jim-2018-000939.479

Case report Psoriatic arthritis (PsA) is an inflammatory arthritis that is typically suspected when a patient presents with inflammatory poly or oligoarthritis, negative rheumatic markers, and skin lesions consistent with psoriasis. Psoriatic plaques are typically found on external surfaces of knees and elbows. Inverse psoriasis is another skin manifestation characterized by erythematous plaques exhibiting minimal to no scaling. A reported 3%–7% of people with psoriasis develop as inverse form. In 13%–17% of patients, PsA precedes the skin manifestation of psoriasis.

We report the case of 26-year-old woman who presented with subacute oligoarthritis. The patient was seen in an outside ED two months prior with left third and fourth toe pain. After unrevealing imaging, she was diagnosed with occult stress fracture. The patient was then seen one month after with severe right knee and back pain. Aspirate of the right knee showed 15,000 WBC with no organisms. Further diagnostic evaluation resulted in negative ANA, RF, dsDNA, anti-CCP, APLS, and Chlamydia/Gonorrhea. After a right knee washout, the patient was discharged on prednisone taper for undifferentiated inflammatory arthritis. She then presented to our institution after further progression of her oligoarthritis. Other than joint pain, she reported skin lesions on her neck present for the past month.

Upon evaluation, the patient had normal vital signs. Her musculoskeletal exam was notable for mid-lumbar tenderness, right knee swelling and warmth, and tenderness to palpation at second and third metacarpophalangeal joints. A skin exam was notable for a right neck well demarcated erythematous plaque, a right posterior ear scaly plaque, and the gluteal cleft with thin plaques. Radiographs of her hands, feet, and spine were unrevealing. Given severe presentation, she was started on Methotrexate.

This patient with late presentation of skin findings, in atypical distribution, was initially misdiagnosed and appropriate treatment therefore delayed. Her skin involvement was consistent with inverse psoriasis. A high suspicion of PsA should be maintained in patients with poly or oligoarthritic in the setting of any new skin lesions or plaques. Arthritis with seronegative labs that is poorly responsive to systemic steroids should also raise suspicion for PsA or other spondyloarthropathies.

483 HELIOTROPE RASH PRECEDING METASTATIC OVARIAN CANCER

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10.1136/jim-2018-000939.480

Introduction Dermatomyositis is a chronic inflammatory disease of the muscle and skin. The cardinal symptom is a heliotrope rash preceding progressive muscle weakness. The disease is rare, incidence of 0.5–0.89 per 100,000, female to male predominance 2:1. The recognition is challenging but important as there appears to be an association with underlying malignancy as a paraneoplastic phenomenon.

Case presentation A 61-year-old Cambodian female presented to emergency department with subjective fever and sharp, non-radiating right eye pain for three days. No associated neuropathies or muscle pain. On examination, patient was afebrile, hemodynamically stable, a circumscribed raised plaquoid lesion noted on right medial eye, erythematous excoriation of right eyelid consistent with heliotrope rash. Musculoskeletal and neurological examination normal. Initial lab work ruled out infectious, immunological, oncological etiology. CT chest/abdomen/pelvis with contrast and colonoscopy completed showed no underlying malignancy. She was prescribed steroid cream, which helped improve the rash to follow-up outpatient but was lost to follow-up until two years later when she presented to emergency department with complain of severe diffuse abdominal pain, intractable nausea/vomiting, and heavy post-menopausal vaginal bleeding. Repeat CT chest/abdomen/pelvis with contrast showed 10 cm left ovarian mass. Lab finding significant for elevated CA 125 of 1661 U/ml. She underwent surgical resection of tumor. Ultimately diagnosed with stage IV ovarian carcinoma and stage IB1 squamous cell carcinoma of the cervix and initiated chemotherapy.

Discussion Dermatomyositis as a paraneoplastic phenomenon in ovarian cancer has been reported in case reports. The diagnosis should be highly suspected based on clinical findings and inconclusive immunological findings. The interval from recognition of dermatomyositis to development of underlying malignancy is variable but often at time of diagnosis or shortly thereafter. Thus patients should receive initial malignancy evaluation and yearly surveillance for malignancy screening to aid in early detection and management

484 RAMSAY-HUNT SYNDROME COMPLICATED BY BACTERIAL MENINGITIS, SUBARACHNOID HEMORRHAGE AND CEREBELLAR STROKE

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10.1136/jim-2018-000939.481

Purpose of study Herpes zoster oticus, known as Ramsay Hunt syndrome, is the reactivation of the varicella zoster virus in the geniculate ganglion. Reported complications include meningoencephalitis, posterior circulation strokes, and dysphagia. This is an unusual case of Ramsay Hunt syndrome complicated by bacterial meningitis, subarachnoid hemorrhage, and cerebellar stroke.

Methods used Retrospective case report

Summary of results 88-year-old Filipino woman with several comorbidities presented with a three-day history of right ear pain associated with pinna swelling, fever, chills, and right facial droop. The family noted vesicular lesions in the right ear and her trunk prior to presentation. On exam, she was found to have purulent discharge from the ear canal. Neuroimaging showed localized enhancement of the external auditory canal and mastoid. Vancomycin, piperacillin/tazobactam, otic ciprofloxacin, intravenous acyclovir, and methylprednisolone were started. Ear drainage grew methicillin-susceptible *Staphylococcus aureus*. On hospital day three, she developed fever; antibiotics were switched to ampicillin and cefepime. Lumbar puncture revealed opening pressure 11 cmH20, glucose 78, protein 480, white blood cell 1100 with 63% neutrophils consistent with bacterial meningitis picture. Methylprednisolone was stopped after seven days, but her leukocytosis with left shift persisted. Repeat neuroimaging found a right cerebellar hemorrhagic stroke, subarachnoid hemorrhages in the right sylvian fissure around the foramen magnum and superior cervical spinal canal, and the left temporal lobe. Repeat LP found glucose 104, protein 366, RBC 16000, WBC 140 (99% lymphocytes). VZV DNA PCR was negative.

Serial CT images showed improvement in subarachnoid bleeds. She was discharged to an acute rehabilitation facility. She completed a 14 day course of acyclovir and a 21 day course of cefepime and ampicillin. At ten month follow up, the patient had persistent right eye ptosis with cranial nerve VII paralysis.

Conclusions Multiple intracranial complications in Ramsay Hunt syndrome is rare. Physicians should be aware of the risks of intracranial complications in the elderly with Ramsay Hunt syndrome.

485 TUBO-OVARIAN ABSCESS ON FIRE

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10.1136/jim-2018-000939.482

Purpose of study Tubo-ovarian abscess is a polymicrobial adnexal infection that is a sequela of an ascending pelvic inflammatory disease. Treatment can range from total abdominal hysterectomy and bilateral salpingo-oophorectomy to conservative intravenous antibiotics and drainage. This is a case of a tubo-ovarian abscess causing recurrent abdominal and thoracic abscesses due to coryneform *Actinomyces europaeus*.

Methods used Retrospective case report

Case presentation 49 year old female with history of endometriosis, methamphetamine abuse and multiple abdominal surgeries presented with left lower quadrant abdominal pain, fever, nausea, abdominal distension and vaginal bleeding. Imaging revealed multiple pelvic and abdominal abscesses. Empiric ciprofloxacin, ceftriaxone and then metronidazole were started. Source control was attempted with CT guided drainage. Cultures grew *Peptostreptococcus prevotii*, *Prevotella melaninogenica*, *Corynebacterium* species. Vancomycin, piperacillin/tazobactam and gentamicin were added to metronidazole. Unfortunately, she left against medical advice. She returned one week later with dyspnea. Due to respiratory failure and sepsis she was intubated. Imaging showed left sided subdiaphragmatic and loculated pleuritic abscess. CT guided chest tubes and abdominal drain were placed. Cultures grew *Prevotella disiens*, *Candida albicans* and *Corynebacterium* species.Vancomycin, piperacillin/tazobactam, and micafungin were started. *Corynebacterium* species and *C. glabrata* and *albicans* were sent for sensitivities. Due to continued septic shock she underwent exploratory laparotomy, total abdominal hysterectomy with bilateral-oopherectomy, adhesiolysis. Pathology confirmed tubo-ovarian abscess. After 18 hospital days, patient was discharged with a 14 day course of amoxicillin/clavulanate. Speciation and sensitivities of *Corynebacterium* species returned one week after discharge with *A. europaeus* sensitive to penicillin. Amoxicillin 1000 mg was started with plan for 6 months course. One week later, patient returned with recurrent culture negative left pleural effusion that was successfully drained. Patient was discharged with close outpatient follow up.

Conclusions Physicians should be aware of fast growing aerobic coryneform bacteria like *A. europaeus* and others, as it can change long term clinical outcomes.

486 PUZZLING RASH IN A 2 YEAR OLD

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Case report 2-year-old male presented with a generalized itchy rash which was initially papular, then became vesiculopustular starting in the lower extremity, spreading upwards to involve the arms, trunk, and face with a history of fever 3 days prior to admission up to 103° F with no other complaints. None of the family members had any recent rashes. He had been started on oral clindamycin, but referred for further management due to lack of improvement. He had an itchy pustular lesion on the dorsum of his right hand and diffuse, scattered vesicular rash over both lower extremities and trunk, sparing the inguinal area, fingers and toes, with a few of them appearing punched out on the first day. A complete blood count revealed mild leukocytosis, eosinophilia and thrombocytosis. Differential diagnosis included urticaria, insect bites, varicella, herpes simplex virus or coxsackievirus rash with potential bacterial superinfection, impetigo, or scabies. Viral serology, cultures and inflammatory markers were obtained. He was empirically started on intravenous acyclovir and clindamycin. Upon further questioning, the rash had appeared like a mosquito bite while he was near a lake about 3 weeks ago. Itchy rash accompanied by eosinophilia suggested papular urticaria since all viral, bacterial cultures and serology were negative. Clindamycin and acyclovir were discontinued, dexamethasone and antihistamines were started with good results.

Discussion Papular urticaria is a common pruritic hypersensitivity reaction to insect bites which could include mosquitoes, fleas, bed bugs and other insects. Occurring more commonly in children 2 to 10 years of age. It is a very itchy rash, usually described as starting with wheals at the onset which then becomes papular. The treatment modality of choice is usually symptomatic with antihistamines and topical or systemic steroids. Lesions could reoccur even with no recent bites.

Conclusion A good history and high index of suspicion is warranted to diagnose this condition, to prevent unnecessary testing, therapy and also save health care costs. The lesions are mostly self-limited, and treatment is symptomatic. If secondary bacterial infections occur, topical or systemic antibiotics may be needed. Rigorous use of an effective insecticide may prevent insect bites and, accordingly papular urticaria.

487 THE SIGNIFICANCE OF EARLY CLINICAL DIAGNOSIS IN TREATMENT AND PROGNOSIS OF INFANT BOTULISM

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Case report Infant botulism is a potentially debilitating neuroparalytic disease caused by toxins produced by Clostridium botulinum, and rarely by C. butyricum and C. baratii. We present the case of a 2 month old female with no significant past medical history, who presented with weakness and poor feeding with high clinical index of suspicion for botulism. This case is novel for demonstrating efficient clinical diagnosis allowing for early treatment, shortened hospital stay and decreased complications.

Clinical case Our patient was a 2 month old healthy female who was noted to have progressive generalized weakness, an overall tired appearance, poor latch during feeding, as well as constipation for 10 days. The parents denied any ingestion of canned products or honey. On examination, patient was stable with normal vitals and no dysmorphic features. She had bulbar signs including poor pupillary constriction in response to light, lid lag with ptosis on the left, a weak gag reflex, and an almost absent suck reflex. Workup was obtained including labs (CBC, CMP, TSH, CK), blood, urine and spinal fluid bacterial cultures, and imaging (head U/S, KUB, mandibular XR and CXR) all of which were normal. A stool sample was sent for isolation of suspected botulinum pathogen and toxin, but prior to confirmatory results the patient was treated with

Botulism Immune Globulin Intravenous (BIG-IV) about 24 hours after admission. Within 1 week, she had noted improvement with feeding and muscle strength. No pediatric intensive care was required.

Discussion This case represents a rare but life threatening infection and the importance of early identification based on clinical skills rather than diagnostic testing in the treatment of infant botulism. Although the incidence in the United States is about 2 in 1 00 000 live births, it is essential to recognize the symptoms even in the absence of an obvious trigger, as this illness can lead to respiratory failure. About 70% or more of infants with botulism will require intensive care for mechanical ventilation, and the average hospital stay is about 44 days. Strong clinical diagnostic skills can allow for timely treatment of infant botulism and reduce mean hospital stays from 4–6 weeks to about 2 weeks, as well as minimize any hospital-acquired complications.

488 A RARE CASE OF DISSEMINATED COCCIDIOIDOMYCOSIS OF THE GALLBLADDER

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Purpose of study Disseminated Coccidioidomycosis (cocci) of the gallbladder is an extremely rare entity, with only one other case reported in the literature.

Methods used A Retrospective case report

Summary of results A 60-year-old Hispanic male with Diabetes mellitus type 2 and previous right wrist disseminated osseous cocci from past presented with acute onset dyspnea, right upper quadrant (RUQ) pain, and progressively worsening fatigue in the last two weeks. Laboratory studies revealed diabetic ketoacidosis. Thereafter, patient began to develop fevers, hiccups, non-productive cough, and worsening RUQ pain, not responding to empiric broad-spectrum antibiotics. Chest x-ray showed a lingular patchy alveolar density and a 7 mm left mid-lung pulmonary nodule. Computed Tomography revealed numerous cavitary pulmonary nodules in the chest, in addition to a mildly distended gallbladder containing stones, and minimal wall thickening. Gallbladder sonogram demonstrated sludge, calcified stones in the gallbladder, and a 5.6 × 3.5 cm multiloculated pericholecystic fluid collection. Transcutaneous drainage of the pericholecystic fluid collection was performed. Due to discordance between the volume of fluid and the size of the pericholecystic fluid collection seen on imaging, a fistulogram was performed. Fistulogram demonstrated a contained pericholecystic abscess with a sinus tract to the gallbladder, suggesting that a sinus tract had been formed secondary to a chronic underlying manifestation. Subsequently, a cholecystostomy drain was placed into the gallbladder and 10 cc of turbid bilious fluid was evacuated; fungal culture grew Coccidioidomycosis immitis. Cocci serology showed complement fixation of 1:16. Whole body bone scan showed increased uptake at right wrist. He was started on liposomal amphoteric B and continued at the infusion center for 12 week duration. He continues to have cholecystostomy tube until delayed cholecystectomy is performed.

Conclusions Dissemination of coccidioidomycosis to gallbladder is very rare. Despite medical therapy there is a lack of evidence for best timing for cholecystectomy.

489 'A BROKEN HEART GROWS FUNGUS'

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Introduction Heroin intravenous drug abuse(IVDA) remains an aversive epidemic affecting approximately 948,000 Americans reported in the 2016 National Survey on Drug use and Health. Illicit drugs as well as anabolic steroids have been implicated in the development of heart failure (Andersson, 2018). Currently, there is limited literature on invasive *Canadid glabrata* in an otherwise immunocompetent individual with cardiomyopathy.

Case presentation This a physically fit 29 year old male body builder with history of hepatitis C and nonischemic cardiomyopathy secondary to anabolic steroid and IV heroin abuse who presented with worsening SOB, fever and night sweats. Upon admission, he was febrile and tachycardic at a rate of 120bpm with abnormal liver function tests and blood cultures positive for *C. glabrata*. Chest X-ray revealed cardiomegaly with pulmonary vascular congestion. Transthoracic and transesophageal echocardiograms identified a left ventricular ejection fraction of less than 10 percent without evidence of thrombus or vegitation. Hepatitis serology was only positive for HCV and HIV screening was negative. Due to his cardiac findings, aggressive treatment with IV Micafungin 150 mg was initiated and later decrease to 100 mg for a total duration of 2 weeks. There was low suspicion for metastatic foci of infection and repeat blood cultures 48 hours after the last administration of Micafungin were negative for growth.

Discussion Therapy duration for canadidemia has not been well documented and reported cases associated with *C. glabrata* is limited. This case highlights the successful treatment of *C. glabrata* fungemia in an otherwise immunocompetent individual with end stage nonischemic cardiomyopathy and history of IVDA. The incidence of systemic fungal infections found to be associated with *C. glabrata* have increased over the years and it has been previously reported that mortality rates are the highest in *C. glabrata* when compared to other species of *Candida* (Abi-Said, 1997). *C. glabrata* has been found to have fluconazole resistance with an ability to form biofilms, and IV enchinocandin is the preferred first line antifungal regimen (Rodrigues, 2014).

490 GRAPE SEED EXTRACT FOR VERRUCA PLANTARIS

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Abstract 490 Table 1

Complex with E6 protein	Binding affinity (kcal/mol)
Procyanidin C1	−8.6
Procyanidin B1	−8.4
EGCG	−8.3
Quercetin-3-glucoside	−7.9
Procyanidin B2	−7.7
Resveratrol	−6.6
Vitamin A palmitate	−5.4

Abstract 490 Table 2

Complex with E7 protein	Binding affinity (kcal/mol)
Procyanidin C1	−8.0
Procyanidin B1	−7.5
Procyanidin B2	−7.3
Quercetin-3-glucoside	−7.1
EGCG	−7.0
Resveratrol	−6.2
Vitamin A palmitate	−5.0

Purpose of study Grape Seed Extract (GSE) contains procyanidins, resveratrol, and quercetin, which protect against oxidative stress and genomic integrity. They may serve as potential therapeutics against carcinogenesis. In one clinical trial oral GSE reduced hyperpigmentation from chloasma. Similarly, a case study showed topical vitamin A eradicated warts on the back and hands. Human papillomavirus (HPV) strains 1, 2, 4, 60 and 63 are responsible for verruca plantaris, benign epithelial tumors. HPV E6 and E7 oncoproteins inactivate tumor suppressors p53 and Rb to promote cell growth.
Methods used Crystallographic structures were downloaded from the Protein Data Bank. Computational molecular docking analysis was performed with Python Prescription AutoDock Vina. MacPyMol, a molecular visualization program, identified biochemical interactions.
Summary of results High affinity interactions result from stronger intermolecular forces between ligands and targets, resulting in greater binding site occupancy and biologic response. Drug potency is determined by ligand efficacy and binding affinity. These data show procyanidins, particularly C1 and B1, interact with E6 and E7.
Conclusions E6 and E7 may be potential targets for GSE compounds. Pharmaceutical companies may modify them to increase binding affinities and in efforts to prophylax against or treat plantar warts. Future *in vivo* and *in vitro* studies are needed to confirm our results and determine agonist or antagonist activity.

491 NEW DELHI METALLO-BETA-LACTAMASE POSITIVE MULTI-DRUG RESISTANT ESCHERICHIA COLI IN A PATIENT WITH TWIN PREGNANCY

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Introduction Treatment of Enterobacteriaceae infections has become more challenging as the prevalence of multi-drug resistant/carbapenem resistant enterobacteriaceae (MDR/CRE) organisms has increased. New Delhi metallo-beta-lactamase (NDM) is a relatively new carbapenemase with recent geographical dissemination. Treatment options for NDM producing organisms are limited and may include tigecycline or polymyxins. Monotherapy is generally not recommended for serious infections and may result in higher mortality. Combination therapy with ceftazidime/avibactam and aztreonam appears to be synergistic *in vitro* against NDM producing CRE. We describe a case of sepsis due to NDM positive *Escherichia coli* (*E. coli*) with persistent infected nephrolithiasis during pregnancy.
Case description 27 year-old Indian female with twin pregnancy at 24 weeks presented with fever, chills, and dysuria. History was significant for extensive antibiotic use due to multiple complicated UTIs, recurrent infected nephrolithiasis, and recent travel to India where she underwent multiple medical procedures. 3 weeks prior to admission she was treated with ceftazidime/avibactam at another facility for MDR *E. coli*. Workup revealed WBC of 18.7 and urine culture grew MDR/CRE *E. coli* with minimum inhibitory concentration (MIC) $\geq$16 for imipenem and $\geq$16 for meropenem. Xpert Carba-R Assay detected the blaNDM gene. E-test showed susceptibility to fosfomycin (MIC 0.25) and colistin (MIC 1) with resistance to vabomere (MIC 16). Hospital course was complicated by bilateral hydronephrosis requiring ureteral stents. Resolution of clinical symptoms and leukocytosis was achieved with ceftazidime/avibactam plus aztreonam while inpatient and suppressive fosfomycin 3 g twice weekly after discharge.
Conclusion NDM may lead to antibiotic resistance by transfer of a novel genetic sequence via plasmids. Clinical suspicion for NDM producing organisms should be high with high MICs for carbapenems and recent travel to India or Pakistan. In order to optimize treatment outcomes and minimize use of second-line, more toxic agents combination therapy with ceftazidime/avibactam plus aztreonam should be considered when treating NDM producing organisms in immunocompromising conditions such as pregnancy.

492 THE SIGNIFICANCE OF UNKNOWN VARIANTS

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Introduction Hereditary Spastic Paraplegia (HSP) is a rare cause of neuromuscular deficits. Occurring in 1–10/100,000. It is characterized by gait ataxia and spastic paresis. HSP can be subdivided into two types: pure and complicated. While pure HSP is as described above, complicated can present with many other symptoms. Subtype SPG31 accounts for 3% of HSP patients. This subtype classically presents as pure HSP, but rarely as a complicated type with peripheral neuropathy.
Case 15 y/o male presents w/three years of progressing atrophy and weakness of his distal musculature and sensory loss. Patient has numbness, unsteady gait, and weakness. PMH: None SocHx: Benign FHx: Benign ROS: Benign

PE: lower extremity distal atrophy, pes cavus, hammer toes, wide based gait, footdrop b/l, overall tone was spastic, brisk patellar reflexes b/l, positive Babinski b/l

DDx: Diabetes, Charcot Marie Tooth, familial amyloid polyneuropathy, CIDP, ALS
Tests MRIs normal; EMG showed a sensorimotor axonal neuropathy; TSH, CMP, CBC, CMT normal
Treatment Patient was thought to have a hereditary motor sensory neuropathy. Referral was made to a neuromuscular specialist after results for CMT panel came back negative
Referral Special attention was given to the brisk reflexes and ankle clonus. Patient continued to have progressing ataxia.

DDx of referral: Familial Spinal Atrophy, HIV, adrenomyeloneuropathy, Hereditary Spastic Paraparesis, lead poisoning, West Nile, ALS, copper def., B12 def
Testing B12 normal, folate normal, copper and ceruplasmin low, VLCFA abnormal C26:22 ratio, HSP testing showed variant of unknown significance of SpG31

Treatment Patient considered to have a myeloneuropathy. Dr. Hubner, and Dr. Beetz were contacted on the significance of a SpG31 variant. Patient given copper supplementation and baclofen 10 mg TID. Using this patients' information with others it has been determined that SpG31 is significant and rarely includes a polyneuropathy.
Discussion This case demonstrates a rare complication of an uncommon disease. It also shows the possibility of an anchoring bias and using the whole physical exam for a correct differential. It demonstrates the importance of using cohort studies to determine the clinical cause and significance of genetic variants

493 RAPID DECOMPENSATION OF A TODDLER THAT TESTED POSITIVE FOR METHADONE

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Case report A 21 month old male with history of reactive airway disease was found unresponsive in his crib by his grandmother. There were no significant symptoms other than mild nasal congestion prior to being found unresponsive. When the emergency medical providers arrived, he was found to apneic and bradycardic. Chest compressions were not required but bag mask PPV was given. On arrival to the hospital, he continued to be apneic with a GCS of 3. Thus, he was promptly intubated. The pupils were noted to be pinpoint and sluggish which normalized with Narcan. Initial labs were significant for a leukocytosis, mild transaminitis, and mild elevated BUN and creatinine. Chest x-ray, EKG, urine drug screen, acetaminophen and salicylate levels were unremarkable. Comprehensive drug screen taken but results were sent outs. Patient was admitted to the PICU and started on a Narcan drip. In the PICU, he was positive for rhinovirus, but other infectious work up including meningitis panel were negative. A brain MRI showed acute infarction of bilateral cerebellar lobes, a mass effect on the fourth ventricle and subsequent mild hydrocephalus. MRA brain did not show a thrombus or hemorrhage. An EEG was consistent with diffuse encephalopathy. He was also noted to have nonspecific T wave changes on repeat EKG and up trending troponin levels. An echocardiogram showed compensated dilated cardiomyopathy with abnormal wall motion of the septum. Extubated on day 2. Late on day 3, patient was found to be bradycardic, hypotensive with unreactive, unequal pupils. A stat CT head confirmed worsening hydrocephalus with a low lying cerebellar tonsils. An extra-ventricular device was placed to relieve the increase ICP. The patient was subsequently transferred for an emergent occipital decompressive craniotomy. Repeat MRA revealed a superior sagittal sinus thrombus. A thrombophilia and metabolic work up did not reveal any significant abnormalities. The comprehensive urine drug screen later resulted positive for Methadone. Non-accidental trauma work-up was negative. After a prolong stay in inpatient rehabilitation, patient went home with mother after she was cleared by CPS. The patient currently is getting outpatient OT, PT and speech therapy but continues to struggle with right hemiparesis and dysphagia

494 EVALUATION OF THE EFFICACY OF AUTOLOGOUS PLATELET-RICH PLASMA IN POST-OPERATIVE MOHS SURGERY PATIENTS: A PROSPECTIVE CASE SERIES

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Case report Autologous plasma rich in platelets (PRP) is a derived blood product whose application and value in both clinical therapy and the cosmetics industry is still being assessed. Although the effectiveness of PRP as an antibacterial and regenerative agent in wound healing trajectories highlights its potential therapeutic value, more studies are still needed to understand this possible therapy's effectiveness, mechanism of action, and ideal dosing; especially in post-operative Mohs surgery patients. In this study, we characterized the efficacy of autologous PRP on the closure of wounds healing by second intent in patients who had recently undergone Mohs surgery for the removal of a non-melanoma skin cancer. After screening and selection of suitable patients for our study, we administered autologous PRP to these select patients' wounds and followed their healing trajectories over a 12 week period, assessing for regression, improvement, and complete recovery of their wounds via use of the Bates-Jensen Wound Assessment Scale.

495 PERONEUS TERTIUS COMPARTMENT SYNDROME IN NOVEL POPULATION

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Case report Compartment syndrome is a well described condition in which pressure builds up within an extremity muscle compartment resulting in ischemic damage to the contained nerves and muscles. A lower extremity compartment syndrome of the anterior extensor retinaculum (AER) has been previously described in a pediatric population. However this case series reports five adult cases with similar symptoms termed peroneus tertius compartment syndrome (PTCS). The peroneus tertius compartment is covered by the anterior extensor retinaculum of the ankle and contains the deep peroneal nerve, the peroneus tertius muscle, some of the fibers of the extensor hallucis longus (EHL), and the tendons of the extensor digitorum longus and tibialis anterior. In these five cases, distal tibia/fibula fractures resulted in swelling and the characteristic signs and symptoms of a compartment syndrome including writhing pain out of proportion to the injury, pain localizing to the dorsal ankle on passive plantar flexion of toes that was worse on plantar flexion of the great toe, and loss of sensation in the first web space. Peroneus tertius compartment pressures ranged from 50–110 mm Hg at time of surgery. No direct link to fracture pattern was found but all five cases had a fibular fracture above the ankle mortise indicating the need for awareness with such fibular fractures. Recommended treatment for PTCS involves release of AER anywhere along its course between the tibia and fibula. In four of the five cases, the AER was released just medial to the fibular insertion. The final case of the pilon fracture was released in the central portion of the AER during the open

reduction and internal fixation of the pilon fracture. If left untreated PTCS could result in weakness or loss of function of the peroneus tertius muscle, contracture of the EHL, likely permanent loss of sensation of the first web space, and loss of function of the downstream muscles innervated by the deep peroneal nerve, extensor digitorum brevis and extensor hallucis brevis. Further three cases also had transient posterior tibial nerve involvement indicating possible additional complications of PTCS. These five cases stand to educate about the presence of PTCS in the adult population and its negative long term sequelae.