University of Colorado **Anschutz Medical Campus**

36th ANNUAL STUDENT RESEARCH FORUM

COLLEGE OF NURSING

GRADUATE SCHOOL

SCHOOL OF DENTAL MEDICINE

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OF PHARMACY SCHOOL OF

PUBLIC HEALTH

DECEMBER 8, 2021
ANSCHUTZ MEDICAL CAMPUS
Virtual

36th ANNUAL
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS
STUDENT RESEARCH FORUM

Wednesday December 8, 2021

Poster Sessions
1:00-2:00 pm
2:00-3:00 pm

ANSCHUTZ MEDICAL CAMPUS
Virtual

The Student Research Forum organizing committee wishes to acknowledge, with gratitude, the financial support for student research provided by:

The University of Colorado Denver
School of Medicine Dean's Office *And*
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Poster Session Judges

The organizing committee wishes to acknowledge their appreciation to the following serving as judges for the Annual Student Research Forum. Without their generous contribution of time and talent the forum would not be possible. Thank you!

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The organizing committee is especially grateful to the following schools, departments, divisions, and programs for their generous contribution of financial support for the forum and/or a $320 research prize awarded to the top scoring posters at the event.

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The Graduate School

Primary Student Presenter: Amal Alhadad

Additional Presenter(s): Arya Tehrani, Charisse Surio

Presenting School: Pharmacy

Degree Seeking: PharmD

Year: 4th

Mentor: Meghan Jeffres

Poster Title: Clinical outcomes of Ceftriaxone 1 gram vs. 2 gram daily for the treatment of gram-negative Enterobacteriaceae bloodstream infections

Final Category: Microbiology and Infectious Diseases

Abstract:

Within our health system empiric ceftriaxone dose for patients, outside of central nervous system (CNS) infection, is inconsistent. It is theorized that a regimen of ceftriaxone 2 g daily is more likely to achieve pharmacodynamic goals and therefore improve patient outcomes. However, increasing dose exposure of antibiotics may lead to more adverse events including Clostridium difficile infection (CDI). This study evaluates the clinical outcomes of patients with gram-negative Enterobacteriaceae bloodstream infections when treated with ceftriaxone 1 gram (g) versus 2 g daily.

Methods: This study was conducted as a retrospective chart review of patients receiving either 1 g every 24 hours or 2 g every 24 hours of intravenous ceftriaxone for gram negative bloodstream infection. Patient data was pulled from the University of Colorado Health electronic medical record from January 1, 2018 through August 1, 2021. Patients ≥ 18 years of age with evidence of gram negative Enterobacteriaceae bloodstream infection, received either 1 g or 2 g of ceftriaxone for a minimum of 72 hours were included. Patients receiving both 1 g and 2 g dosing regimens were excluded. The quick Pitt score (qPitt) was used to determine the patients' level of severity using 5 domains: hypothermia, hypotension, respiratory failure, cardiac arrest and Glascow coma score (GCS). The primary outcome was frequency of treatment failure 72 hours post initiation of ceftriaxone therapy, and secondary outcomes included 30-day mortality, 30-day infection-related readmission, and frequency of CDI within 60 days of index infection. Data was analyzed using Fischer's exact analysis using SPSS version 27.

Results: A total of 405 patients were included in the cohort, 168 patients in the 1 g group and 237 patients in the 2 g group. Of the cohort, 68.9% were female with an average age of 65 years, and the main source of infection was pyelonephritis (84.1%). Baseline characteristic data between the 1 g and 2 g groups of height ($p=0.02$), weight ($p=0.01$), race ($p<0.01$), and duration of therapy ($p<0.01$) were statistically significant. There was no difference between groups in any other variables. Patients' qPitt scores between the 1 g versus 2 g groups were similar: 0 (46.4% vs 48.9%), 1 (35.1% vs 31.2%), 2 (12.5% vs 13.9%), 3 (5.4% vs 5.5%), 4 (0.6% vs 0.4%).

Treatment failure between 1 g versus 2 g groups was not different (16.7% versus 21.1%, p=0.31). No significant difference was observed between the two groups for 30-day mortality (1.2% in 1 g group versus 3.4% in the 2 g group, p=0.21), 30-day infection related readmission (4.2% in 1 g group versus 5.5% in the 2 g group, p=0.65) or CDI (0% in 1 g group versus 0.4% in the 2 g group, p=1.00).

Conclusion: In this retrospective cohort analysis, the frequency of early treatment failure was not different between patients receiving 1 g versus 2 g daily of ceftriaxone. Patients with gram negative bloodstream infections secondary to pyelonephritis do not appear to need higher doses of ceftriaxone to achieve positive clinical outcomes.

Primary Student Presenter: Kseniya Anishchenko

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Tracy Cushing

Poster Title: The Knowledge and Attitudes of Pediatricians Toward Whole Food Plant-Based Diets

Final Category: Education

Abstract:

Purpose: There has been abundant evidence showing the health benefits of a plant-based diet, yet many physicians do not stress the importance these diets as an important aspect of chronic disease prevention and treatment. Pediatricians have an important role in dietary education of children, and there is scarce data focused specifically on pediatricians' knowledge regarding plant-based nutrition. Our study assessed pediatrician's general nutritional knowledge and attitudes regarding whole food plant-based diets.

Methods: A cross-sectional study was done using a previously implemented questionnaire that was distributed among a sample of pediatricians in the United States. Survey items were scored based on nutrition knowledge and attitudes toward plant-based diets, and then analyzed and compared among participants.

Summary: Of 117 respondents, 95 (81.1%) were general pediatricians and 75 (64.1%) were following a vegetarian or semi-vegetarian diet. 42 (36%) of the participants had been in medical practice for more than 15 years. 94 (80.3%) of participants received ≤10 hours nutrition education in medical school, while 77 (65.8%) of participants had ≤10 hours of nutrition-specific continuing medical education since residency. In terms of pediatric-specific medical knowledge, 73 (62.4%) of participants were uncertain or disagreed with the notion that lacto-vegetarian diets for children are similar to pediatric dietary recommendations for reduced chronic disease risk, and 21 (17.9%) did not agree that children can grow and develop normally on vegetarian and vegan diets.

Conclusions: Pediatricians are exposed to very little nutrition education hours during medical school and in their continued education training. A significant portion of pediatricians in our survey had low average knowledge base in vegetarian nutrition. Increasing education hours for pediatricians regarding plant-based diets may help them better counsel their patients on their dietary decisions.

Primary Student Presenter: Leslie Barnard

Presenting School: Public Health

Degree Seeking: PhD

Year: 2nd

Mentor: Marian Betz

Poster Title: The effect of Extreme Risk Protection Orders on the Concept of Voluntary Out-of-Home Firearm Storage: Results from a Qualitative Study in Two States

Final Category: Healthcare and Public Health

Abstract:

Purpose of Study: Reducing firearm access during a crisis can prevent suicide. Multiple states have developed storage maps identifying locations for voluntary, temporary out-of-home firearm storage. Non-voluntary options such as Extreme Risk Protection Orders (ERPOs) allow designated "petitioners" to request the temporary restriction of firearm access for someone with imminent risk of harm to self or others. However, ERPO laws have been controversial, and their implementation occurred at the same time as voluntary programs. We sought to understand how ERPO laws impact views of voluntary storage options.

Methods: Between 10/2020 and 5/2021, the study team interviewed stakeholders in Colorado and Washington State, including firearm ranges and retailers, law enforcement agencies (LEAs), and public health and firearm rights organizations. Semi-structured interviews were conducted and recorded. We used a mixed deductive and inductive approach to code transcripts and analyzed coded data to identify dominant themes.

Summary of Results: We conducted 95 interviews with 100 participants (31 firearm retailers/ranges, 17 LEAs, 52 organizations). Themes about the effect of ERPOs on voluntary, temporary firearm storage were views or concerns that: (1) ERPOs further alienate those who might have sought or offered voluntary storage by (a) putting all parties (LEA and firearm owners) at risk of physical harm during enforcement and (b) their potential to be used inappropriately, and (2) voluntary storage providers may or may not be willing to store firearms resulting from an ERPO.

Conclusion: While both voluntary and non-voluntary firearm storage approaches can be used to reduce firearm suicide risk, the simultaneous presence of both options can raise challenges. Our study suggests the need to clearly distinguish between voluntary and non-voluntary storage. Understanding stakeholder views on voluntary and non-voluntary storage options support the development of acceptable and feasible programs for out-of-home firearm storage during times of suicide risk.

Primary Student Presenter: Moncia Bianchini

Presenting School: Pharmacy

Degree Seeking: PhD

Year: 3rd

Mentor: Richard Lindrooth

Poster Title: Impact of High-Dose vs Standard-Dose Influenza Vaccine on Respiratory-Related Hospitalizations: A Fuzzy Regression Discontinuity Design

Final Category: Microbiology and Infectious Diseases

Abstract:

The high-dose (HD) influenza vaccine is approved for use in adults ages ≥65 with evidence for reducing influenza infections and hospitalizations. This study aimed to determine the impact of the HD vs standard-dose (SD) influenza vaccine on hospitalizations among adults ages 50-80. METHODS: A fuzzy regression discontinuity design was used to estimate the causal effect of the HD vaccine on respiratory hospitalizations. This design takes advantage of the discontinuity in likelihood of receiving the HD vaccine at age 65 to compare the outcomes of adults just older and younger than 65. Data was extracted from IQVIA claims database for adults with an insurance claim for a HD or SD vaccine during the 2012-2018 influenza seasons. Outcomes and covariates were identified using diagnoses codes. The primary outcome was respiratory-related hospitalization. Covariates included demographics, comorbidities, and history of receiving the HD vaccine. RESULTS: The study included 384,180 individuals: 0.3% of adults 50-64 received the HD vaccine vs 52% of adults 65. Receipt of the HD vaccine decreased the probability of respiratory-related hospitalizations by 0.5% points (95% CI -0.8%, -0.2%) vs the SD vaccine (p=0.002) for adults who received HD because it was approved for their age group. Results were robust to specification and sensitivity tests. CONCLUSIONS: The results of this study show the HD vaccine reduced the rate of respiratory-related hospitalization compared to the SD vaccine among adults who received HD vaccine because of their age. The results suggest that extending approval to adults ages 50-64 would reduce respiratory-related hospitalizations among those who become eligible.

Primary Student Presenter: Caitlin Blades

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Aaron Mason

Poster Title: An Objective Assessment of Outcomes of Endoscopic Sagittal Craniosynostosis Release

Final Category: Surgery

Abstract:

Introduction: One in 2,200 newborns is diagnosed with craniosynostosis. The sagittal suture is involved most often. Endoscopic strip craniectomy with post-operative helmet-guided re-modeling has risen in popularity over the past decade as a treatment method. An objective outcome of results has been elusive. Since machine learning now enables an objective evaluation of head shape, we sought to determine if the head shapes of patients treated endoscopically for sagittal craniosynostosis were normal at the end of treatment.

Methods: After IRB approval, patients treated with endoscopic strip craniectomy/helmet re-modeling between 2017 and 2021 were collected from our institutional EPIC database. Patients with pre and postoperative calvarial 3D imaging were included in the assessment. Objective evaluation of head shape using an existing machine learning algorithm based on a normative statistical model (age 0-10 years) was performed at the end of the treatment course to calculate the risk of patients presenting abnormal head shapes associated with craniosynostosis.

Results: Twenty-six patients were identified and analyzed. Our quantitative evaluation method identified 19/26 (73%) with a normal head shape post-operatively at discontinuation of helmet therapy with risk scores ranging from 0.79% to 20%. Within the group with normal outcomes, 4/19 (21%), 9/19 (47.5%), 4/19 (21%), and 2/19(10.5 %) were operated upon at 2-3, 3-4, 4-5, and 5-6 months of age, respectively.

Conclusion: In this cohort, objective evaluation of surgical outcomes shows that minimally invasive endoscopic treatment followed by helmet-guided remodeling successfully creates normal head shapes in 73% of patients with sagittal craniosynostosis. An analysis of those for whom treatment failed may identify reasons for which treatment was not successful.

Primary Student Presenter: Rachael Branscomb

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Lori Sussel

Poster Title: Comparative Analysis of Fetal Ferret Pancreas Development

Final Category: Metabolism and Endocrinology

Abstract:

Comparative Analysis of Fetal Ferret Pancreas Development. RL Branscomb, (M.D., SOM), JF Engelhardt, and L Sussel, Barbara Davis Center for Diabetes, Aurora, CO.

Cystic fibrosis (CF) is a progressive, multisystemic disease that affects more than 30,000 individuals in the US. Cystic fibrosis-related diabetes (CFRD) is the most significant co-morbidity, impacting >50% of adult patients. Studies in young children with CF indicate that defects in islet function is an early clinical feature of CF, but the cause of this dysfunction remains controversial. To begin to understand the potential origins of CFRD, it would be optimal to model CFRD in an animal model; however, CFRD is not well-modeled in mice. Alternatively, CFRD occurs spontaneously in the ferret model of CF, suggesting this would be a useful model to characterize whether there is a developmental origin of pancreas dysfunction in CF patients. Because the development of the fetal ferret pancreas has not yet been characterized, the purpose of this project is twofold: 1) to characterize wild type ferret pancreas development as a baseline for comparison with a CF ferret model, and 2) determine whether pancreatic developmental defects contribute to CFRD in adults. Fetal ferret tissues were embedded and sectioned, and immunohistochemistry was employed to identify key markers of development. In this study we demonstrate that the ferret, mouse, and human pancreas appear similar in early development, but as development progresses, ferret pancreatic islet formation appears more similar to humans. Future studies will use similar analyses to determine whether CF ferrets display altered pancreatic islet development.

Primary Student Presenter: George Burnet

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Barry Platnick

Poster Title: Muffins and Meditation: Combating Burnout in Surgical Residents. G Burnet (MD, SOM), C Platnick (MD, SOM), A Sauaia (MD, Ph.D), K Jaiswal (MD), and KB Platnick (MD), Department of Surgery, University of Colorado Anschutz Medical Campus, Denver, CO.

Final Category: Surgery

Abstract:

Muffins and Meditation is a wellness program for University of Colorado surgical residents and medical students. This study was designed to assess the impact of the program through validated tools measuring mindfulness, self-compassion, flourishing, and burnout. Our hypothesis was that participants with more frequent attendance would: 1) be more mindful and self-compassionate and 2) experience less burnout and more flourishing. An optional one-hour weekly breakfast conference was led by a senior surgical faculty member, and the time was protected from all clinical duties. Following a guided meditation, participants were given time for reflection and dialogue about their training experiences or led in a wellness exercise. TRANCE (tolerance, respect, anonymity, non-retaliation, compassion, egalitarianism) principles were utilized to create a safe and open environment. Residents were surveyed through REDCap at the end of the study period. When answering the two-question Maslach Burnout Inventory, 35.7% of residents reported feeling burned out by their work once a week or more, and 29.7% reported feeling more callous toward people once a week or more. After multivariate analysis, the only independent predictors of increased burnout were “not being married or in a committed relationship”, lower positive affect, and higher negative affect. Qualitative feedback was overwhelmingly positive, and residents expressed gratitude for the conference, the opportunity for self-reflection, and open dialogue with attendings and colleagues. Although we failed to identify independent associations between attendance and burnout rates, flourishing ratios, self-compassion, or cognitive and affective mindfulness scores, our survey results provided qualitative evidence of the value this conference holds for residents.

Primary Student Presenter: Melissa Carpenter

Presenting School: Medicine

Degree Seeking: MD

Year: 1st

Mentor: Mark Myerson

Poster Title: Morphology Features of the Calcaneus and Arch Height in Patients with Insertional Achilles Tendinopathy

Final Category: Surgery

Abstract:

Within the adult population, insertional Achilles tendinopathy with calcification and degeneration of the insertion is a common disorder. Presently, there is little understanding of the etiology, pathogenesis, and biomechanics of this disease entity, although excessive tension at the Achilles insertion associated with calcaneus abnormalities has been considered a contributing factor. Multiple imaging modalities have been used to investigate a possible correlation between calcaneus morphology and insertional tendinopathy. However, no prognostic criteria have yet been found. In this study, it was hypothesized that there are differences in both calcaneus morphology and foot arch height in patients with insertional Achilles tendinopathy and individuals without. Medical records of 87 patients with symptomatic Insertional Achilles tendinopathy (study group) and 30 patients with neither clinical nor radiographic signs of Achilles tendinopathy (control group) were retrospectively reviewed. To assess the morphological features of the calcaneus in the two groups, a new angular analysis, "The Posterior Tuberosity Inclination Angle (PTIA) was introduced. It is a combination of the shape of the posterior calcaneal tuberosity (Posterior Tuberosity Angle) and the position of the Calcaneus (Calcaneal Pitch Angle) measured in weightbearing lateral view radiographs. These three angles were used to assess the morphology of the calcaneus. The ratio of the Medial Cuneiform Base Height/Cuboid Height, and the ratio of the Medial Cuneiform Base Height/Fifth Metatarsal Height were used to assess the arch height. The hindfoot alignment was evaluated in the study group with further dividing patients into three subgroups (a neutral alignment heel, a varus heel, and a valgus heel). The morphology of the calcaneus was compared between the study and the control groups. In the study group, both the morphology of the calcaneus and the arch height were compared among the three subgroups, and correlation between calcaneus morphology and hindfoot alignment, calcaneus morphology and arch height were studied as well. Statistical analysis revealed the study group had a significantly larger PTIA (7.12 degrees of difference) and Posterior Tuberosity Angle (7.77 degrees of difference) than the control group. Within the study group, 61 patients had a neutral hindfoot alignment, 15 patients had a varus hindfoot, and 11 patients had a valgus hindfoot. Among these three subgroups, there were significant differences of the Calcaneus Pitch Angle, PTIA, and Medial Cuneiform Base Height/Cuboid Height between the valgus and varus heel groups, and valgus and neutral heel groups. PTIA had a significant correlation with the ratio of

Medial Cuneiform Base Height/Fifth Metatarsal Height. The newly introduced angular measurement (PTIA), reports information of both the position and the shape of the calcaneus, is found to be significantly higher in patients with insertional calcaneus tendinopathy than the controls. The findings of this study can guide diagnosis and surgical treatment planning for treatment of insertional Achilles tendinopathy in particular when the patient has combined malalignment issues in the hindfoot and midfoot.

Primary Student Presenter: Lorraine Davis

Presenting School: Graduate

Degree Seeking: PhD

Year: 4th

Mentor: Daniel Sherbenou

Poster Title: MYC Inhibition Overcomes IMiD Resistance in Heterogeneous Multiple Myeloma Populations

Final Category: Hematology and Oncology

Abstract:

Multiple myeloma (MM) is an incurable plasma cell malignancy. Immunomodulatory drugs (IMiDs) are critical for disease control, yet resistance develops. IMiDs act by inducing Cereblon-dependent degradation of the transcription factors IKZF1 and IKZF3, which leads to IRF4 and MYC downregulation (collectively termed the "Ikaros axis"). We therefore hypothesized that in IMiD resistant MM, IMiDs fails to downregulate the Ikaros axis. To measure IMiD-induced Ikaros axis downregulation, we designed a flow cytometry assay to measure relative IKZF1, IKZF3, IRF4 and MYC protein levels in MM cells following IMiD treatment. We performed this in MM cell lines and patient samples grouped by ex vivo IMiD sensitivity. Our hypothesis was supported in MM cell lines, as resistant lines lost IMiD-induced decrease of all Ikaros axis proteins. However, when assessed in patient MM cells, we observed IMiD-induced downregulation regardless of IMiD sensitivity. We next used mass cytometry in patient samples to reveal that individual Ikaros axis proteins were differentially expressed between MM subpopulations. When correlating this with ex vivo IMiD sensitivity of subpopulations, we observed that low IKZF1/3 corresponded to resistance. Interestingly, most resistant populations still expressed MYC. We therefore assessed whether MYC is critical in resistant cells and found that 88% (7/8) of resistant patient samples were sensitive to MYC inhibition. While our findings in patients did not support our initial hypothesis, our data suggest a mechanism where the Ikaros axis no longer drives MYC expression in IMiD resistant MM, and resistant MM cells remain dependent on MYC. This suggests targeting MYC may be an effective strategy to eradicate IMiD resistant MM.

Primary Student Presenter: Eva Dindinger

Presenting School: Graduate

Degree Seeking: PhD

Year: 2nd

Mentor: Jeanelle Sheeder

Poster Title: Risk of luteal phase pregnancy with modified intrauterine device insertion eligibility

Final Category: Child-Maternal Health and Reproductive Services

Abstract:

Objective: To determine rates of luteal phase pregnancy (LLP) in adolescents and young adults (AYA) initiating intrauterine devices (IUDs) using modified insertion guidelines.

Methods: We assessed a randomly selected cohort of AYA receiving IUDs at a Title-X clinic between 2009-2019. IUD manufacturers' guidelines state that IUDs should only be inserted following a negative pregnancy test, ≤7 days of last menstrual period (LMP) or switching from prescribed contraception. In this cohort, IUDs could also be inserted if people reported abstinence or 100% condom use. We created two groups: within manufacturers' guidelines and outside the guidelines. We computed rates of LPP and compared them using Fisher's exact tests.

Results: We assessed 3,535 insertions: 56.3% were within guidelines; follow-up pregnancy status was documented in 60.4% and was similar across groups (p=0.99). Patients within guidelines were younger (median (range): 20 (11-24) vs 21 (11-24.9) years; p=0.009). Of patients outside guidelines 67% reported 100% condom use, 30% reported abstinence, 3% reported withdrawal, breastfeeding, or initiated EC with their IUD insertion. Overall, the rate of LPP was 0/1,992 (95%CI:0-0.31%) within guidelines and 1/1,543 (95%CI:0-0.59%) outside guidelines; p=0.44. For those with documented pregnancy status these rates were: 0/1,210 (95%CI:0-0.3%) within guidelines and 1/926 (0.1%95%CI:0-0.6%); p=0.44. EC was dispensed to 53 patients outside guidelines; 0 pregnancies occurred.

Conclusion: AYAs experience barriers accessing sexual and reproductive healthcare. Same-day IUD insertion may improve access for these people. Adopting a more liberal eligibility criteria that allows providers to insert IUDs when patients report abstinence, or condom use does not result in more LPP.

Primary Student Presenter: Allison M. Dubner

Presenting School: Graduate

Degree Seeking: PhD

Year: 4th

Mentor: Mary CM Weiser-Evans

Poster Title: Role of smooth muscle-derived vascular progenitor cells in atherosclerosis

Final Category: Cardiovascular

Abstract:

Purpose: Atherosclerosis is a major cause of morbidity and mortality worldwide, but current therapies fail to adequately meet clinical needs. Emerging evidence implicates the outer layer of the blood vessel, the adventitia, in the pathogenesis of atherosclerosis. Specifically, it has been suggested that expansion of adventitial microvessels, the vasa vasorum (VV), drives atherosclerosis progression by facilitating inflammatory cell infiltration. Our group previously identified a unique population of multipotent resident vascular stem cells (AdvSca1-SM cells) that derive from mature vascular smooth muscle cells (SMCs) and reside in the vessel adventitia, where they are poised to respond to vascular injury. We hypothesized that in the setting of atherosclerosis, AdvSca1-SM cells contribute to VV expansion to drive disease progression. Methods: We generated a highly specific lineage tracing mouse model in order to track AdvSca1-SM cells in vivo even if they differentiate into other cell types. Lineage tracing mice were placed on either normal chow or Western diet for 8 or 16 weeks, then vascular tissue was analyzed using IF microscopy, scRNA-Seq, and flow cytometry. Results: scRNA-Seq and flow cytometry revealed that AdvSca1-SM cells in atherosclerosis primarily differentiate into mature SMCs, modulated SMCs, and myofibroblasts. Contrary to our preliminary data, AdvSca1-SM cells very rarely differentiate into endothelial cells. Additionally, despite previous evidence of SMCs gaining a macrophage-like phenotype in atherosclerosis, we identified only rare instances of AdvSca1-SM cells contributing to macrophage populations. Conclusions: As in our findings in acute vascular injury, AdvSca1-SM cells in atherosclerosis predominantly differentiate into SMCs and myofibroblasts. Future studies on advanced lesions will define the functional role of AdvSca1-SM cells in atherosclerotic plaque progression.

Primary Student Presenter: Vincent Fu

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Matthew Zuckerman

Poster Title: Digital MD: A Novel Social Media and Digital Scholarship Elective

Final Category: Education

Abstract:

Background: Seventy-five percent of medical students use social media, and one in five medical students are creating and using medical educational resources online and connecting with peers and mentors on social networks (e.g. Twitter, Instagram, LinkedIn, Doximity). Practicing physicians are increasingly utilizing social media as a means to connect with patients, seek advice from peers, and expand their fund of knowledge; at the same time, patients also desire increased digital access to physicians--especially in the wake of the COVID-19 global pandemic.

The current medical curriculum lacks coursework to support student doctors in such digital scholarship and to educate them about the importance of patient confidentiality, online professionalism, and using social media to network with colleagues. Many schools offer policies but rarely provide formal mentorship in this field; online activities are either prohibited or regulated, and rarely mentored or taught. This starkly contrasts the rest of the practice of medicine, which is built upon structured mentorship and reflective practice.

Program Objectives: The Digital MD curriculum was formulated based on student survey, pre-existing materials, and discussion with key stakeholders (physicians, campus digital media, national social media leaders). Digital MD equips learners with the conceptual understanding and technical skills necessary to utilize digital media in their practice. The ultimate outcome is to satisfy an unfulfilled need in medical education and develop effective pedagogy in digital literacy for physicians.

Detailed Description: Digital MD accomplishes its objectives through 7 weekly online modules that involve preparatory work, asynchronous discussion, content creation, and a zoom discussion session.

- Module 1: What is Social Media and Digital Scholarship?

- Module 2: Legal and Ethical Pitfalls of Online Citizenship

- Module 3: Transitioning from Lurker to Contributor/Social Media Activism

- Module 4: Developing a Professional Identity/Personal Branding

- Module 5: Digital Scholarship Educational Theory

- Module 6: Everyone is Creative with Adobe Suite (Guided Lab)

- Module 7: Capstone Presentations, Review, & Feedback

Illustrative Example of Results: Each Digital MD student completes a capstone project in the form of an image, video, or audio contribution to ongoing and current topics in medicine. They are then encouraged to share their piece on social media, engaging with other online citizens in discussions. In March 2020, a student published an evidence-based infographic titled “COVID-19: Myth vs Fact” during a time when much was misunderstood about the novel coronavirus. In December 2020, another student contributed to an ongoing thread with an infographic illustration of COVID-19 outcome statistics, which has garnered well over 20,000 impressions and over 3,000 engagements--including a commentary repost by a well-known MD/MPH and translation into Arabic--despite the student having only created the account ten days prior. These examples, among others, illustrate the immediate and impactful online influence that medical students gain after completing our course.

Key Points:

- Social media is an important and increasingly critical part of communication and

professionalism

- Resources are available, expanding, and proven to be feasible

- Has meaningful impact on students with creation of capstone projects and enhanced

social media engagement with real world impact

Primary Student Presenter: Bruck Gezahegn

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: David Wagner

Poster Title: Interleukin-2 and Forkhead Box P3 is Elevated in a Subset of Multiple Sclerosis At-Risk Patients with Elevated CD4+ CD40+ T-cells.

Final Category: Immunology and Autoimmune Diseases

Abstract:

Purpose of study: Multiple Sclerosis (MS) is an autoimmune demyelinating disease of the central nervous system. The immune system goes haywire and attacks the myelin, an insulating sheath of the nerves utilized to increase the speed and efficiency of electrical impulses. The underlying genetic predisposition is not well understood and requires investigating associated immunological molecular attributes. CD40+ CD4+ T-cells (Th40) are elevated in MS patients and correlated to inflammation. Therefore, this study investigates the level of Th40 cells and associated cytokines in at-risk individuals.

Methods used: T-cells isolated from first-degree relatives of MS patients were stained for CD3, CD4, CD40, IL-2, IL-10, and Foxp3. The gates were set such that the upper left/right and lower right quadrants had less than 1% of events. Data was analyzed using GraphPad Prism from GraphPad Software, Inc.

Summary of results: Isolated T-cells from at-risk patients show elevated Th40 levels in a subset of patients. The increase in Th40 levels was correlated with decrease in IL-2 and Foxp3 levels. On the contrary, at-risk patients with lower Th40 levels had relatively higher IL-2 and Foxp3 levels with higher IL-10 levels.

Conclusions: IL-2, IL-10, and Foxp3 levels are crucial to modulate the immune system via anti-inflammatory and regulatory T cells (Tregs). The correlated higher levels of Th40 cells might explain increasing inflammation due to lack of IL-2, IL-10, and Foxp3 levels. Thus, Th40 levels can provide a potential immunological marker to track the progress/risk of at-risk MS patients.

Primary Student Presenter: Drew Gottman

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Bradford Smith

Poster Title: A Scale-Free Model of Ventilation-Induced Lung Injury.

Final Category: Pulmonary and Critical Care

Abstract:

Acute respiratory distress syndrome (ARDS) is characterized by the accumulation of pulmonary edema (PE) and atelectasis in alveoli, often leading to life-threatening hypoxemia and the need for mechanical ventilation. While mechanical ventilation is a necessary life-saving intervention, it can also exacerbate ARDS and propagate lung injury. A common practice for analyzing the progression of ventilator-induced lung injury (VILI) relies on interpretation of histological cross sections of injured lungs from mice; however, it remains a challenge as to how disparate regions of injury should be correlated with one another. To answer this question, we subjected mice to two-hit models of acute and ventilator-induced lung injury, prepared histological samples, and segmented the corresponding regions of atelectasis and PE with machine-learning software. We conceptualized the dynamics governing the progression of VILI as analogous to those governing earthquakes. We discovered that, like earthquakes, sizes of VILI regions are power-law distributed and exhibit scale-free behavior (Fig. 1). Our work also builds on previous models of VILI that demonstrate a similar pattern in the progression of alveolocapillary perforation sizes – an aptly-named "rich-get-richer" scheme that exhibits preferential attachment. Knowing that scale-free networks exhibit preferential attachment, we suggest that areas of injury act along "fault lines". That is, we can cluster areas of injury according to regional influences with varying levels of confidence (Fig 2.). The advantage of our current model is that we can correlate regions of lung injury with minimal assumptions of the actual mechanism, allowing us to build a simple model that generalizes to a variety of injuries and allows for simple inspection of their visual patterns.

Primary Student Presenter: Salina Haville

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Kevin Deane

Poster Title: Evaluating Transitions from Pre-Rheumatoid Arthritis to Clinically-Apparent Inflammatory Arthritis

Final Category: Immunology and Autoimmune Diseases

Abstract:

Rheumatoid Arthritis (RA) has a 'pre-RA' period defined as elevated antibodies to citrullinated protein antibodies (ACPA) before clinically-apparent Inflammatory Arthritis (IA). ACPA elevations can predict future IA in symptomatic individuals; however, it is unclear how ACPA relates to future IA in asymptomatic individuals. There is limited understanding of how individuals who develop IA in prospective studies compare to those with new RA found through standard referrals.

We identified 86 ACPA(+) individuals (CCP3, Inova) without IA who were followed prospectively for incident IA. We also evaluated 57 CCP3+ patients with EarlyRA at a baseline visit <30 days from confirmed IA. We evaluated joint symptoms, examination findings and disease activity through incident IA, and between individuals who converted to IA and patients with EarlyRA.

19/84 (22%) of anti-CCP3+ participants developed IA ('converters') at a median of 509 days of follow-up. At baseline, CCP3+ converters reported longer morning stiffness and had higher levels of CCP3 and RFIgM compared to CCP3+ subjects who did not develop IA. 'Converters' without any joint symptoms at baseline trended towards a longer duration to IA compared to those with baseline symptoms (median 686 vs 363 days, p~0.09). At the time of diagnosis of IA, 'converters' had less symptoms, disease activity and lower CCP3 than patients with EarlyRA.

In CCP3+ individuals, morning stiffness and higher CCP3 and RFIgM were associated with incident IA; in addition, a subset of CCP3+ individuals without symptoms at baseline developed IA. These findings impact prediction models for future IA. The lower disease activity in 'converters' to IA versus EarlyRA indicates that prospective follow-up of ACPA+ individuals could identify IA when disease activity is less, perhaps indicating a stage of disease more responsive to therapy.

Primary Student Presenter: Rebecca Henkind

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Catherine Velopulos

Poster Title: Left Out in the Cold: Homicide Amongst Persons Experiencing Homelessness

Final Category: Healthcare and Public Health

Abstract:

Purpose: Average life expectancy for a person experiencing homelessness (PEH) is 20-30 years less than the general population, largely attributable to higher rates of chronic diseases. Few studies explore other causes. Our goal was to characterize risk factors that exist for PEH who experience a death by violence.

Methods: We examined all adult victims of homicide reported through the National Violent Death Reporting System (NVDRS) from 2003-2018. Comparison of factors was performed across victims who were identified as homeless and not-homeless. We utilized the U.S. Department of Housing and Urban Development (HUD) Point-In-Time (PIT) Data and the United States Census Bureau Population Estimates to estimate homicide rates per 100,000 for the general and homeless populations for adults age 18+.

Results: PEH are over ten times as likely as others to die by homicide. While shelters are often avoided by PEH due to violence, most incidents involving PEH took place outside. PEH are three times more likely to experience death by random homicide.

Conclusions: Interventions into homeless homicide should focus on risk factors specific to PEH including the markedly increased rates of alcohol/ substance abuse problems and mental health issues among homeless victims.

Primary Student Presenter: John Hesling

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Vikhyat Bebarta

Poster Title: Characterizing Pediatric Supermassive Transfusion and the Contributing Injury Patterns in the Combat Environment

Final Category: Surgery

Abstract:

Purpose: To evaluate the injuries, clinical findings, and prehospital interventions predictive for pediatric supermassive transfusion (SMT), which we define as receipt of >80mL/kg of blood products.

Methods: We analyzed pediatric trauma data from the DOD Trauma Registry from January 2007 – 2016, stratifying patients into two cohorts based on blood products received in the first 24 hours post-injury: 1) 40-80mL/kg for massive transfusion (MT); or 2) >80mL/kg for SMT. We evaluated demographics, injuries, prehospital interventions, and clinical findings.

Results: Our dataset included 3439 pediatric casualties, of which 536 met inclusion parameters (≥40mL/kg of blood products received). The MT cohort included 271 patients (50.6%) versus 265 patients (49.4%) in the SMT cohort. Survival to discharge was reduced in the SMT cohort (78% vs 86% for MT; $p<0.011$). Multivariable analysis of injuries revealed serious injuries (Abbreviated Injury Scale 3-6) to the extremities (OR 2.13, 95% CI 1.45-3.12) and abdomen (OR 1.65, 1.08-2.53) were associated with SMT. Wound dressing (41% versus 29%; $p=0.003$), tourniquet (23% vs 12%; $p=0.001$), and intraosseous (IO) access (17% vs 10%; $p=0.013$) usage were increased in the SMT group. Age-adjusted hypotension was greater in the SMT group (41%, n=100 vs 23%, n=59; $p<0.001$), with no statistical difference in tachycardia (87%, n=223 vs 87%, n=228; $p=0.932$).

Conclusions: Our research demonstrates that pediatric SMT patients have increased risk of mortality and highlights the seriousness of extremity injuries in pediatric trauma patients. Prehospital interventions of wound dressing, tourniquets, and IO access were more frequent in the SMT cohort. Our research determined that hypotension was associated with SMT.

Primary Student Presenter: Hannah Hicks

Presenting School: Graduate

Degree Seeking: PhD

Year: 5th

Mentor: Rebecca Schweppe

Poster Title: The Role of a More Invasive Phenotype in Response to MAPK-Directed Therapies in Thyroid Cancer

Final Category: Hematology and Oncology

Abstract:

Advanced papillary thyroid cancer (PTC) and anaplastic thyroid cancer (ATC) are the leading causes of endocrine cancer death. Mutations in the MAP kinase (MAPK) pathway are common in PTC and ATC, especially in BRAF. However, therapies targeting the MAPK pathway are not approved for PTC patients, and despite the approved combination of BRAF and MEK inhibition to treat BRAF-mutant ATC, these patients often progress. An emerging mechanism of resistance to targeted therapies is an invasive phenotype switch in which cells transition from a proliferative, therapy sensitive population to an invasive, therapy resistant population. Using Matrigel Chamber Invasion assays, we showed that BRAF-mutant PTC and ATC cells resistant to BRAFi exhibit an increase in invasion when treated with BRAFi while sensitive cells do not. We further identified an increase in the levels and secretion of fibronectin (FN1) in response to BRAFi treatment in resistant cells. Treatment with either FN1 or conditioned media from BRAFi-treated resistant cells phenocopies BRAFi-treatment by also increasing invasion. However, depletion of FN1 blocks this response. Interestingly, ERK inhibition also mitigates the invasiveness observed in response to BRAFi or FN1 in resistant cells. We further observed that dual BRAF and ERK inhibition slows tumor growth in vivo in a BRAFi-resistant patient-derived xenograft model. These data indicate that thyroid cancer cells resistant to BRAF inhibition exhibit a more invasive phenotype characterized by increased FN1 and a pro-invasive secretome. Further, dual inhibition of BRAF and ERK ablates BRAFi-induced invasion and slows tumor growth in vivo, providing a potential therapeutic strategy for BRAF-mutant thyroid cancer patients.

Primary Student Presenter: Alex Hoffner-Heinike

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Micol Rothman

Poster Title: Novel use of a “bootcamp” series within the Project ECHO model for training providers in the care of gender diverse patients

Final Category: Education

Abstract:

Purpose: Many transgender and gender diverse (TGD) adults report lack of access to clinically competent medical providers. To bridge the gap in knowledge in providing TGD healthcare, we instituted a longitudinal monthly series via Project ECHO (Extension for Community Healthcare Outcomes), which is an educational telementoring model. After a year of the program, the team created a four-session weekly “bootcamp” series to enhance knowledge of new participants that joined the longitudinal series. The goal of this study is to evaluate the effectiveness of the “bootcamp” model in increasing participant comfort with topics related to TGD healthcare and to evaluate the impact of “bootcamp” participation on enrollment in the longitudinal ECHO series. Methods: The “bootcamp” took place over four consecutive weeks in February 2021. Participants were recruited from the ongoing series as well as through targeted mailings and word of mouth. Results were collected from self-reported pre- and post-“bootcamp” surveys as well as from attendance data. Results: The “bootcamp” had 90 participants. Per Figure 1, Participants reported a 13.8% increase (2.9 to 3.3 on a 4-point scale, p=0.007) in overall comfort in providing care to transgender patients and an 8.6% increase (3.5 to 3.8 on a 4-point scale, p=0.026) in comfort providing care for cisgender patients. The “bootcamp” also helped to bring new registrants to the longitudinal series with 17 of the 90 bootcamp participants registering for at least one session of the longitudinal program which already had 122 registrants. Conclusion: The ECHO model is an effective tool to educate providers on care management for TGD patients. The novel use of a “bootcamp” also highlights a way to introduce and recruit new participants to an ongoing longitudinal ECHO curriculum.

Primary Student Presenter: Joy Huang

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Christene Huang

Poster Title: Hind Limb Transplantation with Hypothermic Machine Perfusion Using Preservation Solution in a Small Animal Model

Final Category: Surgery

Abstract:

Purpose: Vascular composite allograft (VCA) transplantation can be used to treat combat-related injuries to the hands or face, but such grafts are susceptible to ischemic reperfusion injury. The aim of this study was to investigate the benefits of 24 hour hypothermic machine perfusion (HMP) preservation in transplantation of rodent hind limbs.

Methods: 6 hind limb transplants were performed using 12-16 week old Male Brown Norway rat recipients and donors. One donor limb was subjected to 24 hours cold ischemia with HMP using heparinized KPS-1®, while the contralateral limb was subjected to static cold storage (SCS). Changes in weight, vascular resistance, and pH were measured. The recipients were sacrificed post-operative day one (POD1).

Results: All 3 recipients of the HMP limbs died before POD1 due to unclear etiology, while all 3 recipients of the SCS limbs survived to POD1. HMP KPS-1® limbs gained significantly more weight than SCS limbs ($p=0.02$). Among the HMP KPS-1® limbs, there was no significant change in vascular resistance from baseline at 6 hours or 24 hours ($p=0.2$ and 0.5), but the perfusate did become significantly more acidotic over 24 hours ($p=0.04$).

Conclusions: Extended HMP preservation of hind limb VCAs led to 100% early mortality in our series of hind limb transplants in a small animal model, with 100% survival to POD1 with SCS. These findings suggest that unlike in kidney transplantation, preservation solution may not be a viable perfusate for HMP in VCA transplantation. Additional studies are required to explore alternative perfusates for storage of VCAs.

Primary Student Presenter: Shaquia Idlett-Ali

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Shawn Hochman

Poster Title: Assessment of spinal cord stimulation-based modulation in the spontaneous hyperexcitability model of neuropathic pain

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Spinal cord stimulation (SCS) is used clinically for relief of chronic neuropathic pain. The gate control theory presents a theoretical framework of the therapy's mechanism of action associated with Aβ sensory afferent recruitment, but the true mechanisms remain unclear. Preclinical studies frequently investigate mechanisms leading to modulation of stimulus-evoked pain, despite the primary function of therapeutic SCS being modulation of chronic, stimulus-independent pain. Here, we utilized an ex vivo spinal cord-dorsal root ganglia preparation to generate a model of spontaneous hyperexcitability in sensory nociceptive circuits using 4-aminopyridine (4-AP). Applied 4-AP selectively increased Fos immunolabeling in superficial dorsal horn neurons - consistent with selective recruitment of pain circuitry (n=2). We characterized spontaneous activity by recording from sensory afferents in lumbar dorsal roots (DR), Lissauer's tract (LT), and neurons in the superficial dorsal horn (DH). 4-AP led to the emergence of spontaneous activity manifesting as rhythmic dorsal root potentials with superimposed burst firing, and coincident rhythmic field potentials with superimposed spikes in LT and the subjacent DH (n=4). To investigate modulation of spontaneous nociceptive activity by gate control theory mechanisms we assessed the effects of clinically-analogous SCS at dorsal column (DC) and dorsal root (DR) recruitment threshold intensities. We observed that 50 Hz SCS at DC threshold intensity depressed spiking activity in LT/DH during SCS, but it could not modulate field potentials or produce prolonged modulation following cessation of stimulation (n=4). These results demonstrate the utility of a 4-AP model of spontaneous hyperexcitability and the limitations of presumed selective Aβ recruitment as underlying SCS modulation of spontaneous nociceptive activity.

Primary Student Presenter: Rabbia Imran

Additional Presenter(s): Danielle Gilbert, Laura Meimari

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Janet Meredith

Poster Title: Implementation of an alcohol abuse health literacy program in a local Burmese refugee community.

Final Category: Healthcare and Public Health

Abstract:

This study is a community-participatory based health initiative targeting problematic alcohol use within the adult Burmese Refugee community in Denver, Colorado. In a preliminary assessment performed by former University of Colorado School of Medicine students, members of the participating community identified a lack of health literacy regarding alcohol use as a priority for community-based participatory intervention. This study continues the partnership with community stakeholders to develop and implement a culturally appropriate health education program focused on problematic alcohol use. Education about problematic alcohol use has the potential impact for the community beyond addressing immediate adverse health effects. Alcohol intervention should mitigate long-term negative effects on family life, including decreasing unemployment and intimate partner violence, both concerns identified by the community during the previous phases of this project. The health education program will be created with feedback from small research focus groups and designed to improve health literacy surrounding alcohol use. The education program will consist of four educational sessions conducted in English over a one-year period, with the engagement of a certified interpreter. The sessions will include the effects of problematic alcohol use and the impact of alcohol in general on physical and mental health. Participants will receive a pre-session survey to examine their beliefs and knowledge surrounding alcohol use and the impact of problematic alcohol use on their family and community. Following the session, participants will be given a post-session survey to examine changes in perception, knowledge, and comfort surrounding problematic alcohol use to assess learning and contributing factors. Participants will also be asked to participate in an optional, post-session audio interview to discuss the impact of the session in more detail. The audio interviews will be analyzed to probe for participant quotes that represent shared themes of responses. From this mixed methods approach, we hope to explore themes of problematic alcohol use and means for intervention in a refugee population living domestically.

Progress to date includes attending community activities, survey and interview design, IRB application and approval, and preliminary focused conversations with employees of local non-profits working within

the community.

Key Terms: Alcohol abuse, Burmese, refugee community, health literacy, community-based research

Primary Student Presenter: Rabbia Imran

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Patrick Duffy

Poster Title: Low Completion Rate of Patient Reported Outcome Measures (PROMS) in Burn Clinic:

An Opportunity for Improvement

Final Category: Surgery

Abstract:

Burn injuries are morbid and have lasting effects. Past studies have demonstrated that laser therapy can decrease scar thickness, and improve pigmentation, pliability, texture, heat sensitivity and contractures. Various validated outcome measures are used to assess subjective and objective burn patient outcomes after laser therapy. We aimed to assess the rate of completion of three measures for patients evaluated at the UCHealth Burn and Frostbite Center. A retrospective chart review was performed of patients who underwent at least one laser treatment from May 2019-June 2021 to assess the rate of completion of the Patient Observer Subjective Assessment Scale (POSAS), The 5D Pruritus Scale, and The Nerve Pain Scale. Records were considered adequate if all three measures were completed for the baseline assessment and for the first treatment. 45 patients were identified as having undergone 205 laser therapy sessions. 24 (53%) patients were classified as adequate. All measures were absent for 54 (26.3%) sessions. Only 7 (16%) patients had all three measures completed for all sessions. 8 (18%) patients missing the provider evaluated POSAS were consequently classified as inadequate (Figure 1.). These three measures allow clinicians to longitudinally track burn scar outcomes and identify improvements after laser therapy. Our results demonstrate low provider completion rates result in considerable inadequate data. This represents an opportunity to re-evaluate the current process of collecting these measures at our institution. Future work will focus on identifying barriers to completion and utilizing a user-centered design approach to redesign the process for obtaining these important measures.

Primary Student Presenter: Kayvon Jabbari

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Christodoulos Kaoutzanis

Poster Title: Macromastia and Reduction Mammoplasty: Analysis of Total Cost of Care and Opioid Consumption at 10-Years Post-Operatively

Final Category: Surgery

Abstract:

Background: Reduction mammaplasty is commonly performed with over 100,000 procedures annually. Despite a persistent number of patients with macromastia desiring reduction mammaplasty, insurance companies are less willing to pay for the operation. Macromastia has also been associated with increased opioid consumption. The purpose of this study was to evaluate total cost-of-care and opioid consumption in patients with macromastia and compare those who underwent reduction mammoplasty versus those that did not have surgery.

Methods: PearlDiver, a national database encompassing private payers with fifty-three million unique patients, was queried from 2010-2020. Patients with macromastia and those who underwent reduction mammaplasty were included utilizing International Classification Codes 9 and 10 and Current Procedural Terminology codes. Total cost-of-care and morphine milligram equivalents were calculated up to 10-years post-operatively for both cohorts. Cohorts were matched based on age, obesity and Charlson Comorbidity Index, and comparative statistics were calculated using t-tests.

Results: Of the 333,854 patients diagnosed with macromastia, 48,348 underwent reduction mammoplasty. Total cost-of-care one year after diagnosis of macromastia among patients who underwent reduction mammoplasty was higher compared to those that did not (Table 1). At 6 through10 years, there was no significant difference in total cost-of-care between the two cohorts. At every successive follow-up beyond 30 days post-operatively, macromastia patients not receiving reduction mammaplasty had a statistically significant higher morphine milligram equivalents consumption (Table 2).

Conclusion: Patients with macromastia who undergo reduction mammaplasty have less opioid consumption compared to patients that do not undergo reduction mammaplasty, with no long-term increases in total cost-of-care.

Primary Student Presenter: Austin Jolly

Presenting School: Graduate

Degree Seeking: MD/PhD

Year: 6th

Mentor: Mary Weiser-Evans

Poster Title: The Epigenetic Remodeling Protein Brg1 is implicated in Vascular Progenitor Cell Contribution to Pathological Vascular Remodeling and Fibrosis.

Final Category: Cardiovascular

Abstract:

Vascular fibrosis describes irreversible stiffening of the blood vessels that develops in response to many forms of cardiovascular disease including hypertension and atherosclerosis. We identified a unique population of multipotent smooth muscle-derived progenitor cells that reside in the adventitial layer of mouse arteries and express the stem marker Sca1 (AdvSca1-SM cells). After acute vascular injury, AdvSca1-SM cells expand in the adventitia, differentiate into myofibroblasts, and greatly contribute to vascular fibrosis. The chromatin remodeling protein Brahma-related gene 1 (Brg1) is upregulated in AdvSca1-SM cells in response to vascular injury, but how Brg1 influences AdvSca1-SM differentiation remains unknown. Using in vitro systems and animal models, we aim to define the role of Brg1 in AdvSca1-SM cells. We hypothesize that Brg1 modulates chromatin to preferentially drive AdvSca1-SM cell differentiation towards pathologic myofibroblasts and inhibition of Brg1 will disrupt AdvSca1-SM – myofibroblast differentiation and reduce vascular fibrosis.

Results: Mice subjected to carotid ligation and treated with the Brg1 inhibitor PFI-3 exhibit decreased vascular fibrosis, smaller neointima, and decreased expansion of AdvSca1-SM cells as compared to control mice. In vitro, AdvSca1-SM cells stimulated with TGF-β express myofibroblast genes such as αSMA and periostin, and co-treatment with PFI-3 blocks TGF-β induced myofibroblast gene expression at the mRNA and protein level. Ultimately, these results support the conclusion that Brg1 is a major regulator of AdvSca1-SM myofibroblast differentiation and may be a targetable protein to treat vascular fibrosis.

Primary Student Presenter: Katherine Ketcham

Presenting School: Medicine

Degree Seeking: MD

Year: 1st

Mentor: Mark Deutchman

Poster Title: Tough Enough to Wear Pink: A Community Approach to Address Breast Cancer Needs in Rural Colorado

Final Category: Healthcare and Public Health

Abstract:

According to the National Cancer Institute, about 1 in 8 U.S. women will develop invasive breast cancer throughout their lifetime. When a person gets diagnosed with cancer, it is an immediate life-changing moment. As a community, Tough Enough to Wear Pink (TETWP) addresses the fears and financial burdens a cancer diagnosis adds to a family's life.

TETWP is a nationwide organization that started in 2004. It bridges the western lifestyle to breast cancer in a community. Since its creation, the organization has spread nationally. Gunnison, Colorado, a frontier community in the heart of the Rocky Mountains only has a population of 6,403 but has been the number one TETWP fundraiser for five years and counting! The organization and community's support greatly impacts the lives of individuals going through cancer.

The vision of TETWP is for Gunnison Valley Health (GVH) to become the best rural hospital in the United States for women's service and breast cancer care. The mission of TETWP is to provide innovative and best practice medicine by utilizing state-of-the-art equipment and technology, a skilled staff, and to incorporate a multidisciplinary team.

Total fundraising since 2005 is $4,742,000 and this has funded a variety of programs including, "Mammo Mondays," "Lucy's House," "Make it a Great Day," "Tough Enough Pass," "Tuffy," "Bucky," and "Betty Ann," our three vehicles, "Sparky's Fund," "Friends of Pink," "Team Smile," "Pink Sisters," "Catalyst Coaching," and "Blue Sky Cleaning." Together these programs provide transportation and housing to patients so that they can attend their treatments in Denver, provide financial assistance, provide preventative care for uninsured and underinsured patients, and by purchasing a Hologic 3D Tomosynthesis Mammography Machine.

This research study is looking at how effective TETWP is in creating a comprehensive continuum of cancer care through ongoing and continuous data collection from patients that utilize their programs.

Primary Student Presenter: Yue Li

Presenting School: Pharmacy

Degree Seeking: PhD

Year: 1st

Mentor: Dmitri Simberg

Poster Title: Variability of opsonization of iron oxide nanoparticles with

complement C3 in different species and strains: a quest for a predictive animal model

Final Category: Other

Abstract:

The complement system plays a key role in opsonization and immune clearance of engineered nanoparticles. Understanding the efficiency, inter-subject, and inter-strain differences of complement opsonization in preclinical species can help with translational nanomedicine development and improve our ability to model complement response in humans. Dextran-coated superparamagnetic iron oxide (SPIO) nanoparticles and a wide range of non-magnetic iron oxide nanoparticle formulations are widely used in magnetic resonance imaging and as clinically approved iron supplements. Previously we found that opsonization of SPIO nanoworms (NW) with the third complement protein (C3) proceeds mostly via the alternative pathway in humans, and via the lectin pathway in mice. Here, we studied the pathway and efficiency of opsonization of 106 nm SPIO NW with C3 in different preclinical species and commonly used laboratory strains. In sera of healthy human donors (n = 6), C3 opsonization proceeded exclusively through the alternative pathway. On the other hand, the C3 opsonization in dogs (6 breeds), rats (4 strains) and mice (5 strains) sera was either partially or completely dependent on the complement Ca2+-sensitive pathways (lectin and/or classical). Specifically, C3 opsonization in sera of Long Evans rat strain, and mouse strains widely used in nanomedicine research (BALB/c, C57BL/6 J, and A/J) was only through the Ca2+-dependent pathways. Dogs and humans had the highest between-subject variability in C3 opsonization levels, while rat and mouse sera showed the lowest between-strain variability. Furthermore, using a panel of SPIO nanoparticles of different sizes and dextran coatings, we found that the level of C3 opsonization (C3 molecules per milligram Fe) in human sera was lower than in animal sera. At the same time, there was a strong predictive value of complement opsonization in dog and rat sera; nanoparticles with higher C3 deposition in animals showed higher deposition in humans, and vice versa. Notably, the opsonization decreased with decreasing size in all sera. The studies highlight the importance of the consideration of species and strains for predicting human complement responses (opsonization) towards nanomedicines.

Primary Student Presenter: Samantha Magliato

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: David Howell

Poster Title: Virtual Neuromuscular Training to Reduce Injury Risk After Concussion: A Pilot Study in Healthy Adults

Final Category: Bone or Skeletal

Abstract:

Sports-related concussion is associated with an increased risk of musculoskeletal injury following return to play potentially due to an inability to effectively meet the complex cognitive and motor demands of sport. Interventions affecting neuromuscular control may reduce injury risk after concussion. Our purpose was to determine the efficacy of an 8-week virtual Neuromuscular Training (vNMT) program using a novel, smartphone-based platform in healthy adults.

Participants 22-30 years completed initial self-reported and clinically obtained measures used in concussion diagnosis and management (Table 1). Participants were randomized (stratified by sex) to control or vNMT conditions. vNMT group participants completed an 8-week intervention of three 30-minute guided workouts per week using a smartphone-based platform. Participants returned for follow-up testing after 8 weeks. We performed an intent-to-treat analysis comparing pre and post outcomes between groups.

At the time of analysis, n=18 participants had completed both pre and post intervention visits: 8 in the vNMT group (24.9±1.1 years; 75% female) and 10 in the control group (26.4±3.0 years; 70% female). Although not surprising given we were testing non-impaired individuals, we observed no significant between-group differences for any measurement obtained (Table 2). The vNMT group demonstrated fewer errors (Cohen's d = 0.84) in the multiple hop test at the post-intervention assessment compared to the control group, although this did not reach statistical significance.

This study is the necessary first step in assessing the efficacy of a smartphone-based rehab program in a healthy population. Our future work seeks to shift clinical practice by integrating this model into concussion management to reduce musculoskeletal injuries following return to sport after concussion.

Primary Student Presenter: Vincent Mainella

Presenting School: Pharmacy

Degree Seeking: PharmD

Year: 4th

Mentor: Victoria Stevens

Poster Title: Management of Adverse Effects from High-Dose Insulin Therapy in Calcium Channel Blocker/Beta-blocker Overdose: An Observational Study

Final Category: Cardiovascular

Abstract:

Toxicities brought about by calcium channel blocker (CCB) and beta-blocker (BB) overdose lead to similar physiologic manifestations, and are associated with a high risk of mortality. The use of high-dose insulin (HDI) for treatment of these toxicities leads to comparatively improved outcomes versus typical vasopressor therapies. However, existing studies do not definitively describe supportive care for the adverse effects of HDI (e.g., hypoglycemia, hypokalemia, and hypervolemia). The lack of data in these areas represents an opportunity to further characterize both HDI, and its supportive care. A retrospective chart review of patients admitted to UCHealth between 2015 and 2020 was conducted. Patients who received at least 0.5 units/kg/h infusions of regular insulin for the treatment of suspected and/or confirmed beta-blocker or calcium channel blocker overdose were induced. The primary outcome was the amount of patients who experienced hypoglycemia (blood glucose < 70 mg/dL) and/or hypokalemia (potassium < 3.3 mg/dL). Need for dextrose infusions (D10W, D20W, D50W) was assessed. Fluid overload was evaluated by the total cumulative fluid status of patients after HDI/dextrose therapy. Additional data on if patients needed continuous renal replacement therapy (CRRT) for an indication of fluid overload was also collected. A total of 10 patients were included in the study. Median age 44 (IQR: 37.5–48), majority female (70%), and median hospital length of stay was 11.5 days (IQR: 3.5–41.8). Patients overdosed on verapamil (50%), amlodipine (20%), propranolol (10%), and atenolol (10%). One patient had an unknown overdose but was presumed to be and treated as a CCB/BB by toxicology. Median initial and maximum rates of HDI were 1 unit/kg/h (IQR: 1–1) and 10.5 units/kg/h (IQR: 5.5–14.3), respectively. Median total duration of HDI infusion was 1.8 days. Six patients incurred hypoglycemia and nine experienced hypokalemia. The average number of push-dose dextrose administrations per patient was 5.5 (standard deviation (SD): 6.5), and the median duration of supportive care dextrose infusion 4.8 days. The median cumulative volume status of patients after HDI and dextrose infusion therapy was positive 10.6 liters. Nine patients were placed on continuous renal replacement therapy over the course of their hospital stay. Four of those patients (44%) were started on CRRT for fluid overload according to nephrology consult notes. HDI therapy is beneficial in the treatment of CCB/BB overdose. Many patients will experience one or more side effects of insulin therapy. Treatment and management of these side effects can lead to volume load and possibly contribute to the

need for renal replacement therapy.

Primary Student Presenter: Jane Manalo

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Natalie Serkova

Poster Title: Advanced Vessel- and Cell-Size MRI to Assess Chemo-Radiation Treatment Response in Pediatric Ependymoma Models

Final Category: Hematology and Oncology

Abstract:

Introduction: Ependymoma (EPN) is an aggressive pediatric brain tumor that contributes significantly to poor overall outcomes in children1. The benefits of chemotherapy in pediatric patients with EPN have not been defined2, and EPEN treated with surgery and radiation therapy can still recur in 23-66% of patients3. Our group has previously established aggressive behaviors of EPN, including high tumor cellularity, cytological anaplasia, high mitotic index, tumor necrosis, and the presence of inflammatory cells such as M2-type myeloid cells4. The purpose of this study is to develop and optimize an advanced mpMRI protocol (cell-size, vessel-size and inflammation imaging) to characterize the phenotype and chemo-radiation treatment (CRT) response in an orthotopic mouse of patient-derived xenografts (PDX) of pediatric EPN.

Methods: All animal protocols were reviewed and approved by the University of Colorado IACUC. Female severely immune deficient (SCID) mice were used for intracranial orthotopical inoculation of disaggregated tumors from pediatric EPN patients (n=22). Once the intracranial tumor reached at least 5 mm3, the animals were assigned to a placebo and CRT groups (10 Gy radiation plus 30 mg/kg 5-fluorouracil, Figure 1). All radiation treatment was performed on the animal image-guided precision XRAD irradiator, using MRI and CT guided EPN localization. For each MRI session, the animal was inserted into a Bruker 9.4 Tesla BioSpec MRI scanner with a Bruker mouse head array RF cryo-coil. Each session consisted of an mpMRI protocol based on the following optimized sequences:

• High resolution T2w turboRARE (sagittal and axial) for tumor volume

• Diffusion weighted imaging (DWI) for tumor necrosis and edema

• Selective size imaging using filters via diffusion times (SSIFT)

• Vessel size imaging (VSI) (fast T2* during 10 mg/kg iron-oxide ferumoxytol injection)

• Quantitative T2maps (qT2) for inflammation (before and 24hr after ferumoxytol injection)

Analytical methodologies included (i) conventional volumetric analysis, apparent diffusion coefficient

(ADC) values and T2 relaxation times using ParaVision NEO software; in house MATLAB simulations to calculate SSIFT iAUC, vessel size imaging (VSI) and density indices (Q).

The qT2 were repeated 24 hours after SPION injection. This protocol was performed before CRT, immediately after CRT, and two weeks after CRT.

Results: High-resolution turboRARE Tw2-MRI (48 microns in-plane resolution) clearly showed that all EPN PDX were inoculated and homed at the proper anatomical location for EPN, the cerebellum (Figure 2). The sensitivity of T2w-MRI scans was 0.2 mm for the smallest tumor detected; the median tumor volumes at the baseline were 21±12 mm3. They also revealed increased blood vessel densities (0.54±0.12), high SSIFT iAUC (7.1±1.2) indicative for EPN cell size of 14±3 microns, and low ADC values (as low as 0.58x10-3 mm2/s) in EPN as compared to the normal cerebellum. The 5-day CRT with 2Gy/day and 30 mg/kg 5-FU resulted in a significant decrease in the tumor volumes (Figure 2), accompanied by the increased ADC values and decreased SSIFT iAUC and cell size two weeks after CRT (Figure 3). Interestingly, the most immediate response, seen on ferumoxytol-enhanced VCI and qT2 (-4 ms median), seen as soon as 2 days after the CRT, was related to a decreased blood vessel density and an increased presence of inflammatory macrophages and microglial cells in irradiated EPN (Figure 4).

Discussion: Orthotopically implanted PDX EPN xenografts closely mimic histological features, anatomical location and radiologic features of the primary tumors. Our advanced mpMRI protocol followed by novel MATLAB algorithm analysis allows for a unique characterization of pediatric EPN as well as assessing the tumor response to a clinically relevant CRT protocol in a mouse model. A significant decrease in vessel size density and an increase in inflammatory cells were seen as soon as 2 days after CRT. The late response (2 weeks post CRT) is characteristic by decreased ADC values and cell size, resulting in significantly decreased tumor volumes.

Summary: We successfully developed a comprehensive mpMRI protocol for an orthotopic pediatric EPN model, which can be readily translated into human imaging. In addition to the volumetric MRI assessment, we introduce cell size imaging based on the intrinsic distinguishing feature between cancerous (14 microns) and normal brain cell (5 microns). The relation of ferumoxytol-enhanced transverse relaxation rates R2* and R2 provides in vivo VSI mapping of the mean caliber of cerebral vessels, while decreased T2 values in qT2 are reflective for iron accumulation in inflammatory cells such as macrophages and microglial cells immediately after CRT.

Primary Student Presenter: Andrew Mariotti

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Adeel Faruki

Poster Title: Patient and Operational Outcomes of Propofol Sedation versus Fentanyl, Versed and Diphenhydramine Sedation for Endoscopies and Colonoscopies at an Academic Medical Center

Final Category: Healthcare and Public Health

Abstract:

Purpose: In this project we compared the difference in patient and operational outcomes for two different sedation techniques prior to gastrointestinal (GI) procedures: Monitored Anesthesia Care (MAC) using propofol administered by physicians, and Nurse Administered Sedation (NAS) with fentanyl, versed, and diphenhydramine. We hypothesize that MAC will yield improved outcomes compared to NAS. Our first aim was to determine if MAC improved outcomes for patients defined by pain scores. Our second aim was to determine if MAC improved operational outcomes for hospital efficiency as defined by decreased PACU length of stay (LOS). Methods: We will test this hypothesis and evaluate aims using a retrospective cohort analysis under STROBE guidelines. On 8/1/21, the University of Colorado Hospital (UCH) changed its anesthesia procedures in the GI suite from NAS to MAC. We took advantage of this shift to identify our MAC cohort and compare to historical NAS outcomes. Data will be abstracted from the UCH electronic medical record (EMR). Cohort inclusion criteria is defined as patients who have undergone procedures in the GI suite and were sedated using MAC procedures between the dates of 8/1/2021 and 10/31/21. Results: Power calculations yielded a Cohen's d value under 0.2 for powers ranging from 80-95% showing our data is sufficient to detect small differences between MAC and NAS. Preliminary results show decreased PACU LOS up to 10 minutes and decreased overall pain scores. Conclusions: Preliminary data shows decreased perioperative times due to decreased PACU LOS. This provides opportunity to see more patients and increase access to care. Patients also reported decreased pain during recovery.

Primary Student Presenter: Gabriella Mayne

Presenting School: Other

Degree Seeking: MA

Year: 3rd

Mentor: K. Joseph Hurt

Poster Title: Neurosteroids and Steroid Hormones in Preterm Birth

Final Category: Child-Maternal Health and Reproductive Services

Abstract:

Chronic stress is a risk factor for preterm birth, however objective measures of stress in pregnancy remain elusive. Neurosteroids such as allopregnanolone (ALLO) play important roles in stress physiology. Low stress-responsive ALLO is associated with perinatal depression in humans, and animal models with low ALLO exhibit reduced gestational length. We hypothesized women who deliver preterm have lower maternal ALLO compared with women who deliver at full term. We evaluated maternal serum ALLO and five other steroid hormones in gestation and investigated associations with preterm birth. We performed a nested case-control study using biobank serum samples. We included healthy women with singleton pregnancy and excluded mothers with major medical illness, preeclampsia, or chronic hypertension. We matched preterm cases with term controls (1:1) by gestational age (GA) at first blood sample and least difference in time between samples (N=27 per group). We used a new high-performance liquid chromatography-tandem mass spectrometry assay for ALLO and five other steroids. We used T-test, linear and logistic regression as statistical tests. High maternal serum ALLO late in pregnancy was inversely associated with odds of preterm birth (at 32 weeks' gestation OR=0.94, 95% CI:0.92–0.97; P<0.001). We found no significant difference in mean maternal serum ALLO in direct comparison of preterm and term groups. Higher early pregnancy cortisol, cortisone and pregnanolone associated with increased odds of preterm birth. The clinical utility of these potential maternal steroid biomarkers deserves further evaluation.

Primary Student Presenter: Alec McCranie

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Sarah Tevis

Poster Title: "Should I Stay or Should I Go": Second Opinion Retention in Breast Cancer Care at a Large Metro Healthcare System.

Final Category: Surgery

Abstract:

Background: Patients with breast cancer commonly seek second opinions. Previous studies have demonstrated that up to 16% of patients who receive second opinions had a change in diagnosis when seen by the second physician. Despite this, nearly 80% of patients returned to their initial physician for treatment. This study aimed to evaluate the retention rate for breast cancer patients seen within a large metro healthcare system and describe the patient, disease and treatment characteristics associated with transferring care to the second opinion provider.

Methods: A retrospective chart review of patients with breast cancer who were seen at a large academic medical center or an affiliated site within the healthcare system was conducted between July 1, 2020, and July 30, 2021. Patient demographics, tumor characteristics, treatment plans and treatment locations were reviewed. Descriptive statistics were used to describe the population. Univariate analysis was used to evaluate the relationship between retention of second opinion patients and their demographics, tumor and treatment characteristics.

Results: 70 patients with breast cancer sought second opinions. Second opinion patients represented 5.4% of all new patients seen during the study period. 69 (98.6%) were female and 1 (1.4%) was male. The average age of the patient was 54 years old 43 (61.4 %) had private insurance, 18 (25.7) had Medicare, and 6 (8.6%) had Medicaid. 21 patients (30%) were diagnosed with DCIS, 21 (30%) with stage 1 breast cancer, 20 (28.6%) with stage 2 breast cancer, and 9 (12.9%) with stage 3 breast cancer. Majority of patients (72.9%) were seen in our multidisciplinary clinic (MDC). Of the patients who sought an additional opinion at our institution, 15 patients (21.4%) were seen as a 3rd or 4th opinion. 29 (41.4%) patients received a different treatment recommendation and of these, 14 (45.2%) were recommended to undergo additional treatment. Overall, 65.7% of patients received surgical treatment at our institution but only 54.3% of patients received all their treatment at one of our sites. Ultimately 38 (54.3%) patients received their surgical treatment at our parent medical center and another 8 (11.4%) received surgical treatment at another site within our healthcare system. On univariate analysis insurance type, cancer stage, presence of a gene mutation, appointment type, provider specialty, and treatment recommendations were not associated with retention. Patients who consulted with plastic

surgery during their second opinion visit more frequently received their surgical care at our institution ($p<0.05$).

Conclusion: Patients who sought second opinions were retained at high rates at our medical center. Exploring the characteristics of patients who did and did not remain at our institution for treatment following their second opinion will allow us to better understand our patient population and their treatment priorities. We hope to use the information gained through this work to design interventions that will help improve the experience for patients with breast cancer who seek second opinions and improve the retention rates within our healthcare system.

Primary Student Presenter: Michael Nash

Presenting School: Graduate

Degree Seeking: MD/PhD

Year: 5th

Mentor: Stephanie Wesolowski

Poster Title: Predisposition to NAFLD by Maternal Western Diet Involves Loss of Reparative Macrophages and Antioxidant Activity in Non-obese Juvenile Non-human Primates.

Final Category: Child-Maternal Health and Reproductive Services

Abstract:

Purpose: Predisposition to juvenile non-alcoholic fatty liver disease (NAFLD) can be programmed in early life by maternal Western diet (WD), but the mechanisms are poorly understood. Methods: We studied livers from 3yo juvenile non-human primates exposed to maternal WD or Control (C) diet during pregnancy, switched post-weaning at 7 mo to either C or WD, yielding 4 groups: (C/C, WD/C, C/WD, WD/WD). Results: WD/C animals had unchanged body weight, adiposity, and liver fat. Second harmonic generation imaging and picrosirius red staining showed increased fibrillar collagen deposition in the liver periportal region, suggesting stellate cell activation. Single cell RNAseq of WD/C liver immune cells showed non-reparative macrophage (MØ) and dendritic cells, characterized by decreased pro-inflammatory and anti-inflammatory cytokine genes, decreased oxidative phosphorylation, and less M2 polarization. Bulk whole liver RNA-sequencing, TBARs analysis, and western blotting revealed increased oxidative stress, decreased SIRT3 and NRF2 antioxidant pathways, and impaired mitochondrial quality control. Postnatal WD (C/WD and WD/WD) drove liver MØ recruitment and ER stress response, which was not present in WD/C. Compared to all other groups, WD/WD livers had worsened TBARs, increased collagen deposition, and an RNA profile of increased collagen synthesis and inflammation. Conclusions: Our results suggest that maternal WD exposure remodels immune cell function and promotes early fibrosis by hindering oxidative stress resolution and by driving mitochondrial dysfunction, whereas postnatal WD promotes MØ recruitment and ER stress, accelerating inflammation and fibrosis when paired with maternal WD. These results support that maternal diet plays a critical role in driving juvenile NAFLD risk, even in the absence of obesity.

Primary Student Presenter: Adom Netsanet

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Steven Abman

Poster Title: Antenatal Betamethasone Preserves Lung Structure and Function and Prevents Pulmonary Hypertension in Chorioamnionitis-Induced Bronchopulmonary Dysplasia

Final Category: Pulmonary and Critical Care

Abstract:

Background: Bronchopulmonary dysplasia (BPD), the chronic lung disease of preterm birth, is characterized by arrested lung development, abnormal lung function, and increased risk for pulmonary hypertension (PH). Clinical studies have shown strong associations of antenatal stress from chorioamnionitis (CA) with risk for BPD. Antenatal steroids improve many complications of prematurity; however, it remains uncertain whether they reduce markers for BPD in the setting of antenatal inflammation.

Hypothesis: We hypothesize that antenatal betamethasone (BM) administration will help preserve lung alveolar and vascular growth and reduce PH in a rat model of CA-induced BPD.

Design/Methods: Intra-amniotic endotoxin (ETX; 10 μg/sac) or saline (CTL; 50ul/sac) was administered to rat pups via laparotomy of pregnant dams at embryonic day 20 (E20; term, 22 days). BM (BM; 0.2mg/kg) was administered to dams at E20. Pups were delivered by C-section at E22. Four subgroups were identified: saline (CTL), ETX, BM, and ETX+BM. Functional and morphometric analyses were performed at DOL14.

Results: In comparison with CTL, antenatal ETX impaired lung growth, increased resistance, reduced compliance, and increased RVH at DOL14. Maternal BM treatment of ETX-exposed fetal rats preserved distal lung structure and function and prevented RVH. BM treatment reduced total lung resistance by 15.3% and improved compliance by 9.5% ($p<0.05$). BM also preserved lung complexity and alveolar growth as measured by radial alveolar counts (RAC; ($p<0.05$), increased vessel density, and improved RVH by 42.3% ($p<0.05$).

Conclusion: Antenatal BM preserves lung growth and structure, restores function and prevents RVH in this BPD model. We speculate that in the subgroup of pregnancies complicated by CA, antenatal steroids can reduce the risk for BPD.

Primary Student Presenter: Khoa Nguyen

Presenting School: Medicine

Degree Seeking: MD

Year: 1st

Mentor: Michael Graner

Poster Title: Osteoblast Exposure to Chordoma Exosomes Alters the Tumor Microenvironment

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Chordomas are extremely rare tumors of the sarcoma group; nonetheless, they are the most common tumor of the sacral and cervical spine. Within the tumor microenvironment, exosomes – secreted vesicles with multifaceted activities – are involved in tumor communication and material exchange. Our prior novel investigation showed chordoma exposure to chordoma exosomes resulted in different protein expression profiles for proteases, cytokines, and chemokines compared to control. We are now investigating how chordoma exosomes influence osteoblasts, the normal cells within the tumor microenvironment. We believe chordoma exosome-exposed osteoblasts will experience alterations to signaling, metabolism proliferation, and secretion of modifying material into the extracellular matrix.

ARF-8 chordoma cells were grown in DMEM+10% XO-Free (exosome-depleted) FBS.

Conditioned medium was subjected to differential centrifugation, ultrafiltration, and

ultracentrifugation to acquire ARF-8 exosomes. Purified ARF-8 exosomes were applied to

osteoblasts (in triplicate) while control osteoblasts remained untreated. Both control and treated

triplicates underwent proteomic and signaling pathway analyses.

Osteoblast exposure to chordoma exosomes resulted in contrastingly opposite variations and concentrations of proteins between the control and the XO-exposed osteoblasts. Signaling pathway analysis demonstrated notable remodeling of epithelial adherens junctions.

Acknowledgements: Appreciation is expressed to the University of Colorado Department of

Neurosurgery and the CU Research Track program for funding and program execution, lab

personnel in the Graner laboratory for technical support, and the CU Anschutz Proteomics team for proteomics analysis assistance.

Primary Student Presenter: Thy Nguyen

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Nanette Santoro

Poster Title: Effects of a Eucaloric High Fat Diet on Anterior Pituitary Trophic Hormones, their Targets and Adipocytokines in Normal Weight Women

Final Category: Child-Maternal Health and Reproductive Services

Abstract:

Introduction: Obesity in women is associated with decreased fertility, adverse pregnancy outcomes and relative hypogonadotropic hypogonadism, which we termed reprometabolic syndrome. We previously demonstrated that acute hyperlipidemia and hyperinsulinemia recapitulates this phenotype in normal weight women and exerts differential effects on the hypothalamic-pituitary-gonadal, adrenal and thyroid axes. We hypothesized that a eucaloric high-fat diet (HFD) designed to elevate insulin and circulating free fatty acids would also impact anterior pituitary trophic hormones and adipocytokines.

Methods: 17 normal weight (BMI 18-24.9) healthy, cycling women (mean age 29±8) underwent frequent blood sampling (q10 min) in the early follicular phase (days 2-5) for 4 hours starting at 7 am, during a pre-diet cycle. They were subsequently provided a prescribed, eucaloric HFD (48% calories from fat) for the duration of their next menstrual cycle and the frequent blood sampling was repeated in their post-HFD cycle. Serum TSH, free T4 (fT4), total T3 (tT3), cortisol, GH, prolactin (PRL), IGF-1, HMW adiponectin, and leptin were measured by immunoassay. Wilcoxon signed-rank tests were used to compare hormone levels before and after the HFD intervention.

Results: There was a small but significant decrease in tT3 ($p=0.01$) and cortisol ($p=0.02$) after the HFD. No changes in TSH, fT4, PRL, GH or IGF-1 were observed in response to the HFD. Similarly, leptin and adiponectin levels were not significantly different (Table).

Conclusion: A one-month HFD, designed to induce the reprometabolic syndrome of obesity, resulted in differential effects on the hypothalamic-pituitary-gonadal, adrenal, and thyroid axes, implicated in reproductive function. The observed decrease in morning cortisol after the HFD is novel. Studies have not addressed the impact of eucaloric HFD on thyroid hormones and the clinical significance of the small reduction in tT3 is unclear.

Primary Student Presenter: Tien Thuy Nguyen

Additional Presenter(s): Folake Adegboye, Nathan Ewing

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Janet Meredith

Poster Title: Exploring Community Member Experiences with Mental Health Care in Order to Improve Medical Education.

Final Category: Education

Abstract:

By reducing pre-clerkship education to one year, the University of Colorado School of Medicine (CU SOM) has reduced already limited pre-clinical coursework in psychiatry and mental health care. The importance of caregivers and family members in the experience of mental illness is not a specific learning objective in pre-clinical education. The objective of this community-based participatory research study is to identify issues facing patients with mental health problems in the Denver Metro area that could be mitigated through changes in medical school education. This study will 1) describe the attitude and beliefs of the mental health care received and the impact of the current mental health system on patient and family wellbeing, 2) determine the gaps and barriers faced by community members attempting to receive care 3) identify potential opportunities for improving mental health medical school curriculum. In the initial phase of this project, we collaborated with Mental Health Colorado and reviewed 70 online public testimonies from the Colorado Behavioral Health Task Force. Qualitative thematic analysis and Natural Language Processing were used to analyze and interpret the results. The results identified barriers of the mental health system and helped develop 50-60 innovative solutions, which support a service-learning curriculum that could potentially mitigate these issues. Next steps include conducting 50-75 one-on-one virtual interviews and 5-10 focus groups amongst mental health community members (I.e., patients, caregivers, family members, etc.) through the database of National Alliance of Mental Illness CO, conducting a survey of CU SOM medical students and residents in primary care and psychiatry to assess the amount of mental health-specific instruction received during their medical training, and developing a pilot service-learning course.

Primary Student Presenter: Eniola Ogundipe

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Vijaya Vemulakonda

Poster Title: Prenatal and Early Postnatal Outcomes for Fetuses with Anatomic or Functional Renal Agenesis.

Final Category: Child-Maternal Health and Reproductive Services

Abstract:

Introduction: There has been increased interest in fetal intervention for previously "lethal" anomalies such as bilateral renal agenesis or other diagnoses associated with in utero renal failure (functional renal agenesis). While there have been rare reports of successful births following intervention, there is a paucity of data regarding the risks, benefits, and outcomes of intervention. To address this gap, this study reviewed our experience with fetal intervention for anatomic or functional renal agenesis.

Methods: A retrospective review was conducted for patients referred to the Colorado Fetal Care Center (CFCC) for evaluation of complex CAKUT anomalies. Patients were included if they had severe oligohydramnios associated with bilateral renal agenesis, renal dysplasia, or other etiologies consistent with primary renal failure. Eligibility for amnioinfusion was determined by a multidisciplinary team including social work and psychology.

Results: 7 patients met eligibility criteria. Mean age at presentation was 29 years. 86% (6/7) of patients identified as white, and 86% (6/7) of patients were married. Postnatal data was available for 5/7 cases. Respiratory intervention occurred in 3/5 cases. 2/5 cases survived to dialysis. 30-day mortality was 60% (3/5). 1-year mortality was 80% (4/5).

Conclusions: Individuals carrying a pregnancy complicated by anatomic or functional renal agenesis face a difficult choice when considering intervention. In this small cohort, patients considered eligible were more likely to be white and married. While these diagnoses are considered lethal without intervention, intervention is associated with significant morbidity and mortality. These findings reinforce that treatment of these cases should be considered experimental and large-scale multicenter trials are needed to determine the optimal indications for prenatal intervention.

Primary Student Presenter: Amanda Otamendi

Presenting School: Public Health

Degree Seeking: MPH

Year: 2nd

Mentor: Nicole Kelp

Poster Title: Characterization of Centers for Disease Control and Prevention Communications via Social Media Regarding the COVID-19 Pandemic and Effects on Public Engagement and Response. AL Otamendi, (MPH, CoSPH), NC Kelp, G Sivakumar, SA Alderfer, K Murphy, and D Lan

Final Category: Healthcare and Public Health

Abstract:

This observational study analyzed how the methods and language used in COVID-19 Facebook posts of the Centers for Disease Control and Prevention (CDC) affected engagement with posts and responses. We performed a content analysis of 470 CDC Facebook communications regarding the emerging COVID-19 pandemic from January-July 2020. We found that while the CDC only used videos in their posts 16.4% of the time (70 of 426 analyzed posts), video posts had a significant impact on the amount of engagement with the post. Specifically, video posts had an over 10-fold increase in reactions and an over 4-fold increase in comments and shares compared to posts without a video. We also found that CDC advice on masks was correlated with fewer neutral and more negative comments. This study reveals that messaging that advises the public on potentially controversial personal behaviors during an emerging, uncertain health issue should be refined to increase engagement with and positive reception of the messages. We have begun a retrospective analysis of how the CDC and other public health agencies communicated about another emerging infection disease, Zika, to make comparisons between communication strategies and public responses for diverse emerging diseases.

Primary Student Presenter: Carson Platnick

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Kristen Nadeau

Poster Title: Adipose Insulin Resistance Relates to Perturbed Renal Hemodynamics in Obese Youth with and without Type 2 Diabetes

Final Category: Metabolism and Endocrinology

Abstract:

Objectives: There is a need to better understand the pathophysiology of early diabetic kidney disease (DKD) in youth with type 2 diabetes (T2D). The objective of this study was to compare intrarenal hemodynamic function between obese youth with and without T2D and relate these measures to adipose insulin resistance (IR).

Methods: We assessed insulin sensitivity and kidney function in obese youth with (n=31, 15.8 ± 1.8 years, BMI 35.6 ± 6.6 kg/m2, HbA1c 6.9 ± 1.6, 58% female), and without (n=20, 15.3 ± 2.1 years, BMI 38.2 ± 7.4 kg/m2, HbA1c 5.45 ± 0.3, 30% female) T2D. A hyperglycemic clamp was performed with 20% dextrose to maintain mild hyperglycemia (~190-200 mg/dl) for 240 minutes. Free fatty acid (FFA) labs were collected at baseline, and every 10 minutes during the steady state (190-240 minutes). FFA suppression was calculated as baseline FFA subtracted from steady state FFA and used to estimate adipose IR. Iohexol and p-aminohippurate clearances were used to measure glomerular filtration rate and renal plasma flow, respectively. Gomez equations were used to calculate parameters of intrarenal hemodynamic function. Statistical comparison was done using the nonparametric Mann Whitney test, and correlations were determined using nonparametric Spearman's rho.

Results: FFA suppression was attenuated in youth with T2D compared to obese controls (55.6% vs. 92.1%, $p<0.0001$). Impaired FFA suppression was associated with higher intraglomerular pressure (Spearman r= -0.49, p=0.005), higher efferent arteriolar resistance, (Spearman r= -0.53, p=0.002) and higher renal vascular resistance (Spearman r= -0.59, p=0.0005).

Conclusions: Youth with T2D exhibited impaired FFA suppression compared to obese control participants, indicating adipose IR. Impaired FFA suppression was associated with perturbed renal hemodynamic parameters, indicating a potential role for adipose tissue IR in the development of early DKD.

Primary Student Presenter: Amy Rao

Additional Presenter(s): Armaan Yaseyyedi,

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: William Cornwell

Poster Title: Right Ventricular Performance During Exercise in Patients With Heart Failure

Final Category: Cardiovascular

Abstract:

PURPOSE: To characterize resting and exertional right ventricular (RV) function during exercise among patients with heart failure with reduced ejection fraction (HFrEF).

METHODS: Six patients (five males, 60±9yrs) completed invasive cardiopulmonary exercise testing (CPET) on upright cycle ergometry with conductance catheters for real-time RV pressure-volume (PV) analysis, as well as radial arterial catheterization for blood pressure monitoring. Data were collected at rest, two submaximal levels of exercise (Steady-States 1, 2) below ventilatory threshold, and peak effort. Breath-by-breath gas-exchange parameters were determined by indirect calorimetry. Cardiac output (Qc) was determined by direct Fick.

RESULTS: Cohort characteristics are displayed in Table 1. VO2Max was severely reduced (11.8±5.0) and ventilatory efficiency was severely abnormal (46±15). Exercise Qc increased from rest to Steady-State 1, but there were no increases thereafter at higher workloads or at peak effort. Exercise myocardial energetics (stroke work) were also blunted with a modest increase from rest to Steady-State 2. Diastolic reserve (dpdtmin) increased modestly from rest to Steady-State 1 only. Table 2 displays exercise hemodynamics and gas-exchange parameters. An example figure of hemodynamics and RV PV loops during exercise is displayed in Figure 1.

CONCLUSION: HFrEF patients experience impairments in RV contractile and lusitropic reserve, and energy utilization during exercise. These findings demonstrate how exertional RV dysfunction contributes to impairments in functional capacity.

Primary Student Presenter: Julie Ressalam

Presenting School: Public Health

Degree Seeking: PhD

Year: 1st

Mentor: Eric Campbell

Poster Title: Medical Aid in Dying in Colorado: A Targeted Survey of Physician's Attitudes and Experiences

Final Category: Healthcare and Public Health

Abstract:

Purpose of Study: To examine the nature, extent, and consequences of physicians' participation in Medical Aid in Dying (MAiD).

Methods Used: An anonymous, multi-wave, mailed survey (RR= 55%). Our participants included a targeted sample (n=583) of Colorado physicians caring for potential MAiD patients.

Summary of Results: MAiD participation was primarily defined as having MAiD discussions, conducting MAiD consultations, providing MAiD referrals, and writing a MAiD prescription. Our study found 81.1% of respondents were willing to discuss MAiD with a patient, 88.3% to refer for MAiD, 46.3% to be a consultant, and 28.3% to be an attending. Fewer felt prepared to discuss MAiD (54.4%), provide a MAiD referral (62.8%), be a consultant (30.7%) or be an attending (18.0%). More than half of respondents (52.3%) had discussed MAiD with a patient, 27.3% provided a MAiD referral, 12.8% had been MAiD consultant and 8.5% a MAiD attending. Among MAiD consultants and attendings, 75% reported their most recent MAiD case was emotionally fulfilling and professionally rewarding, though 75% also reported it was time consuming and 49% reported it was ethically challenging.

Conclusions Reached: While the majority of physicians surveyed were both prepared and willing to discuss MAiD and provide MAiD referrals, much fewer stated they felt prepared or willing to serve as a MAiD attending or consultant. This disconnect was further cemented among those that had served as a MAiD consulting physician or written as prescription as a MAiD attending. Several barriers to participation were documented; but the experience was reported to be emotionally fulfilling and professionally rewarding to those who recently served as an attending or consulting physician.

Primary Student Presenter: Caitlin Robinson

Presenting School: Medicine

Degree Seeking: MD

Year: 1st

Mentor: Mitchell Cohen

Poster Title: The Impact of Resuscitative Trauma Research on Clinical Guideline Development.

Final Category: Healthcare and Public Health

Abstract:

Traumatic injury is the leading cause of death in individuals <45 years. Clinical research in this population is challenging and few major advances in the treatment of trauma have been due to randomized clinical trials (RCTs). RCTs are the gold standard for evaluating practice change, however, the heterogenicity of trauma resuscitation results in few RCTs impacting clinical care guidelines (CCGs).

This critical analysis reviews RCTs that have been conducted in resuscitative medicine to determine if they have contributed to CCGs. Secondary objectives were to evaluate CCGs to determine if RCTs form the foundation for evidence-based medicine in trauma and determine the aspects of RCTs that increase the impact on guideline updates.

ClinicalTrials.gov was queried to identify RCTs. Trials were reviewed for inclusion based on primary outcome, and type and timing of intervention. Trials were scored based on degree of incorporation into CCGs. CCGs from ACS and EAST were used to determine the overall impact each trial had on advancing resuscitation guidelines. Guidelines were independently assessed to determine the basis of evidence for treatment recommendation.

RCTs in trauma impact CCGs significantly less than those in other practice areas. Different aspects of RCTs evaluated are in the table, with the probability of that aspect influencing CCGs. Two factors significantly correlate with the integration into CCGs: number of enrolled patients (p=.002) and number of publications (p=.007). CCGs are predominantly based on observational and retrospective research.

Resuscitative RCTs are failing to impact clinical practice. Characteristics of trial design may help to increase trial effectiveness. Improving development of RCTs and integration into CCGs will have a major impact on public health.

Primary Student Presenter: Madison Rose

Presenting School: Graduate

Degree Seeking: PhD

Year: 6th

Mentor: Rebecca Schweppe

Poster Title: The Regulation of Apoptosis by Cooperative Src and MAPK Signaling

Final Category: Hematology and Oncology

Abstract:

The Regulation of Apoptosis by Cooperative Src and MAPK Signaling M Rose, (Ph.D., GS), LA Pike, VL Espinoza, and RE Schweppe, Department of Endocrinology, University of Colorado Anschutz Medical Campus

Advanced thyroid cancer (TC) patients have poor survival rates due to lack of effective therapies. Genetic alterations in the MAPK pathway account for most driver mutations expressed in TC, but clinically there has been mixed success targeting this pathway. We've shown that combined Src (Srci) and MAPK inhibition (MEKi) results in synergistic inhibition of growth in vitro and in vivo, and increased apoptosis in BRAF- and RAS-mutant cells, while PIK3CA-mutants are resistant. Here we further delineated the mechanism(s) of apoptotic regulation by dual Srci and MEKi. Reverse Phase Protein Array (RPPA) was performed on a panel of TC cell lines treated with Srci and/or MEKi. Western blotting was performed using Odyssey Imaging, growth and apoptosis assays were performed using Sulforhodamine B or CellTiter-Glo, and Caspase-Glo 3/7 assays. All stats were calculated in GraphPad Prism 9. RPPA identified the pro-apoptotic protein BIM as a key regulator of response. Western blots showed a 6-fold induction of BIM in cells that are sensitive to combined Srci and MEKi, and a ?3-fold induction of BIM in resistant cells. Overexpression of BIM in resistance cells promoted sensitivity to combined Srci and MEKi. A previous study (Sale et al.) showed that low Bcl-xL expression in melanoma compared to high expression of Bcl-xL in pancreatic cancer (PC) predicted sensitivity to an MCL1 or Bcl-xL inhibitor, respectively. We showed that TC cells align with PC, expressing high levels of Bcl-xL and so are sensitive to a Bcl-xL inhibitor. In summary, BIM is a key protein regulated by the Src and the MAPK pathways and is sufficient to induce sensitivity to combined Srci and MEKi in a resistant cell. The efficacy of combined Srci and MEKi can be increased through the addition of a Bcl-xL inhibitor.

Primary Student Presenter: Aaron Sadowsky

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Zvonimir Bebic

Poster Title: Expanded Perineal Coverage With Combined Pudendal And Inferior Cluneal Nerve Blocks

Authors: Aaron Sadowsky, MS, Zvonimir Bebic, MD

Affiliations: University of Colorado School of Medicine, Department of Anesthesiology;

Children's Hospital Colorado, Depar

Final Category: Other

Abstract:

Purpose: The pudendal nerve (PN) block is an effective regional technique for perineal anesthesia. If additional dermatomal areas lateral to the PN dermatome are needed, additional blocks are necessary. We present a case report of a six-year-old female for surgical resection of widespread condylomata accuminata of the perineum and buttocks. A combined PN and inferior cluneal nerve block was used. To our knowledge, this is the first report of this combined technique used for perioperative analgesia.

Case Description: A six-year-old 22 kg otherwise healthy female presented for resection and cauterization of widespread condylomata accuminata of the anus and buttocks. The surgeon was concerned for perioperative pain and requested regional anesthesia. A caudal block was considered, however, mother refused. A PN block was suggested, but due to the widespread nature of the lesions, would have been inadequate. Following literature review, ICN was identified as a suitable target in combination with a PN block to achieve wider analgesia (Figure 1). Patient presented to OR, standard ASA monitors were applied, GA was induced with propofol 3mg/kg, and a LMA was placed. No opioid or muscle relaxation was used. Her hips were flexed towards her chest. IT was palpated, cleaned, and identified using a linear US probe. Using an out of plane technique, a 25-gauge needle was passed medial to the IT. 5 mL of 0.25% bupivacaine + dex was injected. The probe was moved cephalad along the IT until the prominence fell from view. Same needle was advanced out of plane until the ischium was contacted (Figure 2). An additional 3 mL of 0.25% bupivacaine was injected as a field block. VSS throughout entire procedure, patient only required 10 mg/kg IV APAP and 0.5 mg/kg of ketorolac. Dermatomal coverage was determined based on extent of surgical site and confirmed in PACU using alcohol swabs. Patient was discharged with minimal pain and returned twice more for further fulguration with same similar results.

Results: Figure 1: Dermatomal coverage of the female perineum, from an inferior view, looking periorly.

Figure 2: Visualization of 25-gauge needle and ischial tuberosity using 6-13 Hz linear ultrasound probe. Hashed arrow represents needle trajectory (out-of-plane) pudendal nerve block. “M” = medial; “L” = lateral.

Conclusions: Combined PN and ICN blocks:

A. May be utilized to reduce perioperative opioid requirements in patients presenting for procedures of the buttocks.
B. B. Allow for wider lateral coverage for perineal surgeries that utilize lateral incisions.
C. C. May be repeated multiple times for a patient to iteratively avoid opioid exposure or use.

This is a single case report of a successful combined approach for PN and ICN regional anesthesia. Further research is recommended.

Disclosures: There are no conflicts of interest for either author. Consent was obtained from mother of the patient.

Primary Student Presenter: Omar Samara

Presenting School: Medicine

Degree Seeking: MD

Year: 3rd

Mentor: Andres Henao-Martínez

Poster Title: Cytokine Levels In Sepsis and TNF Association with Mortality but not Sepsis Severity or Infection Source: a Systematic Review and Meta-analysis

Final Category: Microbiology and Infectious Diseases

Abstract:

Introduction: Sepsis is a global health problem associated with significant morbidity and mortality and is attributed to elevated cytokine levels. However, anti-cytokine therapies have failed to lower sepsis mortality in clinical trials. Quantifying cytokine levels in sepsis is required to establish their role in pathogenesis. This systematic review and meta-analysis characterizes levels of key cytokines in the circulation of sepsis patients and relates TNFα levels to mortality and patient characteristics.

Methods: Medline, Embase, Cochrane Library, and Web of Science Core Collection databases were searched from 1946 to May 2020 for studies in English disclosing cytokine levels in sepsis. Keywords included sepsis, septic shock, purpura fulminans, and tumor necrosis factor (TNF)α. The primary clinical outcome evaluated was 28-day mortality. Data analyses were performed using a random-effects model to estimate pooled odds ratios (OR) and 95% confidence intervals (CI). This systematic review is registered in PROSPERO under number CRD42020179800.

Results: A total of 3656 records were identified. After exclusions, 109 studies were included in the meta-analysis. Among studies in sepsis patients, 72 disclosed TNFα levels, 25 showed interleukin (IL)-1β levels, and 6 presented interferon (IFN)γ levels. The pooled estimate mean TNFα level in sepsis patients was 58.4 pg/ml (95% CI, 39.8-85.8 pg.ml; I2 = 99.4%). Pooled estimate means for IL-1β, and IFNγ levels in sepsis patients were 21.8 pg/ml (95% CI, 12.6-37.8 pg.ml; I2 =99.8%) and 63.3 pg/ml (95% CI, 19.4-206.6 pg/ml; I2 = 99.7%), respectively. Elevated TNFα concentrations are associated with increased 28-day mortality (P=0.001). In a subgroup analysis, TNFα levels did not relate to sepsis source, sepsis severity, or sequential organ failure assessment (SOFA) score (figure 1). In a metaregression: age, percentage of females and mortality at 28 days associated with TNFα levels.

Conclusion: We estimate levels of TNFα, IL-1β, and IFNγ in human sepsis and show TNFα elevations associated with sepsis mortality. TNFα concentrations did not correlate with sepsis severity. We believe the concept that elevated cytokines cause sepsis should be revisited in the context of these data.

Primary Student Presenter: John Schutz

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Sarah Sibbel

Poster Title: Establishing the Role of Inflammatory Markers in the Diagnosis and Treatment of Acute Hand Infections in the Pediatric Population

Final Category: Bone or Skeletal

Abstract:

Background: Pediatric hand infections are complex clinical problems due to difficulty distinguishing infections of differing severity, presentation, and response to treatment. Generally, superficial infections can be managed non-surgically with antibiotics, while deeper infections may necessitate surgical management and antibiotics. Inflammatory blood markers, including WBC, ESR, and CRP, are reported to aid in determining severity of infection and response to treatment in adults.

Purpose: The purpose was to identify the difference in inflammatory marker levels in pediatric patients with superficial vs. deep hand and wrist infections to determine the utility of markers in diagnosis and treatment.

Methods: This retrospective cohort study included pediatric patients who received treatment for an acute hand or wrist infection at two children's hospitals. Chart review for demographics, diagnosis, treatment, and cause of infection was conducted. Exclusion criteria included: patients >18 y/o, chronic infection, open fractures, no inflammatory markers measured.

Results: 129 patients met inclusion criteria. Logistic regression was used to assess predictive value of markers in treatment and diagnosis. Only intravenous (IV) antibiotic administration was associated with elevated inflammatory markers. Every 1 unit (mg/L) increase in CRP was associated with a 2.14 increased odds (95%CI: 1.09, 4.17) of being given IV antibiotics. Every 1 unit (cells/mm3) increase in WBC was associated with a 1.26 increased odds (95%CI: 1.06, 1.50) of being given IV antibiotics. Every 1 unit increase in WBC was associated with a 1.14 increased odd (95%CI: 1.02, 1.27) of a cellulitis diagnosis. ESR and CRP were not significantly associated with cellulitis diagnosis.

Conclusion: Pediatric hand infections are complex problems and inflammatory blood markers can be a useful tool for aiding in diagnosis and management, particularly in determining need for IV antibiotics and for diagnosis of cellulitis.

Primary Student Presenter: Sarah Seiwald

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Mark Petrash

Poster Title: Human Breast Milk Enhances Cellular Proliferation in Corneal Wound Healing

Final Category: Vision Sciences

Abstract:

Purpose: Corneal wounds from ulcers, trauma, or scarring from infections are often treated with debridement of the cornea epithelium, allowing new epithelial cells to grow in their place. Corneal wound healing requires a cascade of signaling molecules, including epithelial growth factor (EGF) and growth modulating cytokines; however, a topical post-operative treatment with these components is not available. With the rise in use of Traditional Eye Medicine (TEM), human breast milk (HBM) offers a potential, novel treatment as it contains growth factors and cytokines that may play a role in epithelial cell migration and proliferation. This study seeks to investigate the role of HBM in enhancing reepithelialization of the cornea after mechanical wounding.

Methods: Male and female Balb/C mice, 8 to 12 weeks old, were sedated with intraperitoneal ketamine, xylazine and given 0.5% ophthalmic proparacaine prior to creating a 2mm central cornea defect with a 0.5mm Algerbrush. Immediately post epithelial cell layer removal, mice were randomly assigned to one of three treatment groups: HBM, triple antibiotic ophthalmic ointment containing neomycin, polymyxin B, dexamethasone (TAB), or saline. Operated eyes were treated 4 times per day for up to 48hrs. Epithelial defect size was ascertained with fluorescein staining and ImageJ area analyses at 0, 8, 24, and 48 hrs post wounding. Subsets of mice from each treatment group were used for histology and ELISA cytokine analyses.

Results: Wounded corneas treated with HBM demonstrated significantly increased rate of reepithelialization post wounding at 8hrs and 24 hrs compared to TAB and saline treated eyes. Immunofluorescent staining for cell proliferative marker, Ki-67, on HMB treated eye tissue sections showed significantly higher positive cell numbers over TAB treated eyes ($p=0.0063$ at 8hrs, $p=0.0007$ at 24hrs, and $p=0.0014$ at 48hrs). ELISA IL-1β levels showed no significant difference between treatment groups.

Conclusions: Human breast milk treatment on mouse corneas with central, mechanical debridement of epithelium demonstrated improved rate of healing and increased cellular proliferation. Future studies will investigate the potential effect of HBM on endogenous limbal epithelial stem cells in the cornea.

Primary Student Presenter: Brenda Seymour

Presenting School: Graduate

Degree Seeking: MD/PhD

Year: 4th

Mentor: Kristi Kuhn

Poster Title: Indole Promotes Collagen Induced Arthritis through Enhanced Th17 Immunity

Final Category: Immunology and Autoimmune Diseases

Abstract:

Altered tryptophan catabolism has been observed in autoimmunity, but the mechanism by which tryptophan catabolites alter immune cell function is unclear. We have shown that levels of the bacterial-derived tryptophan metabolite, indole, strongly correlate with collagen-induced arthritis (CIA) severity, and that mice fed a tryptophan-deficient diet (TD) are protected from disease. Others have shown that Th17 cells promote the pathogenicity of CII-specific autoantibodies in CIA through altered antibody glycosylation in an IL-23 dependent manner. This led us to hypothesize that indole promotes CIA development by enhancing the IL-23/Th17 axis. To assess the effect of indole on CIA, mice were fed either a TD diet or a standard amino acid (AA) diet starting at day -1. Indole (10mM) or vehicle was added back by oral gavage every other day. CIA was induced by injection of bovine type II collagen (CII) emulsified in complete Freund's adjuvant at days 0 and 21. Supplementation with indole significantly reversed TD-mediated protection from CIA. Indole-gavaged mice also had a significant expansion of Th17 cells in the spleen and colon, as well as increased complement fixation compared to vehicle-gavaged mice. This suggests that CII-specific antibodies in indole-gavaged mice are more pathogenic, possibly due to glycosylation changes. To test whether indole promotes IL-23 production in DCs, bone marrow derived dendritic cells (BMDCs) were stimulated with indole + LPS for 24hr, and cytokine expression was analyzed by qPCR and ELISA. Stimulation with indole + LPS resulted in significantly higher levels of IL-23 compared to LPS alone. In conclusion, our initial data suggests that indole promotes development of CIA through the enhancement of the IL-23/Th17 axis.

Primary Student Presenter: Shea Shipton

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Nathan Clendenen

Poster Title: Preoperative hemoglobin is key indicator for mortality in cardiothoracic surgery

Final Category: Surgery

Abstract:

Purpose of study In the over 900,000 cardiac surgeries performed each year the 30-day mortality is 3.4%. Most risk factors are non-modifiable with a significant exception being pre-operative anemia. This study seeks to understand if pre-operative anemia is a key indicator in patient outcomes following cardiothoracic surgery.

Methods used A retrospective case cohort study with 2,104 patients who underwent cardiac surgery between Jan 2011 and Nov 2020 was performed. Pre-operative cellular components of blood were analyzed in survivors and compared to non-survivors. 9 separate procedures were included in the study along with the variables of age, gender, hemoglobin, mean platelet volume, red cell distribution width and platelet count. Nominal logistic multivariate regression analysis was performed for mortality.

Summary of results For all variables measured pre-operative hemoglobin has the greatest impact on the mortality of the patient.

In a univariate analysis lower Hgb levels, RDW variability and lower platelet counts are associated with mortality. Multivariate analysis indicates that most patients undergoing surgery are anemic, a driving factor behind mortality.

Conclusions Pre-operative anemia levels are often correctable in non-emergent conditions. Given that this variable has the highest amount of influence regarding the mortality of patients it should be corrected in a pre-operative setting.

Primary Student Presenter: Jason Sidrak

Presenting School: Medicine

Degree Seeking: MD

Year: 1st

Mentor: Nicole Christian

Poster Title: Review of American Board of Surgery In-Training Examination Scores to Modify Didactic Curriculum: A Preliminary Analysis

Final Category: Surgery

Abstract:

General surgery residents at the University of Colorado School of Medicine (CUSOM) attend core curriculum didactic conferences to prepare for the American Board of Surgery In-Training Examination (ABSITE), qualifying examination, and post-residency practice. ABSITE scores are one metric residency directors can utilize to assess resident progress and clinical knowledge. The purpose of this study was to evaluate resident performance in specific subtest and subtopic areas and identify areas in need of improvement in the general surgery residency program. A single institution retrospective study was performed utilizing CUSOM 2020 ABSITE score reports. Performance metrics across the five program years were input into RedCAP and statistical analyses were conducted for ABSITE subtest standard scores and incorrect subtest topics. Median deviation from national average scores was calculated by subtracting the national average from each subtest score. 3rd year residents' median subtest scores were below the national average in Alimentary Tract (Al). 5th year residents' median subtests scores were below the national average in Al, Pre-Peri Op care (OP), SCC/Trauma, and Surgical Specialities. Program year five had two subtests, AL and OP, with a median deviation of -50 compared to the national average. Our study shows that CUSOM general surgery residents scored at or above the national average in program years 1,2, and 4 while years 3 and 5 had median subtest scores below the national average in 1 and 4 subtests respectively. Overall trends in the deviation of subtest scores from national averages and identification of program weaknesses over time are pending additional analysis of 2017-2020 scores. Specifying areas of weakness allows for targeted modification of the core curriculum didactic conferences. This study is unique as it is the first to our knowledge to investigate ABSITE subtest standard performance and prospectively use results to modify curriculum. Our methods have the potential to be replicated by other residency directors at CUSOM, surgical programs at other institutions, and the American Board of Surgery to provide further insights into surgical training.

Primary Student Presenter: Katherine Smulligan

Presenting School: Graduate

Degree Seeking: PhD

Year: 2nd

Mentor: David Howell

Poster Title: Physical Activity Predicts Kinesiophobia at Return to Play for Athletes with Persistent Post-Concussion Symptoms

Final Category: Healthcare and Public Health

Abstract:

Purpose: Physical activity (PA) is recommended to improve concussion recovery time, however, fear of pain with movement (kinesiophobia) may limit PA. Our purpose was to examine the correlation between PA level and kinesiophobia between initial evaluation and return to play (RTP) clearance among adolescents who did and did not experience persistent post-concussion symptoms (PPCS).

Methods: Athletes rated kinesiophobia using the Tampa Scale of Kinesiophobia (TSK) at initial (≤14 days post-concussion) and RTP clearance visits. They wore activity monitors to quantify daily step count and exercise frequency/duration between initial and RTP visits. Our primary outcome was TSK score change from initial to RTP visits. We grouped athletes based on symptom duration≥28 days (PPCS) or <28 days (no PPCS), and calculated correlation coefficients between activity variables (Pearson r for normal distribution, Spearman rho for non-normal distribution) and TSK change scores.

Results: We enrolled 41 athletes ages 10-18 years evaluated within 14 days of concussion. Among our sample, 44% developed PPCS (n=18; age=14.5±2.0 years; 50% female; RTP=66.8±6.4 days) and 56% did not (n=23; age=14.9±1.8 years; 48% female; RTP=21.7±1.9 days). For the PPCS group, lower TSK change scores were significantly and moderately correlated with higher daily step count (r=-0.60, p=0.008) and exercise frequency (r=-0.63, p=0.005), but non-significantly correlated with exercise duration (rho=-0.12, p=0.65). Among the no PPCS group, activity variables were weakly and non-significantly correlated with TSK change (step count: r=-0.18, p=0.41; frequency: r=-0.34, p=0.12; duration: rho=0.10, p=0.67).

Conclusions: Higher daily step count and exercise frequency during concussion recovery, regardless of duration or intensity, may help reduce kinesiophobia for those with persistent symptoms.

Primary Student Presenter: Anthony Smyth

Additional Presenter(s): Cian O'Sullivan, Andrew Mariotti

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Emily Gottenborg

Poster Title: Enchancing Patient Portal Enrollment for Improved Quality of Post-Discharege Care at an Academic Medical Center

Primary Authors: A. Smyth1, C. O'Sullivan1, A. Mariotti MHA1,

Secondary Authors: E. Gottenborg MD2, T. Anstett DO2, L. Meimari1, S. Andani, D.

Final Category: Healthcare and Public Health

Abstract:

The time immediately following discharge from a hospital admission is a vulnerable period for patients where preventable adverse events commonly occur due to discontinuity of care. Portals allow patients the opportunity to conveniently use one platform to view their health record, communicate with their care team, participate in telemedicine, and view a list of their current medications in an effort to improve the continuity of care. Their use has been shown to promote patient engagement, improve patient satisfaction, and ensure smooth continuity of care. The purpose of this study was to develop a standardized process to improve inpatient enrollment in the UCHeatlh electronic patient portal, My Health Connection. Researchers implemented various interventions throughout the 679-bed hospital including inpatient rooms and the discharge lounge. Interventions were designed to address barriers to adoption discovered during patient interviews. Interventions in the hospitals discharge lounge yielded the highest success rate. Researchers acting as volunteers in the discharge lounge over a trial period successfully enrolled 67% (n=9) of targeted patients using a scripted intervention designed to employ empathetic engagement. Implementing a standard process for patient portal registration at an appropriate stage during a hospital admission is an effective strategy for increasing portal adoption and mitigating risk during the post-discharge period. Utilization of volunteers for the intervention requires establishing a method of communication between the appropriate staff and volunteers to optimize volunteer time and balance their other responsibilities. Capitalization on the benefits of patient portals can help ensure the delivery of high value care for the post-discharge patient, improving outcomes and overall satisfaction for providers and patients.

Primary Student Presenter: Marisa Sobczak

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: G. Todd Alonso

Poster Title: Glycemic Control in Relation to Technology Use in a Single Center Cohort of Children with Type 1 Diabetes (T1D)

Final Category: Metabolism and Endocrinology

Abstract:

Background: Diabetes technology, including continuous glucose monitoring (CGM) and insulin pumps are improving and being used more commonly. The use of insulin pumps, CGM, and hybrid closed loop (HCL; combining pumps and CGM with algorithms that automatically adjust insulin delivery), are associated with lower A1c trends.

Objective: To evaluate the use of pump, CGM, and HCL technology and their impact on glycemic control among pediatric patients with T1D.

Method: Medical records at the Barbara Davis Center (BDC) were examined to identify patients with T1D between 1/2018 and 12/2020 who at their last visit were <22 years old; had diabetes duration >3 months; and had available A1c, pump usage, and CGM data. Data were analyzed by age group and technology-use group: multiple daily injection with blood glucose meter (MDI/BGM), pump with BGM (pump/BGM), MDI with CGM (MDI/CGM), and pump with CGM (pump/CGM). Glycemic control (A1c) was compared using ANCOVA and controlling for diabetes duration, race, and insurance.

Results: Among 4003 eligible patients, Table 1 shows comparisons of mean A1c and percent of patients with A1c <7.0% by technology use group and age group. Patients in the pump/CGM group had the lowest A1c in each of the age categories. In patients without CGM, pump/BGM users had similar A1c to MDI/BGM users (10.0 vs 10.0, $p<0.001$). The pump/CGM users had a significantly lower A1c than MDI/CGM users (8.1 vs 8.6, $p<0.001$). MDI/CGM users had lower A1c than pump/BGM users (8.6 vs 10.0, $p<0.001$). Patients who used HCL had significantly lower A1c compared to those who used pump/CGM without HCL (7.6 vs 8.3, $p<0.001$; Table 2).

Conclusion: Approximately half of patients are using both CGM and pump, which is associated with lower A1c. While CGM use is associated with a lower A1c regardless of pump use, pump use is only associated with a lower A1c if used with CGM. HCL technology was associated with the lowest A1c.

Primary Student Presenter: Jordan Stellern

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Joshua Gowin

Poster Title: A Meta-Analysis on the Role of Difficulties in Emotion Regulation in Substance Use Disorders

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Background: Stronger ability to regulate emotions successfully has been associated with greater resilience to psychopathology. Individuals diagnosed with substance use disorders (SUDs) have been shown to have higher levels of negative emotionality, and possibly impaired emotional regulation compared to individuals without SUD, but no previous attempt has been made to systematically review the literature to assess the magnitude and robustness of this difference. Methods:
This systematic review and meta-analysis reviewed studies that examined differences in emotion regulation between individuals with and without SUDs using the Difficulties in Emotion Regulation Scale (DERS). Results: We searched PubMed and PyscINFO and identified 22 studies that met our search criteria and performed a meta-analysis of the mean difference between groups for total score and for subscale scores. Individuals with SUDs had significantly greater difficulties with emotion regulation with hedge's g = 1.04 ($p<0.001$, 95% CI = 0.85 - 1.24), a large effect. The difference was robust, remaining significant after removing outliers and studies with risk of bias. The effect had a high degree of heterogeneity ($I2 = 93.0\%$) that was not accounted for by age, sex, primary substance used, or country where the study was conducted. Individuals with SUD also showed poorer emotion regulation on each of the DERS subscales, with the largest deficit in having strategies to manage negative emotions. Conclusions: This meta-analysis provides strong evidence that individuals with SUDs have greater difficulties in emotion regulation than healthy comparison adults.

Primary Student Presenter: Megan Stumpf

Presenting School: Medicine

Degree Seeking: PhD

Year: 1st

Mentor: Raul Torres

Poster Title: Breaking B Cell Anergy: Exploring “Redemption” Cocktails

Final Category: Immunology and Autoimmune Diseases

Abstract:

Autoimmunity affects over 24 million people in the United States. A possible culprit driving certain autoimmunities including systemic lupus erythematosus (SLE) and type 1 diabetes (T1D) are anergic B cells (BND), which are autoreactive B cells that have escaped central tolerance. Recently, autoantibodies (aAbs) against self-antigens were identified in severe COVID-19 and may drive pathology in severe disease. Here, we propose that strong inflammation in disease relaxes peripheral immunological tolerance, thus, breaking anergy in BND cells and producing aAbs.

To study whether BND cells activate with strong inflammation, naïve B cells or sorted B cell subsets were isolated from peripheral blood mononuclear cells of 5 healthy donors and cultured for up to eight days with stimuli combinations, including IL-2, CpG, CD40 ligand, anti-Ig, IL-4, IL-6, IL-1b, and TNF-a. Cell supernatants were tested using cardiolipin and total antibody (Ab) enzyme-linked immunosorbent assays (ELISAs). Cells were stained for cell surface marker expression and measured using flow cytometry.

Of all cocktails tested, the presence of IL-4 limited total Ab and cardiolipin Ab production. IL-6, TNF-a, and IL-1b increased total IgG production and anti-cardiolipin Abs. Activation markers were upregulated on BND cells suggesting successful activation in response to inflammation. However, when B cell subsets were separately stimulated from one donor, unswitched memory cells were the only subset that produced cardiolipin Abs.

BND cells can be activated using inflammatory stimuli mimicking those found in severe COVID-19 to upregulate surface activation markers and elicit aAb production. Individuals may differ in the B cell subtype of their autoreactive B cells or depending on past exposures. Further studies should be done to determine whether the autoreactive unswitched memory cells originate as BND cells in the periphery prior to differentiation.

Primary Student Presenter: Chris Thomas

Presenting School: Pharmacy

Degree Seeking: PharmD

Year: 4th

Mentor: Barrett Crowther

Poster Title: Risk of Clostridioides Difficile Reinfection After Kidney Transplant

Final Category: Microbiology and Infectious Diseases

Abstract:

The purpose of this study is to identify risk factors associated with the recurrence of Clostridioides difficile infection (CDI) 90 days after receiving kidney transplant.

A retrospective cohort study was conducted from 2011 to 2021 to compare the risk of CDI in kidney transplant recipients with a pre-transplant history of CDI to a control population without a history of CDI. The primary outcome was incidence of CDI 90 days post-transplant. The secondary outcome was incidence of CDI 365 days post-transplant. Subgroup analysis included proton-pump inhibitor use, mean post-transplant antibiotic duration, and mean length of index hospital stay. Inclusion criteria were age > 18 years, history of kidney transplant, and clinical diagnosis of CDI in the pre-transplant group.

148 total kidney transplant recipients within the University of Colorado Health system were included (46 pre-transplant, 102 control). The majority of subjects were male (53.4%), White or Caucasian (77.7%), and received a thymoglobulin induction dose of 4.5mg/kg (76.9%). Incidence of CDI 90 days post-transplant was 15.2% pre-transplant vs 2.9% control (p = 0.01, OR, 5.84 [95% confidence interval {CI}: 1.25 – 36.77]). Incidence of 365-day CDI was 28.3% pre-transplant vs 5.9% control (p = 0.0004). Nine (26.1%) subjects in the pre-transplant population experienced delayed graft function vs nine (8.8%) in the control group (p = 0.01).

Kidney transplant recipients with a history of CDI prior transplant have a significantly increased risk of CDI 90 days and 365 days after transplant.

Primary Student Presenter: Scott Tilden

Presenting School: Graduate

Degree Seeking: PhD

Year: 4th

Mentor: Tom Anchordoquy

Poster Title: Toxic of Helpful?

Exploring the Body's Response to Virus-Like Nanoparticles

Final Category: Other

Abstract:

For decades now, nanomedicines have been touted as the future of cancer therapy. However, the field of tumor-targeted nanomedicine has failed to significantly advance toward becoming the primary choice for cancer intervention. The largest obstacle that has yet to be overcome is off-target accumulation of the nanoparticles. Even with engineered “stealth” formulations most of the dose will be taken up by the liver, spleen, and other major organs. Today, chemotherapeutic nanomedicines are still highly dose-limited due to off-target toxicities. We propose a novel approach to “targeting” nanomedicines by focusing on decreasing off-target accumulation rather than directly increasing tumor delivery. Acknowledging a poorly understood “refractory” response to intravenously injected gene therapy vectors, observed in ours and other studies, we hypothesize that virus-like particles can be utilized to limit the off-target accumulation of nanoparticles. Indeed, our results show a significant reduction of dextran deposition in the liver (~13% reduction) and spleen (~40% reduction) with a concurrent increase in tumor dextran accumulation (~27% increase) when the dextran was administered 24 hours after a virus-like particle injection. These data demonstrate that an anti-viral response initiated by an injection of virus-like particles can reduce major organ accumulation of a subsequently administered particle while simultaneously increasing tumor accumulation.

Primary Student Presenter: Satya Raj Trikha

Presenting School: Medicine

Degree Seeking: MD

Year: 1st

Mentor: Josiane Broussard

Poster Title: Prevalence of Obstructive Sleep Apnea in Collegiate Football Players at Colorado State University

Final Category: Healthcare and Public Health

Abstract:

More than 54 million Americans between the ages of 30-69 have some level of obstructive sleep apnea (OSA). OSA increases the risk for several cardiometabolic diseases, depression, and a reduced quality of life. Risk factors for OSA include high body mass index (BMI), large neck size, narrowed airway, and male sex. Indeed, results from previous studies demonstrate higher prevalence of OSA and other sleep disorders in professional football players (50% of football players vs. 25% in the general population), as they present with many of these risk factors. These risk factors are also present in collegiate football players; however, the proportion of younger athletes impacted by OSA is unknown. In the current study, we tested the hypothesis that a higher prevalence of OSA already exists in collegiate football players compared to the general population.

Participants were recruited from the Colorado State University (CSU) football team in the fall of 2019. Following informed consent, anatomical evaluations were conducted to assess neck circumference and unique upper airway features. Participants also completed in-depth healthy history and sleep questionnaires. Participants were then provided instructions and a WatchPat 3000 device for in-home estimations of Apnea Hypopnea Index (AHI), blood oxygen saturation, and body position on 3 consecutive nights. WatchPat data were autoscored and evaluated by 2 sleep physicians.

Fifty-eight young, healthy men completed the study (BMI: 29.0 ± 5.5 kg/m2; neck circumference: 16.7 ± 1.2 in; mean±SD). Based on WatchPat 3000 data analyses, 38% (n=22) of study participants had clinically defined mild to moderate OSA (mild: 5-15 AHI; moderate: 16-30 AHI).

Collegiate football players at CSU present with OSA at a higher rate than non-athletes, but lower than NFL players. It is unknown whether the presence of OSA in younger individuals is associated with elevated risk for development of cardiovascular disease and type 2 diabetes later in life.

Primary Student Presenter: Theresa Welle

Presenting School: Medicine

Degree Seeking: PhD

Year: 4th

Mentor: Katharine Smith

Poster Title: The role of mRNA translation in homeostatic plasticity of inhibitory synapses

Final Category: Neuroscience and Brain and Behavior - Adult

Abstract:

Neurons communicate via synaptic connections, which can generally be characterized as excitatory or inhibitory, depending on whether they promote or suppress neuronal firing. In response to global changes in neural activity, synapses undergo homeostatic plasticity as a compensatory mechanism. Homeostatic plasticity of excitatory and inhibitory synapses plays a key role in sensory development and memory consolidation. Little is known about the mechanisms supporting homeostatic scaling of inhibitory synapses, which is crucial to these neural functions. mRNA translation of genes essential for synaptic function has been shown to support multiple forms of plasticity, including long-term potentiation of inhibitory synapses. In this project, I examine the role of mRNA translation in homeostatic inhibitory synaptic plasticity. Using immunocytochemistry to quantify the expression of inhibitory synaptic proteins and quantitative reverse-transcription PCR to measure the expression of inhibitory synaptic transcripts, I observe that synaptic expression of inhibitory synaptic markers increases during homeostatic scaling of inhibitory synapses in a translation-dependent manner. Further, I observe modulations of mRNA levels as well as increased translational activity of inhibitory synaptic transcripts during this form of plasticity. These results suggest that mRNA translation plays a key role in homeostatic scaling of inhibitory synapses, and that this may include increased translation of specific genes crucial for inhibitory synaptic function and plasticity. In the future, I would like to probe the mechanisms which regulate translation during homeostatic scaling of inhibitory synapses.

Primary Student Presenter: Derek Wengryn

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Vijaya Vemulakonda

Poster Title: Association of an Undescended Testicle Video Decision Aid with Shared Decision-Making

Final Category: Education

Abstract:

Shared decision-making (SDM) has been identified as a key component in improving patient care and outcomes. While patient decision aids have been shown to improve SDM, their use in pediatric urology has not been well-studied. This study evaluates whether an educational video can improve the perception and quality of SDM in the setting of undescended testicle (UDT) consults.

New patients presenting to a tertiary pediatric urology clinic visit with a referral diagnosis of UDT were eligible for the study. Patients were randomly assigned to an intervention group where an educational video on UDT was shown before the visit or a control group where the video was not shown. Parents in both groups were given the SDM-Q-9 survey (SDMQ9) to complete following their visit.

The SDMQ9 was administered to 153 guardians. 92 guardians were randomly assigned to the intervention group and 61 were randomly assigned to the control group. Overall, the educational video group showed a statistically significant greater perception and higher quality of SDM than the control group ($p=0.049$). There were three individual questions that were significantly improved in the educational video group. The first was “My doctor asked me which treatment option I prefer” ($p=0.036$), the second was “My doctor and I thoroughly weighed the treatment options” ($p=0.036$), and the third was “My doctor and I selected a treatment option together” ($p=0.054$)

In parents of children referred for UDT, use of an educational video prior to discussions about treatment increased the quality of SDM. Further research is needed to better understand the role of video education in increasing understanding and engagement in SDM in pediatric urology.

Primary Student Presenter: Kelly Wigglesworth

Presenting School: Medicine

Degree Seeking: MD

Year: 4th

Mentor: Michael Shank

Poster Title: Hereditary Hypophosphatasia In A 30-Year-Old Female With Chronic Bone Pain

Final Category: Metabolism and Endocrinology

Abstract:

Hereditary hypophosphatasia (HPP) is a rare autosomal recessive disorder, characterized by disrupted mineralization of bones and teeth. It is often caused by loss-of-function mutations in the ALPL gene that encodes the tissue-nonspecific isoenzyme of alkaline phosphatase (ALP). Symptoms include defective mineralization of bone, premature loss of teeth, and decreased serum ALP activity. Severe cases may also include fractures, rickets, and respiratory insufficiency. Chronic bone pain is a common symptom, but less specific, and often preceded by gross deformities. Adult onset HPP can be missed, given its uncommon and complex nature. There have been few reports of HPP presenting in adulthood, which were mistaken for osteoporosis. In the current case, the patient was a 30 year old female with a long history of chronic, progressive bone pain since childhood who presented to her family medicine physician. Her ALP level at the time of the visit was 31 U/L (Ref: 35-147 U/L). She previously had low ALP levels intermixed with low-normal. The persistent, distressing bone pain and decreased ALP levels prompted genetic testing, which revealed an ALPL gene .571G>A (p.Glu191Lys) mutation, indicating HPP. Since diagnosis, she has normal DEXA scans, tibial x-rays, and renal ultrasound. Her course of treatment has mostly consisted of pain management with tapentadol, gabapentin, buprenorphine and her geneticist have discussed treatment with hormone replacement and teriparatide--modified parathyroid hormone that promotes bone growth. HPP is important to consider in patients with chronic bone pain, regardless of the consistency of ALP levels. It is also imperative to distinguish bone pain compared to pain of muscular origin, as seen with fibromyalgia. Diagnosis of HPP may provide more treatment options with teriparatide and ALP replacement.

Primary Student Presenter: Margo Wohlfeil

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Rajeev Vibhakar

Poster Title: The Role of CDK12 in Pediatric Medulloblastoma

Final Category: Hematology and Oncology

Abstract:

Medulloblastoma is the most common type of malignant brain cancer in the pediatric population, with different subtypes conferring different prognoses. MYC-driven medulloblastoma (MB) has a poor 5-year survival rate, due to lack of therapeutic targets and frequent metastasis to the CSF. MYC overexpression causes malignant cell sensitization to apoptosis via transcriptional dysregulation and increased proliferation. A CRISPR-Cas9 essentiality screen was done to identify MYC-MB therapeutic targets on 1,140 genes. CDK12 was identified as a top essential gene for MYC-MB viability. Using shRNA genetic depletion as well as small molecule inhibitors of CDK12 in in vitro studies, we observe a decrease in tumor growth and increase in apoptosis. CDK12 inhibition causes a decrease in expression of DNA damage response genes, as well as disruption of transcriptional elongation via RNA polymerase II inhibition. This inhibition desensitizes tumor cells to apoptosis, while enhancing sensitivity to DNA damaging agents. These studies identify CDK12 inhibition as a possible therapeutic target for MYC-amplified medulloblastoma.

Primary Student Presenter: Jonathan Zakrajsek

Presenting School: Medicine

Degree Seeking: MD

Year: 2nd

Mentor: Bill Vandivier

Poster Title: Outcomes Associated with Asthma Exacerbations with Respiratory Failure Treated with Extracorporeal Membrane Oxygenation (ECMO)

Final Category: Pulmonary and Critical Care

Abstract:

Rationale: Asthma affects 20 million adults in the United States resulting in up to 500,000 hospitalizations each year. Patients admitted to the intensive care unit (ICU) for asthma exacerbations requiring invasive ventilation have a mortality of ~7%. Extracorporeal membrane oxygenation (ECMO) is a salvage technique used in patients with respiratory failure to increase delivery of oxygen, remove CO2 and allow time for recovery. Case series and uncontrolled registry studies have examined benefits of ECMO for asthma exacerbations with respiratory failure, but no studies have examined outcomes associated with use of ECMO for asthma exacerbations compared to standard care. Objective: To assess outcomes associated with use of ECMO during asthma exacerbations requiring invasive ventilation compared to standard care.

Methods: Patients were extracted from the Premier Database from 2010-2020 if they had a primary diagnosis of asthma, or a primary diagnosis of respiratory failure with a secondary diagnosis of asthma, and were treated with invasive ventilation. Patients were excluded for age < 18y, no ICU admission, chronic lung disease other than asthma, COVID-19, or if they were not treated with corticosteroids. Hospital mortality was the primary study outcome. Key secondary outcomes included ICU length of stay (LOS), hospital LOS, length of invasive ventilation and hospital costs. Differences in outcomes were assessed using propensity score matching at a 1:2 ratio of ECMO versus no ECMO, and by covariate adjustment of the entire study group.

Results: A total of 20,494 patients with asthma exacerbations requiring invasive ventilation were included in the study, of which 130 were treated with ECMO and 20,364 were not. After propensity matching, ECMO (N=103) versus no ECMO (N=206) was associated with reduced mortality (11.4% vs. 23.3%, p = 0.017) and increased hospital costs, but no difference in ICU LOS, hospital LOS or length of mechanical ventilation (Table). The covariate-adjusted model replicated these findings (Table). When individual patients were assigned a probability of being treated with ECMO equal to the hospital rate where they were admitted, each 10% increase in the hospital rate of ECMO was associated with no change in the odds of mortality (OR, 1.12: 95% CI, 0.82-1.52), p=0.48). ECMO was also associated with increased renal replacement therapy (P = 0.02), shock (P=0.02) and 30-day all-cause readmission (P =

0.01).

Conclusion: ECMO was associated with reduced mortality at the cost of increased morbidity in asthmatics requiring invasive ventilation, indicating that ECMO has the potential to save thousands of lives.