

Patient Education and Career Pathways:

Educating Patients on Diabetic Neuropathy

Maria Elsoury

This quality improvement project consisted of educating patients on diabetic foot health. A large majority of the patient base at Summa Health had an indication on their chart for diabetes. The hospital generally serves a lower-income demographic, and the outreach for diabetic foot health is important. Upon rounding and observing patient charts, it was evident that a lot of the patients did not have symptoms indicative of peripheral neuropathy. This makes patients susceptible to an absence of feeling in their feet when an injury or cut is in place. This, in turn, can result in skin infections and potentially osteomyelitis which are grounds for amputation if it progresses. The objective and summary of the brochure was to indicate to the patient what they could do to prevent it and provide a basic overview of what diabetic foot health is and its importance.

Handout with updated direction on aiding patients in smoking cessation in a primary care clinic

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According to the Centers for Disease Control and Prevention, around 11.5% of adults in the United States consistently smoked cigarettes in 2021. Smoking cessation can be a difficult process and is one seen often in primary care clinics. Therefore, it is essential to have a firm understanding of the most effective methods to help patients quit smoking. We performed a literature review of recent studies concerning the quality of different practices in smoking cessation. A handout was created to function as a comprehensive guide for physicians to help patients stop smoking. This handout outlines the 5 A's of managing smoking cessation; pros and cons of the most prevalent medications used in smoking cessation; and lists other aspects of treatment outside pharmaceuticals including counseling resources, follow-up needs, and risk factors for relapse. We intend on giving this handout to family physicians employed at Mercy Health – Columbiana Primary Care to be used in future practice. To measure the effectiveness of the handout, we will administer a short questionnaire before and after reading the handout asking the reader about their knowledge of the content.

Impact of Neurology Educational Experiences on Student Interest in Neuroscience Specialties

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Purpose: This study aims to investigate the influence that neurology experiences have upon medical students' interest in that field and specifically their decisions to apply to the neuroscience residency programs.

Methods: The 2022-2023 M3 and M4 classes at NEOMED were sent a nine-question survey to complete, which evaluated attitudes towards neurology and how experiences over the entirety of students' higher education have influenced those attitudes. Questions were formulated by medical students, faculty, and statisticians. Reminders were sent to students after two weeks.

Results: We received 87 responses (43 M3's and 44 M4's). After SPSS analysis, there was no statistical significance in student interest in neurology after preclinical coursework or in desire to pursue neuroscience residencies after elective rotation. However, qualitative increases were noted in both categories.

Discussion/Conclusions: Though the results lacked statistical significance, this study provided an informative first step in evaluating whether pre-clinical/clinical experiences enhanced students' interest in neurology. One opportunity to increase the small sample size is to administer this survey to additional medical schools to see if similar trends exist. We found that many students had enhanced interest in neurology before medical school and post-M1/M2 coursework, but the number of residency applications was much lower. What can be done to address this? Additional work is planned which is intended to provide further insight into the critical periods in which students gain or lose interest so that strategies can be developed to maximize student interest as the demand for neurologists increases.

Medical Students as Teachers: Preparing the Next Generation

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There is a well-documented shortage of physicians in rural areas, and since research has shown that medical students from rural areas are more likely to return to rural areas to practice, one of the potential solutions to the healthcare shortage is to recruit medical students from rural areas. Northeast Ohio Medical University (NEOMED) has a rural medical education (RMED) pathway program that brings together medical students interested in rural medicine to participate in a student-centered learning community. To facilitate community involvement and promote healthcare-related career pathways among local rural high school students, faculty and students at NEOMED implemented a program where current rural pathway medical students served as teachers in a local rural high school. Medical students taught multiple sessions throughout the academic year. The sessions included assisting with animal dissections in biology classes and inviting students on field trips to the medical university. This program served as an opportunity for the high school students to meet current medical students and learn more about college, medical school, and healthcare-related fields. For the medical students, by engaging early and meaningfully in these experiences, it may encourage students to pursue careers in medical education and engage deeply in community service and leadership.

Improving Patient Education for Self-Management of Diabetes Mellitus

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Physicians often struggle to educate their patients about diabetes. Patient education is meant to bridge that gap between the physician and patient. However, due to the difficult medical terminology used and the advanced reading level required, low health literacy can lead to worse health outcomes. The NIH and AMA set recommendations that were followed to edit currently used education materials. Using the Flesch Reading-Ease Test, new materials were confirmed to be under an eighth grade reading level. By meeting these goals, it's hopeful that patients will be more informed and more able to conduct self-care.

Improving Portal System Enrollment and Engagemet at AxessPointe

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Patient portals can improve patient-provider communication, strengthen patient engagement, and improve health outcomes. Previously at Axesspointe, enrolling patients into the healow health portal was the responsibility of the front desk team who are often busy with checking in patients, answering phone calls and completing other necessary tasks. The exam rooms had a poster that prompted patients to ask the providers and nurses about the portal, but it did not have sufficient information for the patients to enroll independently. To improve patient interaction with the portal system, an updated poster was created and placed in exam rooms. It contains information about the benefits of the portal system as well as a QR code that takes the patients directly to the enrollment page with instructions on how to create an account. The goal is to see an increase in portal account enrollment as well as increased patient engagement with the portal and app.

Orthopedics:

Role of TUT7 in Age Related Intervertebral Disc Degeneration

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Aging related intervertebral disc degeneration (IDD) is one of the most common cause of chronic low back pain. Intervertebral discs (IVDs) contain collagen, proteoglycans and are avascular. The disc can be organized into three regions, a gelatinous nucleus pulposus (NP), a fibrocartilaginous annulus fibrosus (AF), and cartilaginous endplate; these structures are integral to preserving spinal flexibility. Degeneration of both the NP and AF leads to a loss of osmotic pressure along with dehydration, resulting in disc bulging and ultimately a decrease in disc height. Disc bulging can lead to many neurological and musculoskeletal deficits such as sciatica, analgesia, spinal stenosis, and paresis. Terminal Uridyltransferase 7 (TUT7) uridylates 3'-ends of mRNA and miRNA and may alter their stability and function. TUT7 mediated uridylation of IL-6 targeting microRNA results in increased expression of cells leading to a pro-inflammatory response. Both WT and Tut7KO mice spines were harvested at 56-62 weeks, embedded, cut into 5-8 μ m sagittal sections and stained with hematoxylin and eosin (H&E) and picrosirius red. TUut7KO aged mice showed resistance to aging-related intervertebral disc degeneration compared to age matched WT mice. Disc damage scoring system data suggests that aged Tut7KO mice preserve AF more effectively than NP. Despite having much healthier overall discs, aged Tut7KO mice exhibit more bone remodeling than aged WT mice. Picrosirius red stained images will be used in future studies to visualize and quantify collagen fiber disorganization using polarized light microscopy in aged WT and aged TUT7KO mice.

Recurrent instability after shoulder stabilization surgery at a single pediatric institution: A different approach to defining failure

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Purpose: There is a relatively high recurrence of shoulder instability after primary shoulder stabilization surgery reported in the literature (17-51%). Some attribute this wide range of failures to how recurrence is defined and call for standardization. The purpose of this study is to

propose a different approach to defining recurrent instability using a large series of failures from a single pediatric institution.

Methods: In this retrospective review, a single pediatric institutional database was searched to identify all cases of shoulder stabilization surgery for anterior or multi-directional instability (MDI) over 10 years. Office charts were reviewed for failed cases, defined as any case requiring a second shoulder surgery, reduction of dislocation in the ED, or any subjective complaints of recurrent shoulder instability or pain at last follow-up at least 1 year post-surgery. Mode of failure was assigned using the following categories: objective failure, subjective failure treated surgically, and subjective failure treated conservatively. Cause of failure was also assigned to each case (new trauma, non-traumatic failure, noncompliance, overuse, pain). Failures of index anterior instability and MDI cases were compared.

Conclusion: Using these criteria, significant differences were noted between the anterior and MDI groups. Patients that underwent anterior stabilization were more likely to have objective signs of failure as the result of a new trauma, while those initially treated for MDI were more likely to report recurrence of symptoms without appreciable pathology or traumatic event. In addition to standardizing outcomes in research, appropriately categorizing failure can help guide surgical decisions for primary and recurrent shoulder instability.

THE THERAPEUTIC ROLE OF OSTEOACTIVIN/GPNMB IN POST-TRAUMATIC OSTEOARTHRITIS

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Osteoarthritis is a degenerative disease affecting approximately 530 million individuals worldwide. Currently no disease modifying therapeutic options are available to treat osteoarthritis. We seek to investigate the therapeutic potential of osteoactivin, also known as glycoprotein nonmetastatic melanoma protein B (GPNMB), an anti-inflammatory glycoprotein, in osteoarthritis. We utilized intra-articular recombinant GPNMB (rGPNMB) and GPNMB related-peptide (GPNMBp) injection in a mouse model of post-traumatic osteoarthritis. We performed destabilization of medial meniscus (DMM) surgery of the right knee on C57BL/6 male mice at 10 weeks of age. Treatment groups included control (no DMM surgery or treatment), sham surgery, DMM surgery with PBS injection, DMM surgery with rGPNMB injection (2mg) and DMM surgery with GPNMBp injection (120mM). Injections were performed at 6 weeks post-DMM surgery. Animals were sacrificed at 14 weeks post-DMM surgery and knees were decalcified, fixed, and paraffin embedded. Sections were either stained with Safarin-O and fast green and scored per the OARSI scoring system, or immunostained for aggrecan, matrix metalloproteinase-13 (MMP-13), or GPNMB. Results showed that intra-articular injection led to significantly less severe osteoarthritis in the medial femoral condyle (MFC) of animals treated with rGPNMB or GPNMBp compared to those treated with PBS. Immunostaining results showed that rGPNMB or GPNMBp treatment increased GPNMB and aggrecan staining in articular chondrocytes and decreased MMP-13 staining compared to the PBS treated group. Overall, our preliminary results suggest that rGPNMB and GPNMBp prevent continued cartilage damage following joint injury. This shows rGPNMB and GPNMBp's potential therapeutic use in the treatment of post-traumatic osteoarthritis.

THE IMPACT OF KETOROLAC UTILIZATION ON OUTCOMES IN SPINE SURGERY: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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Purpose: The purpose of this study is to examine the impact of ketorolac utilization with or without other medications in an analgesic regimen on postoperative outcomes following spine surgery.

Methods: A systematic review and meta-analysis of randomized controlled trials (RCTs) was performed using PubMed, CINAHL, MEDLINE, and Web of Science in July 2023. Inclusion criteria were articles that utilized ketorolac, articles concerning spine surgery of any region, full-text English articles, and RCTs only.

Results: Fourteen RCTs were included from 1,007 articles (n=1,137 patients; frequency weighted mean age of 53.9 ± 7.6 years; 610 patients in the ketorolac group). There was no significant difference in the total postoperative morphine utilization between patients in the ketorolac group (n=261) as compared to patients in the non-ketorolac group (n=267) via meta-analysis (p=0.109). There was no significant difference in the postoperative Visual Analog Scale (VAS) scores at 24-hours and final follow-up between groups (p=0.065 and p=0.582, respectively). There was also no significant difference in the 24-hour postoperative morphine utilization or LOS between groups via meta-analysis (p=0.185 and p=0.990, respectively). Overall, patients in the ketorolac group had an absolute lower rate of major complications as compared to patients in the non-ketorolac group (3.8% versus 6.7%).

Conclusion: There is no significant difference in total postoperative morphine utilization, 24-hour postoperative morphine utilization, VAS scores, or LOS after spine surgery between patients receiving ketorolac with or without other medications in an analgesic regimen as compared to patients not receiving ketorolac within an analgesic regimen via meta-analysis of RCTs.

Role of TUT7 in Age-related Intervertebral Disc Degeneration

Mustafa Husein, Adam Ellis, Jacob Moncher, Mohammed Yunus Ansari PhD

Intervertebral disc (IVD) degeneration (IDD) is one of the major causes of low back pain in millions of people worldwide. IDD is characterized by high inflammation, matrix remodeling, drying of nucleus pulposus (NP), and tear in annulus fibrosus (AF). Unfortunately, there is no drug of treatment for IDD. Research is currently being done to find drug-target genes which are associated with IDD pathogenesis. Terminal uridylyltransferase 7 (Tut7) performs the uridylation of mRNA and microRNA and affects their stability and function. However, the role of Tut7 in IDD is unknown. Mouse tail samples from 15-month-old Tut7KO and wt littermates were dissected and processed to investigate the effect of Tut7 in aging-related IDD pathogenesis. The tail samples were stained with H&E, toluidine blue, and picosirius red. A histopathology scoring method was used to determine the severity of IDD in age and sex-matched wild-type and Tut7KO mice. Immunofluorescence staining was used to determine inflammatory markers and matrix-degrading protease expression. The wild-type IVD showed significant IDD and had an average score of 3 for the NP and 2 for the AF. The Tut7KO IVD had an average score of 1 for the NP and AF suggesting improved IVD health. Immunofluorescent staining showed decreased levels of Il-6, Mmp13, and

Cox2 in the Tut7KO discs. We demonstrate here that Tut7 deletion protects mice from aging-related IDD by suppressing inflammation and matrix degradation. Our data shows that Tut7 plays a pathological role in disc degeneration and can be used as a drug target to treat IDD.

Neurodegenerative Disorders:

Mapping the Autonomic Deep Cerebellar Nuclei

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PURPOSE: The present study employs neuroanatomical tracing technology to define the specific sites within the deep cerebellar nuclei that influence the adrenal medulla's sympathetic output. These identified cerebellar areas may ultimately help develop targeted treatments for dysautonomia.

METHODS: A trans-neuronal tracer, rabies virus, was injected into the adrenal medulla of two anesthetized capuchin monkeys. The virus retrogradely transported through interconnected neuron chains. After the virus traversed four synapses, animals were deeply anesthetized, and the nervous system was fixed and cryo-protected via transcardial perfusion. Using a cryostat, we prepared serial sections (50 μm) of the cerebellum in the coronal plane. Neurons containing the trans-neuronal tracer were immunohistochemically labeled using a primary antibody to rabies virus. Cresyl violet staining was used to identify the locations of the deep cerebellar nuclei on separate sections. All sections were mounted onto glass slides and cover slipped. Scanning microscopy digitized the imaged sections. We analyzed these sections to determine the location of labeled neurons within each deep cerebellar nucleus.

RESULTS: Cerebellar output neurons were distributed across all four deep cerebellar nuclei. The majority were identified in the ipsilateral nuclei. The greatest number of neurons were located in the ipsilateral fastigial nucleus.

CONCLUSIONS: Our results demonstrate that rabies virus can be used to successfully identify fourth-order neurons of the deep cerebellar nuclei that influence the adrenal medulla. Neurons that control sympathetic output are distributed across all four deep cerebellar nuclei.

Deep Cerebellar Nuclei's Influence on the Autonomic Nervous System

Labeeb Ahmad, B.S.

Dysautonomia is a prominent and debilitating symptom prevalent in many neuropsychiatric and neurodevelopmental disorders, including anxiety disorders and autism spectrum disorder. Dysautonomia may arise from a problem in how the central nervous system regulates the adrenal medulla. The neural circuits in control of the adrenal medulla's sympathetic output are not fully defined; filling this fundamental gap in knowledge is crucial in understanding how the circuit may go awry in the aforementioned disorders. One group of these circuits is the deep cerebellar's nuclei influence on the output of the adrenal medulla. In order to identify these circuits, the following studies used trans-neuronal transport of rabies virus in non-human primates. First, we injected rabies virus into the adrenal medulla of capuchin monkeys (*Cebus apella*). Then, we prepared frozen sections of the cerebellum (coronal plane). We labeled neurons of the deep cerebellar nuclei using immunohistochemistry. Finally, we scanned sections and plotted the spatial locations of the immunolabeled deep cerebellar nuclei neurons. Our data indicate that all of the deep cerebellar nuclei exert multi-synaptic influences over the adrenal's sympathetic

output, with the greatest number in the fastigial nucleus. This research aims to fill gaps in knowledge that may exert a sustained influence on how the neuroscience field views the autonomic cerebellum. By doing so, this work may ultimately help us develop therapeutic targets for dysautonomia in neuropsychiatric disorders.

ULTRASTRUCTURE OF NPY PROFILES IN THE YOUNG AND OLD CENTRAL INFERIOR COLLICULUS

Joshua C. Harris, Laila S. Almassri, Kristen M. Crane, Nick J. Tokar, Andrew P. Ohl, Jeffrey G. Mellott

The age-related downregulation of GABAergic neurotransmission in the inferior colliculus (IC) leads to impairments characteristic of presbycusis. Studies have demonstrated that Neuropeptide Y (NPY) is expressed by a subset of IC GABAergic cells to dampen excitability. We characterized and quantified the ultrastructure of NPY boutons to determine if NPY is downregulated in the aging IC. We used 3- and 28-month-old Fischer Brown Norway (FBN) rats. Blocks of tissue were taken from the central IC (ICc). Pre- and/or post-embedding NPY immunolabeling was conducted for transmission electron microscopy. Ultrathin sections (~50 nm) were stained for contrast.

Most (~90%) of young NPY positive boutons/synapses formed symmetric junctions and contained either pleomorphic or round vesicles. NPY synapses primarily targeted NPY-negative dendrites. NPY positive dendrites were commonly targeted by excitatory synapses. At old age our data suggest that NPY synapses are downregulated (~25%). Also at old age, NPY synapses were more commonly observed on larger dendrites. Our data also demonstrated that astrocytes may downregulate NPY with age.

Broadly speaking, we found that most NPY boutons had inhibitory synaptic characteristics (symmetric synapse; flat vesicles), which agrees with light level reports. However, a subset of NPY synapses formed asymmetric/excitatory junctions at old age. This change may reflect unique postsynaptic properties of neuromodulator/neuropeptide release at old age. The age-related loss of NPY in the IC may result in impaired neural input driving hemodynamic responses. Taken together, the age-related loss of NPY in the IC may broadly impair hearing by reducing inhibition and/or affecting neurovascular function.

Investigating Methods to Assess Simultaneous Excitatory and Inhibitory Neural Activity in Mongolian Gerbils Primary Auditory Cortex

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Early life stress (ELS) affects attention and learning, along with the balance of excitation and inhibition in neural regions that mediate these behaviors. We have shown that ELS in Mongolian gerbils also impairs the perception of rapidly changing sounds that are critical for vocal communication, and the sensitivity of auditory cortex (ACx) to these sounds (1). These detections rely on the amplitude and relative timing of excitation and inhibition, which we hypothesize is altered by ELS. To test this, we are optimizing a technique to record simultaneously from identified excitatory and inhibitory cell populations in ACx while gerbils detect sounds.

Methods: Various volumes of adeno-viruses (AAV) were injected through a craniotomy: CaMKII-jGCaMP6f, CaMKII-jRGECO1a, and/or mDLX-jGCaMP6f are selectively taken up

and transcribed by excitatory or inhibitory neurons based on the promoter sequence. A 1mm-diameter GRIN (gradient index) lens was implanted at various positions relative to the injection sites. Animals recovered for 3-4 weeks to allow viral expression. The lens allows for real-time analysis of neural activity via fluorescence changes in separate fluorescent channels, distinguishing excitatory and inhibitory neurons.

Results: We are determining the appropriate volume and location of viral injections and lens implantation for simultaneous visualization of inhibitory and excitatory neurons, accurately targeting left ACx. Strong, accurate viral expression in sliced tissue was achieved with 150 nanoliter injections at stereotaxic coordinates 5.1mm anterior and 3.5mm lateral of lambda. Some fluorescence was seen through the GRIN lens. We are currently waiting for viral expression to test additional implanted animals.

Mapping of cell-surface integrin $\alpha V\beta 5$ in brains of Alzheimer's model mice and control mice

Leslie Gonzalez, Christine M. Dengler-Crish, Ph.D.

Cell-surface integrins play important roles in neuroplasticity, and prior research suggests that dysfunction of $\alpha V\beta$ integrins can facilitate beta-amyloid and tau protein pathology accumulation in Alzheimer's disease (AD). Thus, understanding the novel role of integrin dysfunction in AD may open up new treatment options to prevent AD. In the AD brain, it is unknown whether changes in integrin expression occur in the hippocampus, the major brain structure damaged in the disease. Here, we sought to map integrin expression in the hippocampus of transgenic AD 3xtg mice and healthy control mice. Immunofluorescence assays were performed to optimize integrin subtype-recognizing antibodies. After optimization, assays were performed to label $\alpha V\beta 5$ integrins in fixed brain sections from mice. Epifluorescent microscopy was used to image hippocampal sections across CA1, CA2, CA3, dentate gyrus (DG), and subiculum from animal groups that included pre-pathological and pathologically-aged female and male 3xtg mice along with age and sex-matched healthy C57BL6J control mice. Qualitative analysis of integrin expression in hippocampal regions across animal groups revealed, in all animals, highest expression of $\alpha V\beta 5$ in the pyramidal layer of CA3, the granule cell and polymorph layers of DG, and the dorsal pyramidal layer of the subiculum. Lowest $\alpha V\beta 5$ integrin expression was found in the stratum radiatum layer of CA1 and CA3 and the molecular layer of the DG. This work provides new data on distribution of $\alpha V\beta$ integrin subtypes and will support further research into pharmacological strategies against the development of dementia.

Structural and functional alteration in retinal ganglion cells following traumatic brain injury

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Purpose: Circadian rhythm abnormalities are reported in patients following concussion and moderate brain trauma early in the injury timeline. These include abnormal timing and duration of the sleep cycle, reduction of melatonin levels during the night, and alternating expression of clock genes. Although these deficits could be caused by dysregulation within several brain sites, the retina has been postulated as one of the earliest neural structures affected in several neurodegenerative conditions. Melanopsin-expressing retinal ganglion cells (mRGCs) are responsible for maintaining circadian rhythms, thus making the retina an attractive target for

investigating pathological mechanisms. Loss and or changes in morphology of mRGCs has been reported in other neurodegenerations such as Parkinson's disease and glaucoma, however, little is known about the progression of pathology in mRGC axons following traumatic brain injury (TBI).

Methods: Using a combination of in vivo electrophysiology, immunohistochemistry, and high-resolution fluorescent microscopy, we examined anterior visual pathway function, RGC morphology, and synaptic connectivity following a non-repetitive, controlled cortical impact (CCI) injury in animal subjects.

Results: Our results indicate a significant reduction in dendritic field complexity and synaptic innervation in mRGCs without cell loss in the retina of injured subjects 1-week after injury. These mRGC-specific changes were accompanied by border physiological changes in the anterior visual pathway.

Conclusions: Early changes in mRGC morphology may contribute to the irregular sleep patterns observed in TBI patients. The accessibility, isolation, and simplicity of the anterior visual system may provide a useful framework for studying the mechanisms of axonopathy following brain injury.

Defining Hippocampal Neural Circuits That Influence Sympathetic Output

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Purpose: Autonomic nervous system dysregulation, or "dysautonomia," may occur when the central nervous system control over peripheral autonomic organs becomes disrupted. This dysautonomia is common in many neurodevelopmental and neuropsychiatric disorders and commonly co-occurs with learning and memory impairments. One brain region implicated in learning and memory is the hippocampus. Yet, little is known about which regions of the hippocampal formation influence autonomic output. Filling this gap in knowledge may advance our understanding of how to manage learning and memory impairments in dysautonomia. Thus, the present study aimed to identify the hippocampal neural circuits that influence sympathetic output of the adrenal medulla.

Methods: Rabies virus was injected into the adrenal medulla of marmoset monkeys (*Callithrix jacchus*). Following trans-neuronal transport of rabies virus into hippocampal neurons, we then prepared frozen coronal brain sections and immunolabeled infected neurons. Sections were digitized with a slide scanner. Then, we outlined regions of the hippocampus and plotted immunolabeled neurons.

Results/Conclusions: Preliminary results indicate that the subiculum contains the greatest number of neurons that send multi-synaptic projection to influence the adrenal's sympathetic output. These results suggest that the subiculum may have the greatest hippocampal control over the sympathetic nervous system.

NPY mRNA in the Young and Old Central Inferior Colliculus

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The age-related loss of inhibition in the inferior colliculus (IC) contributes to presbycusis. A subpopulation of GABAergic cells in the IC also express Neuropeptide Y to dampen neural excitability. We sought to determine if NPY mRNA is downregulated in the aging IC. We

quantified individual NPY mRNA across the IC subdivisions and classified cells as small, medium or large. We used 3- and 28-month-old Fischer Brown Norway (FBN) rats. NPY mRNA was revealed with single molecule fluorescent *in situ* hybridization and imaged with fluorescent microscopy. Tissue was stained with DAPI and NeuroTrace. Profile areas of each cell were recorded with NeuroLucida.

We analyzed 1,000+ IC cells that expressed NPY mRNA. These cells also express GAD1 mRNA. The densest population of NPY cells are in the dorsal cortex of the IC. Most (~80%) cells expressing NPY mRNA had medium profile areas with an average of 243.2 μm^2 at young age and 237.8 μm^2 at old age. The average number of NPY mRNA in medium young cells was 79.9. The average number of NPY mRNA in medium old cells was 48.3, a 39.5% reduction. Reductions in small and large cells were not as robust.

Our findings demonstrate that NPY mediated inhibition is likely reduced at old age. As NPY dampens neural excitability in the IC, the loss of NPY may contribute to an imbalance of inhibitory/excitatory neurotransmission. Thus, the poor temporal precision routinely present in elderly populations with hearing loss may be driven by the downregulation of NPY.

Neurological Lipid Dynamics: Regulation of Cholesterol Metabolism in the Gut-Brain Axis

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Fibroblast growth factor 15 (Fgf15, human homolog FGF19) is a gut-produced hormone with wide-ranging roles in embryogenesis. In adults, Fgf15 signaling is targeted to the liver, where it reduces bile acid synthesis. Bile acids are synthesized from cholesterol and play a major role in maintaining cholesterol homeostasis. Bile acid and cholesterol metabolism are also affected by alcohol consumption, but the data are conflicting and inconclusive. In this study, we aimed to evaluate how alcohol consumption affects cholesterol metabolism in the liver and brain of Fgf15 intestinal knockout (iKO) mice. Mice were subjected to 10 days of ethanol consumption via a liquid diet followed by an ethanol gavage 9 hours prior to termination to simulate a binge-drinking episode. In the liver, cholesterol levels were not altered by Fgf15 knockout or ethanol consumption, though serum cholesterol and fecal cholesterol excretion were reduced in iFgf15 KO. mRNA expression levels of key enzymes involved in cholesterol metabolism were examined in the hypothalamus. Results revealed significant differences in the expression patterns of *Pppara* and *Hmgcr* between control and iFgf15 KO mice consuming alcohol. Moreover, *Cyp27a1*, *Cyp7b1*, and *Pfkl* demonstrated distinct expression patterns which were not recapitulated in the hippocampus, consistent with the role of the hypothalamus in energy regulation. These results indicate that both ethanol and Fgf15 regulate cholesterol metabolism in the hypothalamus. Further studies examining the cell-specific roles of Fgf15 in cholesterol and energy metabolism will shed light on the role of Fgf15 in the gut-brain axis.

Descending Projections From the Inferior Colliculus to the Superior Olivary Complex

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Projections from the inferior colliculus (IC) to the superior olivary complex (SOC) have been characterized in several species and are thought to play a role in modulating early auditory processing. The main targets of the IC projection are the ventral nucleus of the trapezoid body

(VNTB) and the superior paraolivary nucleus (SPN). A projection from the IC to the VNTB has been shown in mice but projections to other SOC nuclei are uncharacterized, an important issue given the growing prominence of mice in auditory research. We injected an adeno-associated virus into the IC in mice to induce expression of a fluorescent protein by IC neurons. The brain was subsequently fixed by perfusion and cut into coronal sections that were stained with markers for Nissl substance, cholinergic neurons or GABAergic neurons and observed in a fluorescence microscope. We observed a widespread bilateral projection from the IC to the SOC. On both sides, labeled axons terminated heavily in the VNTB and moderately in the SPN. In addition, there was a strong bilateral termination in the lateral superior olivary nucleus (LSO). Across nuclei, labeled axonal boutons were located in the neuropil and in some cases appeared to contact GABAergic or cholinergic neurons directly. Our results demonstrate a robust projection from the IC to the SOC in mice, more widespread than previously reported in any species. We conclude that the descending projection from the IC is likely to modulate auditory brainstem processing bilaterally through direct actions on inhibitory (GABAergic) and modulatory (cholinergic) brainstem circuits.

Morphological changes in optic disc size in 3xtg compared to c57 mice across sex and age group

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It has been noted that structural and functional changes in the visual pathway are associated with Alzheimer's diseases (AD). The retina has been postulated as one of the earliest neural structures affected in AD. Thus, the optic disc and nerve head also may experience morphological changes. This loss may contribute to the early visual deficits seen in AD patients. While amyloid- β accumulation, mRGC loss, and gliosis in the retinas of mouse models of AD are evident, little is known about the progression of morphological changes of optic disc and nerve head. We postulated changes could be found in optic disc diameter across the 3xtg and c57 models as well as age and sex. An ophthalmoscope was used for fundoscopic imaging followed by simple data analysis. After using ImageJ to measure the area of the optic disc, we found that there was a qualitative difference in nerve disc between 3xtg and c57 mouse models. It was also notable that there are quantifiable differences in size of optic disk between 3xtg and c57. Among the female group, the c57 model had increased optic disk size in age 2-4 months and 3xtg increased optic disk size in age 12+, while there was no significant difference in 8-10 month. Within the male group, the 3xtg had increased optic disk size in age group 8-10 and 12+ month, but no significant difference in 2-4-month age group. These changes may be able to provide a framework for understanding the morphology in the progression of AD.

Pharmacology:

Evaluation of Prescribing Patterns in Local Community Intensive Care Unit for Hospital-acquired and Ventilator-associated Pneumonia Compared to Guideline Directed Therapy in Adults

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Purpose: The primary objective of this study is to evaluate antimicrobial prescribing habits of providers at University Hospital Portage Medical Center for the treatment of hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) in the intensive care unit (ICU) throughout 2022. Antimicrobial prescribing habits will be analyzed against guideline recommended therapy by the 2016 Infectious Disease Society of America (IDSA). Secondary objectives are patient outcomes including: length of inpatient and ICU stay, time on mechanical ventilation, and adverse drug reactions. A local unit-based antibiogram has been developed and will be utilized to retrospectively evaluate therapy.

Methods: Patients admitted to Portage Medical Center's ICU in 2022 will be divided by diagnosis of HAP or VAP and will be evaluated for appropriateness of therapy and the patient outcomes as listed above. Paired T-test will be utilized to evaluate therapy in patients based on an updated local unit-based antibiogram or presence of high risk characteristics for prescribed therapy compared to recommended therapy. Time-based secondary outcomes will be evaluated by T-test and adverse drug events will be evaluated by chi-square test. This is an ongoing study with results expected 10/31/2023.

Determination of Breastfeeding Safety with Opioid Use Disorder Treatment Drug Naltrexone

Kamille Miracle, MFM, Ryoichi Fujiwara, Ph.D.

Opioid use disorder (OUD) has increased in diagnosis in the last decade in the United States, alongside the use of medication assisted treatments (MAT). Since a large population of breastfeeding mothers are participating in MATs, the question of drug safety for breastfed neonates has arisen. The three main drugs used for MATs are buprenorphine, methadone, and naltrexone. While buprenorphine and methadone previously have been determined to be safe, naltrexone is a relatively new treatment for OUD and has not been studied extensively. This study aims to show that the doses of naltrexone, buprenorphine, and methadone received by neonates is low enough to be considered safe for mothers to continue their treatment and breastfeed simultaneously. The study uses a predictive model based on Milk/Plasma ratios and published peak serum drug concentrations, determined through a literature review, to estimate the dosage of naltrexone, buprenorphine, and methadone received by neonates through breastmilk. The results of the study showed that the dosage received by neonates through daily breastmilk intake of naltrexone, buprenorphine, and methadone is lower than the published infant therapeutic dosages. Therefore, the study concluded that the naltrexone dose in breastmilk is low enough to be considered safe for mothers to continue their treatment and breastfeed. The study also concluded in accordance with current standards that methadone and buprenorphine dosages received through breastmilk are also low enough to be safe for breastfeeding neonates.

An Answered Call for Aid? Cannabinoid Clinical Framework for the Opioid Epidemic

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Background: The opioid crisis continues in full force, as physicians and caregivers are desperate for resources to help patients with opioid use and chronic pain disorders find safer and more accessible non-opioid tools.

Main body: The purpose of this article is to review the current state of the opioid epidemic; the shifting picture of cannabinoids; and the research, policy, and current events that make opioid risk reduction an urgent public health challenge. The provided table contains an evidence-based clinical framework for the utilization of cannabinoids to treat patients with chronic pain who are dependent on opioids, seeking alternatives to opioids, and tapering opioids.

Conclusion: Based on a comprehensive review of the literature and epidemiological evidence to date, cannabinoids stand to be one of the most interesting, safe, and accessible tools available to attenuate the devastation resulting from the misuse and abuse of opioid narcotics. Considering the urgency of the opioid epidemic and broadening of cannabinoid accessibility amidst absent prescribing guidelines, the authors recommend use of this clinical framework in the contexts of both clinical research continuity and patient care.

Novel independent variant associated with CYP2D6 expression and activity

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Cytochrome P450 2D6 (CYP2D6) is a critical hepatic drug-metabolizing enzymes in humans as it plays a pivotal role in the metabolism of about 20-25% of clinically used medications. The CYP2D6 gene is highly polymorphic, resulting in substantial interindividual variability in its catalytic function and fluctuations in the pharmacokinetics and therapeutic outcomes of CYP2D6 substrate drugs. Though many functional CYP2D6 variants have been catalogued, a significant portion of the variability in the expression and activity of CYP2D6 remains unexplained. In this study, we performed a conditional genome-wide association study (GWAS) to identify novel variants associated with CYP2D6 protein expression in human livers, and further examined the impact of these variants on CYP2D6 activity in 100 individual liver samples. A label-free Data Independent Acquisition (DIA)-based proteomics method was utilized to quantify CYP2D6 protein concentrations. Genotyping on a genome-wide scale was achieved using the Illumina Multi-Ethnic Genotyping Array (MEGA). CYP2D6 activity was determined by measuring the production of dextrophan following an incubation study of dextromethorphan with individual human liver s9 fractions. We identified 31 GWAS lead SNPs that are significantly associated with CYP2D6 protein expressions with a p-value threshold of 5×10^{-8} . When accounting for the effect of the GWAS-identified SNPs and known functional CYP2D6 star alleles, one SNP located on Chromosome 22 (rs1807493) emerged as significantly and independently correlated with CYP2D6 protein expression. Notably, rs1807493 also exhibited a significant association with CYP2D6 activities in human livers, suggesting its potential to be catalogued as a novel and independent genetic variant related to CYP2D6.

Analysis of Current Treatments for Cannabinoid Hyperemesis Syndrome (CHS)

Leo Puhalla, BS, Jessica Lee, BS, BA, Quincy Chopra, MD

Purpose: Cannabinoid hyperemesis syndrome (CHS) is a condition associated with daily, long-term marijuana use and is characterized by cyclic, intense episodes of nausea and vomiting. Recent studies have found that haloperidol, a dopamine antagonist, is superior to traditional

antiemetics such as ondansetron for the management of CHS symptoms. This study compares haloperidol and droperidol in the symptomatic treatment of CHS.

Methods: Participants from both cohorts were enrolled at four emergency departments. The prospective cohort received droperidol and Benadryl, while the retrospective cohort received haloperidol. Data collected in this study include medication dosages administered, number of patients who returned to the emergency department (ED) 7 days following discharge, and ED length of stay.

Results: 100% of patients in the droperidol group (n=17) received a 2.5mg dose, whereas only 27% of patients in the haloperidol group (n=55) received a dose of 2.5mg or less, with an average dose of 4.2mg. ED discharge times were 102±71 minutes and 195±85 minutes for haloperidol and droperidol administration respectively. Comparative analysis of 7-day ED readmission rates between haloperidol and droperidol administration revealed 32.7% patient readmissions in the haloperidol group and 0% in the droperidol group.

Conclusion: Though there is little known about CHS, considerable evidence suggests that the antiemetic properties of dopamine antagonist drugs can alleviate the condition's symptoms similar to if not better than traditional antiemetics. Lower ED return rates and lower dosages required suggest droperidol is more effective than haloperidol in the treatment of CHS.

Describing the current landscape of pass/fail grading schemes within pharmacy education through survey data and semi-structured interviews

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The aim of the study is to determine the current landscape of pass/fail grading schemes within pharmacy skills course settings and its impact on faculty workload, remediation, and student and faculty perspectives. Pass/fail grading systems are utilized by many schools across the United States. Studies have identified evidence of benefits for students in programs that utilize these grading systems, such as enhanced student well-being. Within pharmacy education, optimal methods for assessing and grading various skills have not been fully explored, and this information could benefit faculty as well as students. A survey and semi-structured interview questions were developed by the research team. Survey information was sent to pharmacy practice faculty at United States (US) schools and colleges of pharmacy who instruct skills courses and labs. Survey and interview data collection is in process and results are pending.

Primary Care and Mental Health:

Post-COVID-19 Syndrome and its Effects on Marginalized People

Charles Woolery

Post-COVID-19 syndrome, also known as long COVID, presents with a variety of respiratory and neurological symptoms weeks or months following initial infection. While this illness affects a wide range of patients regardless of acute COVID infection severity, it is disproportionately afflicting ethnic minorities and members of marginalized communities. Common features include difficulty breathing, chest pain, fatigue and headache or brain fog. A lack of resources and patient education in underrepresented communities has contributed to this inequality. This

review was conducted with the purpose of educating patients about pertinent risks of the disease and preventive measures to remain healthy and safe. Methods included a comprehensive review of meta-analyses and other research articles focused on the development, effects, prevention and long-term health outcomes stemming from long COVID. Conclusions support the thesis stating this illness disproportionately affects minorities due to an imbalance of resources and patient education.

How is NEOMED contributing to the primary care physician shortage: A ten-year retrospective study of NEOMED College of Medicine Alumni

Lauriel Powell and Michael Appleman, M.A.Ed.

The nationwide primary care physician (PCP) shortage of 17,800-48,000 PCPs by 2034 threatens patient life expectancy, quality of care, and healthcare costs. Factors contributing to this shortage include physician burnout, diminished interest, and an overestimation of institutional contribution to the PCP workforce. Research shows these estimates to be 41.2% with real numbers closer to 22.3% of residents matching into and staying in primary care. Thus, it is imperative to assess the true-output of PCPs and determine methods for increasing these numbers to ameliorate the shortage. This study's objective was to evaluate Northeast Ohio Medical University (NEOMED)'s contribution to the PCP workforce using a retrospective cohort study from 2000-2009 and 2020.

This retrospective cohort study had a convenience sample of NEOMED medicine matched alumni from 2000-2009 and 2020. Each name was searched in the NPPES National Provider Identifier (NPI) Registry website. The NPI number, primary practice address, and NPI specialty were recorded. Data were then organized by NPI practice specialty and correlated with match specialty to determine those still practicing primary care following graduation and residency completion. Results revealed that of 1130 NEOMED alumni who graduated between 2000-2009 and in 2020, 543 (48%) matched into primary care specialties. Of this number, only 314 (28%) still remain in primary care. These findings align with the literature on the true-output of PCPs by medical universities and illustrate the emergent need to attract more student physicians to primary care.

Evaluation of Simulated Patient Cases Depicting Patients with Disabilities

Raman Bhambra BS, Omar Hameed BS, Dominic Congeni BS, Rachel Bracken PhD, Rebecca Fishbein PhD

People with Disabilities (PWD) face barriers to quality healthcare, including the lack of health professions education focused on caring for PWD. Simulated patient encounters which include individuals with disabilities can increase awareness and reduce stigma among health profession students. However, little work has examined the experience of serving as a simulated patient (SP) as an individual with disabilities. We looked to understand the experience of a patient encounter through the lens of an SP with disabilities. First-year medical students participated and conducted a SP interview with an individual from one of three disability communities: Down syndrome (DS), Blind/visually impaired (BVI), Deaf/hearing impaired (DHI). Focus groups were conducted, and experts consulted to develop, pilot, and refine the case in conjunction with the disability communities. SPs were surveyed after to understand their experience. Thirteen of 17 SPs responded (76.5%) including: 2 BVI; 8 DHI; 3 DS. Questions assessed patient case, accessibility, the desire to be a simulated patient again, and areas for improvement. Most

strongly agreed the case was realistic (62%), they had sufficient information to prepare (76.9%), they understood the information provided (82%), and would like to be SPs in the future (85%). Future implementation including a revised set of directions that will emphasize the use of simpler language. Logistical improvements will also be made. The study reports direct experiences of the participants which are crucial to facilitate.

The Value of a Preclinical Mini-Preceptorship in Developmental Medicine

Falcon, Lauren, B.S. Peters, Lin, MPH. Tyler, Carl, MD, MSc.

Individuals with intellectual and developmental disabilities (IDD) often lack access to physicians who are competent to meet their complex health needs, which increases the likelihood of receiving dissatisfactory healthcare. These patients experience several health disparities such as reduced average life span, inappropriate use of psychotropic drugs, higher rates of social isolation, placement into restrictive environments, fewer preventative health measures, and higher rates of obesity, diabetes, and heart disease. Physicians in all stages of their careers report feeling uncomfortable and less confident when treating those with IDD. During my mini-preceptorship, I engaged in a clinical experience under the mentorship of a developmental medicine physician at an ambulatory clinic with a notable IDD population, created caregiver education material that focused on the evaluation and management of physical aggression in adults with IDD, and participated in a multi-disciplinary network that serves the IDD community. We summarize the educational value of these activities and the lessons learned from the perspective of a medical student. In conclusion, we recommend other clinical sites provide mini-preceptorships in developmental medicine, encourage preceptors to inform medical students about the specific healthcare needs of populations experiencing health disparities, and advocate for the development of instruments that assess educational outcomes achieved in condensed clinical opportunities.

The Association of Food Insecurity and Health Outcomes for People with Serious Mental Illness

Tyler Chinsky, B.A., Sanaiya Ahmed, B.S., Natalie Bonfine, Ph.D.

Introduction: Lacking healthy food options can contribute to multiple preventable health conditions. Some studies show the prevalence of food insecurity in serious mental illness (SMI) patients is 71% compared to 13% in the general population. Food insecurity has been shown to be associated with decreased physical activity, higher prevalence of mental disorders and heart disease and other outcomes in SMI patients.

Methods: Our study considered the relationship between overall health and food insecurity among a sample of people with serious mental illness. We conducted a secondary data analysis from a cross sectional survey of SMI patients at a community facility. We performed two bivariate correlational analyses and a logistic regression between our different variables. **Results:** We found that 43% of our population was food insecure. Food insecurity was not associated with heart disease, diabetes, or physical activity. However, patients with higher food insecurity were more likely to indicate they had daily activity limitations.

Discussion: Our study shows food insecurity has a high prevalence among SMI patients. The association between food insecurity and daily activity limitations could be a new avenue for research aimed at improving the quality of life of SMI patients. This study reinforces how food

insecurity screenings and policy changes could lead to better health outcomes and quality of life for SMI patients.

Improvements of Mental Health Treatments in Prison

David A. Ceraolo B.S.¹, Stacey L. Barrenger, PhD², Casey Bohrman, PhD³,

Background: People incarcerated in prison experience high rates of psychiatric and chronic health conditions, yet little is known about how formerly incarcerated individuals experience prison healthcare services. While the punitive system in the United States has never received any accolades for its healthcare or treatment of its prisoners, this study brings forward the changes that individuals with mental illnesses would like to see changed to encourage better health and safety standards.

Method: Recruitment consisted of participants from three separate sites within the United States included Missouri, New York, and Pennsylvania ($N=43$). Inclusion criteria required having a major mental illness (i.e., schizophrenia, post-traumatic stress disorder, bipolar disorder, major depression) and recently released from prison within the last three years. All participants completed an in-depth interview that asked about their experiences accessing and receiving healthcare in person. Data was analyzed via Dedoose by using descriptive statistics and content analysis.

Results: The most common recommendations to improve prison health services were better mental health and drug and alcohol treatments, along with increased access to these treatments. Additionally, participants identified supportive reentry services and educational or trade school programs as important to their health and wellbeing. Many participants felt that prison health services do not address the root causes of mental illness, substance use, or trauma that contributed them being incarcerated. Access to medications and nutritious food, and overall improvements within the prison systems are additional areas needing improvement.

Exploring Housing Instability, Exercise and Diabetes Among People with Serious Mental Illness

Christina Abd, M.S.¹, Alyssa Battaglia, B.S.², Natalie Bonfine, Ph.D.³

Introduction Homelessness and housing instability are social determinants of health. This study explored the prevalence of housing instability among people with serious mental illness and its correlates with health behaviors (e.g., physical activity) and health outcomes.

Methods This study involves secondary data analysis of anonymous survey data collected from 203 adults with serious mental illness living in community-based settings. Housing instability was defined by any indication of homelessness in the previous 12 months or currently living in an insecure or temporary setting. Bivariate correlational analyses were used to indicate associations between housing instability, demographics, exercise, and health outcomes.

Results About 7 percent of the sample (14 participants) reported housing instability. There was a significant negative correlation between housing instability and moderate/vigorous exercise ($r = -0.140$, $p=0.047$). There was a significant negative correlation between physical exercise and having diabetes/high blood sugar in the past 12 months ($r = -0.146$, $p=0.037$). There was no direct bivariate association between housing instability and diabetes.

Conclusions Our findings indicate that the prevalence of housing instability among people with serious mental illness was relatively small (6.9%), suggesting that people with serious mental

illness living independently in the community tend to have stable housing conditions. Our findings also indicate that housing instability was associated with reduced physical activity. While we could not conclude that exercise mediates the association between housing instability and diabetes, future research should explore how housing instability and physical activity impact various health conditions, including diabetes.

Dermatology:

Undereducation is afoot: Assessing the lack of acral lentiginous melanoma educational materials for skin of color

Vissey M. Elad, MMAS, Trevena Anton, BS, Natalie C. Ganios, BS, Vito W. Rebecca, PhD

Acral lentiginous melanoma (ALM) is a subtype of cutaneous melanoma notorious for poor outcomes that disproportionately affect individuals with skin of color (e.g., African-, Hispanic-, Asian-descent) when compared to mortality rates among non-Hispanic White populations. There are several societal factors that contribute to racial disparities in ALM, including a lack of representative educational material in the context of patient education and medical instruction. A review of literature was conducted to analyze trends in medical education, patient education and the accessibility of these materials. The gaps that were found are representative information for the US population and include risk of disease, patterns of incidence, and differences in disease presentation in skin of color. The atypical presentation of ALM on acral volar skin sites makes early detection challenging and necessitates an increased index of suspicion on the part of physicians and patients alike. Studies underscoring the importance of early detection in reducing mortality risk make the availability of adequate representative educational materials indispensable.

Skin Color Reporting in Squamous Cell Carcinoma-Related Randomized Controlled Trials in the Ten Most Impactful Dermatology Journals: A Systematic Review

Natasha Salmen BS, Deven P Curtis BA, Jennifer Popovsky MD

Introduction: Cutaneous squamous cell carcinoma (SCC) is the second most common form of skin cancer. Skin color may influence the detection and subsequent initiation of treatment of SCC. It is unknown how frequently skin color is reported in randomized controlled trials (RCTs) for SCC. The purpose of this study was to determine the rate of skin color reporting in SCC RCTs in the top ten global dermatology journals by impact factor.

Methods: A systematic review of SCC RCTs was conducted up to July 10, 2023 on PubMed among the included journals. Studies were included if they: involved SCC, were RCTs or clinical trials, directly involved patients, were in English, and were available in full text. Articles were excluded if they did not meet all inclusion criteria.

Results: A total of 39 RCTs were included from a total of 59 articles received on initial search. 23 RCTs reported on skin color (59%), and 16 did not (41%). A subgroup analysis was performed by years of publication. The reporting rates for skin color/race showed Group 1 (prior to 1999) had a 100% rate (n=1), Group 2 (2000-2009) had 53.8% (n=13), Group 3 (2010-2019) had 66.7% (n=21), and Group 4 (2020+) had 25% (n=4).

Conclusion: Nearly half of all RCTs involving SCC published in top journals over the past four decades did not report skin color. Further research is needed to determine the influence of skin color on SCC data.

Erythrodermic Psoriasis: A Case Report

Maximilian Dawson¹, Nathan M. Ryan¹, Vissy M. Elad¹, Vincent Hensperger¹, Kelly Kimball, M.D.²

Erythrodermic psoriasis is a rare, but serious subtype of psoriasis characterized by widespread erythema affecting over 75% of the total body surface area. It is a condition that may be mistaken for pathologies with similar clinical presentation, including seborrheic dermatitis or atopic dermatitis. A missed diagnosis of erythrodermic psoriasis may lead to life-threatening systemic complications including hypothermia, sepsis, and high-output heart failure. In this report, we introduce a case of erythrodermic psoriasis with acute progression after an initial diagnosis of new onset atopic dermatitis. This is a disease that warrants prompt recognition and treatment given its morbidity and risk of patient mortality. Provided its potential for acute development from more common presentations of psoriasis as seen in our patient, erythrodermic psoriasis is a pathology that should remain on the differential throughout the treatment of psoriasis.

Hypopigmented mycosis fungoides- a disease disproportionately affecting marginalized populations: a systematic review investigating health disparities and barriers to diagnosis

Justine Busby, M.A., Abigail Singh, B.A., Natasha Salmen, B.S., Sydney Smith, B.A., Ekim Otucu, B.S., Kelly Kimball, M.D.

This systematic review aims to explore disparities associated with age and skin color in the diagnosis of hypopigmented mycosis fungoides (HMF). HMF is a rare subtype of mycosis fungoides that is histopathologically indistinct from classic mycosis fungoides. It is hypothesized that the hypopigmentation found in HMF is due to a CD8+ phenotype, while classic mycosis fungoides usually has a CD4+, CD8- phenotype. When compared to classical MF, HMF has been historically diagnosed more frequently in younger individuals with skin of color. However, it has been shown there is a delay between the onset of symptoms and diagnosis due to its atypical presentation and clinical similarities to other hypopigmented skin disorders, including vitiligo, tinea corporis, tinea versicolor, pityriasis alba, postinflammatory hypopigmentation, progressive macular hypomelanosis, idiopathic guttate hypomelanosis, sarcoidosis, and leprosy. HMF is easily confused with cutaneous T-cell lymphoid dyscrasia (CLD), which presents similarly clinically with the same T-cell phenotype as HMF. In our search of the literature, our findings support previous assumptions that HMF disparately affects younger populations and individuals with skin of color. The goal of our research is to identify additional factors that may affect the delayed diagnosis of HMF, such as social determinants of health factors and resource availability.

Erythema Elevatum Diutinum: A Case Report with MRI and Histopathology Findings

Justine Busby BS, Margaret McGuigan BS, Diana Albaba BS, Hafsa Hassan BS, Kelly Kimball MD, Kimberly Tamargo MD

Erythema elevatum diutinum (EED) is a chronic leukocytoclastic vasculitis typically found on the skin of the distal extremities, buttocks, and elbows. It is a disease with about 250 cases reported in literature. EED manifests in conjunction with various infections, hematologic disorders, and autoimmune diseases. There are only four previously documented cases of EED in patients with diabetes mellitus, and each patient had an additional predisposing condition connected with EED. Additionally, there are no case reports documenting bone involvement due to EED pathophysiology. This case report describes the first documented case of EED arising in a patient with a single associated predisposing condition of uncontrolled type 2 diabetes mellitus. Additionally, this case is the first documented case of EED presenting with lytic bone lesions confirmed on MRI. These novel findings expand on previously established knowledge regarding pathophysiology and presentation of EED.

Dermatology Pearls for Medical Students

Elham Aldosari, M.S., Hafsa Hassan, B.S., Emil Shteyngarts, M.S., Vissy Elad, M.M.A.S., Margaret McGuigan, B.S., Eliot Mostow, M.D.

Dermatology is a vast subject, yet curriculum constraints only allow a fraction of time to be spent on the subject. The purpose of this project is to create recurrent newsletters targeted for medical students that will educate them and increase their familiarity with prevalent dermatological conditions. A series of thematic newsletters were created by students of the Dermatology Interest Group and distributed to medical students.

The lack of comprehensive dermatological instruction in pre-clinical medical school curricula has created a gap that students must often fill themselves. The Northeast Ohio Medical University Dermatology Interest Group (NEOMED DIG) has introduced a monthly newsletter to supplement dermatological content in the curriculum. These newsletters aim to provide students with easily accessible, clinically relevant reference material, and practice quizzes. The inclusion of practice quizzes in these newsletters serves to encourage readers to assess their existing knowledge and identify any potential knowledge gaps, which they can then address as necessary in their study plans. Each newsletter includes: creation and distribution, thematic focus, visual aids, and interactive learning.

We've established an organized system, where regular content is effectively created and distributed. These newsletters aimed to enhance student interest for the field of dermatology, offer knowledge, and encourage active engagement. Future Plans include: 1.) distribute a survey to students to gather information on the engagement, satisfaction, and perceived efficacy of the newsletter. 2) Explore interdisciplinary dermatology topics in collaboration with other medical interest groups to enhance understanding of how skin conditions relate to other medical fields.

Global Health:

Water, Sanitation and Hygiene Quality Improvement in Nepal Project Summary

Michaela Macko, Bernhard Fassl, Spencer Crocker

Diarrhea and water borne illnesses account for 1.53 million yearly deaths and 80.9 million DALYs worldwide. In rural Nepal, this problem exists as a lack of accessibility to clean water related to poor waste management and sanitation practices. This study was intended to describe features of the current water supply and sanitation system in rural Nepal to recognize areas

which require quality improvement interventions and achieve a goal of identifying directions and priorities of improvement for local stakeholders. The methods of obtaining information on the baseline systems and areas for improvement included discussions with local water and sanitation systems leaders and interviews with locals using a validated, standardized community survey tool (WASH) as a backbone for discussions. Additionally, information regarding diarrheal illness and gastroenteritis incidence was obtained. The results of this study identified potential drivers of the water and sanitation issues including but not limited to lack of funds, unclean storage tanks, and insufficient septic waste management. This research identifies gaps and priorities for interventions and will help determine what future interventions will be most useful and sustainable in the region.

Evaluating Helping Babies Breathe and Helping Mothers Survive intervention outcomes on provider skill acquisition in Nepal's Belkotgadhi Municipality.

Shashank Raghavachari, MS, Bailey J. Brocker, BS, Jackson T. Casteel, BS, Bibek Lamichhane, Prakash Karki, MBBS, Bernhard Fassl, MD

Background: Neonatal birth asphyxia, hypertensive pregnancy disorders, and postpartum hemorrhage influence morbidity and mortality in Nepal, especially in rural districts. Nepal's government, collaborating with global experts, implemented Helping Babies Breathe (HBB)/Helping Mothers Survive (HMS), proven training programs, to help health providers successfully manage these conditions.

Study Objectives: To evaluate trainee knowledge/skill uptake following a combined neonatal-obstetric training program in Nepal.

Methods: The HBB/HMS training program was developed in Nepal from 2021-2022, endorsed by Nepal's Ministry of Health. Nepali master trainers conducted 4-day training courses for rural healthcare providers in the Belkotgadhi municipality during Winter/Spring 2023. All trainees completed a pre-post training knowledge questionnaire and bag-mask ventilation skills test. They also demonstrated competency using OSCE examinations. Training scores were abstracted and analyzed to determine competency transference.

Results: 40 trainees completed HBB training; 39 completed HMS training. Mean newborn care pre-post knowledge scores improved from 13.9 to 17.7 ($p=0.000000000000199$). Maternal care scores improved from 11.3 to 13.9 on Day 1 ($p=0.0000000000164442$) and from 4.9 to 7.3 on Day 2 ($p=0.00000000000000010$). 97.5% of trainees passed bag-mask skills assessments. 100% of trainees passed both neonatal emergency OSCE scenarios. 84.6% of trainees passed all 4 maternal emergency OSCE scenarios.

Conclusions: The HBB/HMS program effectively increases knowledge and skills. Its widespread implementation will improve providers' case management abilities in under-resourced Nepali regions. Furthermore, our result verifies the utility of disseminating HBB/HMS protocols worldwide for overall birth outcome improvement.

Determining long-term health and nutrition outcomes of children who completed treatment in a child malnutrition center for severe acute malnutrition.

Alison Ruf, Diana Arredondo, Mohammad Fahad Butt, Helly Panchal, Pankti Pathak, Shailwi Patel, Harshit Malkan, Kashyap Yadav, Nirav Patel, Allison Judkins, Bernhard Fassl

Background: 2.3 million children 6-60 months die due to severe acute malnutrition (SAM) each year in India; Mota Fofalia Hospital operates a child malnutrition treatment center (CMTC) to treat SAM and related morbidities. These inpatient programs for SAM often result in short term weight gain during the hospital treatment but long-term effectiveness on nutrition outcomes is not well documented.

Objectives: Describe the long-term weight outcomes of children who completed nutritional rehabilitation for SAM.

Methods: This study took place at Mota Fofalia Community Health Center, Gujarat, India, June 2023-Aug 2023, includes all children admitted to the CMTC from 2019-2021. We abstracted demographic and SAM treatment information from the CMTC record. As part of a local quality improvement initiative the local field team performed household visits in a convenience sample of children, performing anthropometric measurements. We calculated changes in the weight-for-age (WFA) z-score, expressed as standard deviations above/below the mean weight-for-age between CMTC discharge date and follow-up.

Results: 224 patients were admitted to the CMTC, 167 could be located/contacted during follow-up, 92 have a complete data record. Average patient age at discharge: 20 months (range 4-58); at follow-up: 67 months (range 46-111). 60 children (65%) showed a positive change in their WFA z-score: (mean: +0.55; range -4.41-3.87). Average CMTC WFA z-score at discharge: -2.93 (ranges -5.79-1.70), at follow-up -2.37 (range -5.98-1.63).

Conclusions: A structured follow-up program after CMTC discharge may increase the proportion of children who maintain weight gain.

Proposing A New Standard Hemoglobin Value Distribution Curve in Efforts to Improve Treatment of Anemia in High Altitude Nepalese Populations.

Luis Pozo, Abhyu Ghimire MD; Allison Judkins MD, Bernhard Fassel MD

Background: Anemia is a significant public health challenge in low resource environments.

Diagnosis and management of anemia in populations who reside at high-altitude is challenging as exposure to high altitude itself has a significant impact on blood hemoglobin concentrations.

Objective: To assist a Nepali medical team with analysis and interpretation of hemoglobin values previously obtained during a community-based screening program and describe rates of anemia using the WHO diagnostic criteria adjusted for altitude.

Methods: As part of a community-based QI initiative, a Nepali medical team carried out a population anemia screening program in 9 villages (elevation 3400-4100m) in Pasang-Lhamu Municipality in November 2022 using a validated point-of-care, handheld hemoglobin screening device. Those found anemic received treatment per government guidelines and were scheduled for retesting after 6 months. The Nepal team abstracted de-identified screening information into an electronic database and requested assistance with interpretation of values obtained during the screening program. The program was approved by local authorities.

Results: 830 screenings were performed, 54% female. The mean hemoglobin concentration $\pm 2SD$ among adults was 15.06 ± 4.58 ; for children aged 5-17: 14.09 ± 3.80 . Using standard (non-altitude adjusted) diagnostic criteria anemia prevalence was 5-8%. Using altitude adjusted diagnostic criteria, 34.51% of adult men, 54.56% of adult women; 68.85% of children under 5 and 22.65% of children 5-17 were anemic. Up to 31% of patients in certain groups met criteria for polycythemia.

Conclusions: Unique diagnostic considerations need to be applied in the high-altitude resident Sherpa population for diagnosing and managing anemia.

Baseline Assessment of Prenatal, Perinatal, and Postnatal Care on Newborn Health Outcomes in Rural Nepal

Phuong Tran, BS, Nicole Price, MS, Spencer Crocker, MS, Bibek Lamicchane, Bernhard Fassl, M.D.

BACKGROUND: Insufficient access to peripartum care is a significant factor for newborn health disparities globally. Across rural Nepal, challenges due to geographic remoteness, limited healthcare infrastructure, socio-cultural and economic factors all play a role in the quality and accessibility of prenatal, delivery and postnatal care. The purpose of this study is to perform a baseline assessment survey in 2 remote districts (Accham, Bajura) of Nepal in preparation of an upcoming healthcare capacity building initiative.

OBJECTIVE: To document baseline health service quality of prenatal, postnatal, and delivery care and to identify areas of needed improvement

METHODS: The study took place in 18 rural villages in the two districts of Nepal, Accham and Bajura, from April until August 2023. Using a previously validated standardized household survey tool, a Nepali study team performed household interviews in recently delivered women (RDW) who gave birth within 2 years. Interviews were conducted in the local language. The survey tool assesses basic demographic characteristics, healthcare quality for prenatal, postnatal, delivery care and documents medical outcomes. Reporting is descriptive.

RESULTS: 182 surveys were completed. Prenatal care: 81% of women had anemia screening and 55% had urine analysis checked. Postnatal care: Only 1.1% of newborns received antibiotics and 47.7% had a health care worker visit within 1 week. Delivery care: Only 30.67% of facilities carried oxygen. Health outcomes: 13% of newborns with low birth weight and 4% reported as sick/unwell.

CONCLUSION: Many elements of peripartum care require improvement to ensure safe motherhood and childbirth.

Diagnoses, treatments, and outcomes in a rural neonatal intensive care unit in India

Diana Arredondo, Fahad Butt, Alison Ruf, Helly Panchal, Pankti Pathak, Shailwi Patel, Harshit Malkan, Kashyap Yadav, Nirav Patel MBBS, Bernhard Fassl, M.D.

Background: The neonatal mortality rate in rural India is twice that in urban areas, where admission to a newborn intensive care unit is commonly not an option. As a pilot project in collaboration with the government, Mota Fofalia Community Health Center (MFCHC), located in a rural community in Gujarat, India, established a small NICU in 2016 to fill the gap of intensive care services in rural areas.

Objective: The purpose of this study is to describe the patient, disease, treatment, and outcome characteristics of patients admitted to a rural Indian NICU.

Methods: The retrospective study took place at MFCHC in May 2023. A team of students from NEOMED abstracted medical record information of infants admitted to the NICU from 2016-2023 from the patient logbook, which documents basic demographic admission, diagnosis, treatment and medical outcomes.

Results: 922 patients (45% female) were admitted to the NICU from January 2016 through June 2023: 21% were preterm births, mean birth weight: 2.39kg, mean admission weight: 2.27kg, and mean age at admission: 5.19 days. Most common diagnoses: neonatal jaundice (457/50%), low birth weight (236/25.8%), and respiratory distress (80/8.8%). 7 patients (0.76%) died and 52 (5.64%) were referred to higher centers; most common diagnoses of deaths and referrals were low birth weight and respiratory distress syndrome.

Conclusions: Neonatal jaundice, treated with phototherapy, is the most common condition at MFCHC's NICU. Rural NICU care in India is feasible and may help reduce overcrowding in urban centers.

Key Practice Indicators for Hypothermia Management for Neonates in Rural Nepal

Nicholas Ventigan, BS, Bernhard Fassl, MD

In rural Nepal, hypothermia in neonates is a common complication due to lack of proper infrastructure and resources at birthing centers. The purpose of this research study is to examine the key factors that help prevent hypothermia in the neonatal period in Nepal in the hospital, health centers, and home to help better understand the practices in Nepal. The study took place in Nuwakot, Nepal from June 2022 to June 2023, where auxiliary nurse midwives were surveyed at different clinics in the community. Each birthing center (hospital, health center, home) gave a priority ranking of 1 (most important) to 14 (least important) for newborn temperature management procedures. Generally, all birthing centers followed the same procedures and prioritized each similarly, with the exception of home births, which presented much more variation in the ranking of each procedure. 100% of home birth surveys explained the reason for their ranking as due to geographical remoteness. Among all birthing centers, procedures ranked 1-7, 10, and 12-14 were prioritized the same for >50% of surveys. Procedures ranked 8, 9, and 11 had <50% agreement on priority for neonatal temperature management. When the baby is cold, each clinic uses kangaroo mother care as needed. Overall, temperature management practices for neonates are typically consistent depending upon the birthing location.

Social, cultural, and economic factors contributing to iron-deficiency anemia in a rural district of Nepal

Bailey Brocker, B.S., Jackson Casteel, B.S., Shashank Raghavachari, B.S., Prakash Karki, M.D., Bibek Lamichhane, Bernhard Fassl M.D.

Introduction: Iron deficiency anemia is a severe public health problem in Nepal. The purpose of this project is to provide a description of the social, cultural, and economic factors that influence dietary iron deficiency in the highest risk groups: women of childbearing age and their children.

Methods: This study took place in Nuwakot, Nepal in May 2023 and was part of a healthcare quality improvement initiative of the Nepali government. A team of Nepali community health experts conducted a 28-question standardized nutrition survey in a convenience sample of 23 anemic women (Hgb less than 10g/dl) identified during screening events. Survey responses were converted to categorical data and indexed themes. Descriptive statistics for these and any numerical responses were reported.

Results: The majority of household food supply is grown at home (average 60%). Rice and potato are the most popular crops, and products such as salt and oil are purchased. Travel times to markets averaged 40 minutes and ranged as high as 4 hours. 68% of reported meals consisted of a variation

of “dal-bhat” (lentil soup with rice, with or without vegetables); only one report included meat. There were an average of 2.8 meals per day. 77% reported access to vitamins; only 53% of those reported taking iron. 4 of 9 women reporting breastfeeding were doing so less than 8 times per day. 76.5% of women believe they are receiving inadequate nutrition or experience food insecurity.

Conclusion: Food insecurity and lack of food diversity are serious problems contributing to nutritional deficiencies.

Current State of Maternal and Neonatal Healthcare Access in a Remote Nepal Municipality

Deven P Curtis BA, Anthony Baumann, DPT, Allison Judkins MD, Bibek Lamichhane, Rajak Mijan, Prakash Karki, Bernhard Fassl MD

Background: A large proportion of women in rural Nepal lack access to basic healthcare during pregnancy and childbirth. The purpose of this study is to describe the current state of infant and maternal healthcare access for this population.

Methods: This study was performed in the 13 rural village district clusters (VDCs) in the Nuwakot District, Nepal June 2022. Data was obtained by a team of international experts using standardized household survey questionnaires among 498 recently delivered women (< 24 months postpartum) based on WHO perinatal and antenatal care goals.

Results: 45.4% of the 498 surveyed women were screened for anemia prenatally, 84.7% had access to soap and running water or alcohol-based hand rub during delivery, and 83.1% of deliveries had oxygen equipment available. 90.54% deliveries occurred in a healthcare facility, 45.4% of women received an oxytocin injection, and complications occurred in 40.1% of deliveries. 27.1% of women were given antibiotics and 94.0% of the babies were immediately dried. 96.0% of babies were placed skin-to-skin, 2.4% had delayed cord clamping, and 26.1% received postnatal follow up within 6 weeks. 0 maternal and 0 neonatal deaths were reported.

Conclusions: Antenatal delivery and postpartum care continue to show deficiencies and are in need for further improvement

Cultivating Food Security: An Examination of Food Acquisition and Scarcity in Rural Nepal

Niki Price, MS, Phuong Tran, Bibek Lamichhane, and Bernhard Fassl, MD

Introduction: Food insecurity and nutritional challenges are commonly observed especially in rural and remote regions of Nepal. In anticipation of launching a comprehensive health initiative in Achham and Bajura districts in collaboration with the Nepal government, a Nepali study team conducted a nutritional and economic survey to identify major nutrition related health challenges.

Objectives: To describe prevalence of food insecurity, food procurement challenges and household economic means in 2 remote districts of Nepal.

Methods: A Nepali team of public and community health experts conducted a standardized economic and nutrition household survey in a convenience sample of households in Achham and Bajura districts over a span of six months in 2023. In this qualitative survey, answers to open-ended questions were grouped into indexed themes and transferred into an electronic format for de-identified descriptive analysis.

Results: A total of 364 surveys were completed. Respondents were 100% female reporting an average household income of 190,544 Nepali rupees. 73% of households reported running out of food; Food source: on average 37% of food is grown at home vs 62% of food is purchased at the market. Major obstacles to food procurement were reported to be lack of funds and lack of land/fields to grow crops.

Conclusions: Food scarcity and poverty are significant challenges in Accham and Bajura. Economic and nutritional programs need to be considered in future health strengthening interventions.

Measuring the Effectiveness of a Nutritional Rehabilitation Program for Severe Acute Pediatric Malnutrition in Rural India

Mohammad Butt, Allison Ruf, Diana Arredondo, Nirav Patel, Allison Judkins, Bernhard Fassl

Background: Severe acute and chronic malnutrition (SAM) remains a major contributor to childhood morbidity and mortality and perpetuates intergenerational poverty. India contains 1/3 of all children with SAM. The purpose of this quality improvement study is to determine the effectiveness of a novel nutritional rehabilitation program in a dedicated childhood malnutrition treatment center (CMTC).

Objective: To determine the proportion of SAM children who achieve 10% weight gain after CMTC admission

Methods: This retrospective study is part of a quality-of-care initiative of the Mota Fofalia Community Health Center in Gujarat, India. We reviewed CMTC medical records of all children admitted with SAM between 2018 and 2020 and abstracted demographics, admission/discharge weights, heights, and mid-upper-arm circumferences from medical records. Z-scores for weight-for-age, height-for-age and weight-for-height were calculated using WHO standards for malnutrition severity. Results: Of 224 patients were admitted, 194 had complete data sets and were analyzed: 103/53% females; mean age: 20 months (range 4-58). Upon admission, 153/79% patients were severely malnourished (<-3SD); 39/20% were moderately malnourished (between -3SD and -2SD); 163/84% had an HFA z-score <-2SD; 167/87% had a MUAC of <12cm (red zone). 193 children gained weight; average weight gain 8.8%; average change in WFA z-score upon discharge +0.661 (range -0.1 to +2.8 and SD 0.4); 83/43% children achieved the target weight gain of ≥10%. The median length of stay was 13 days.

Conclusion: Further refinements to the SAM treatment protocol are needed to achieve target weight gain.

Prevalence of Anemia within the Belkotgadi Municipality of Nepal

Jackson Casteel, B.S., Bailey Brocker, B.S., Shashank Raghavachari, B.S., Prakash Karki, M.D., Bibek Lamichane, Bernhard Fassl, M.D.

Background: Anemia is a global health issue that affects millions, particularly in underserved populations. The WHO estimates 30% of women aged 15-49, 38% of pregnant women, and 40% of children aged 6- 59 months are anemic. Nepal is one country at greater risk for this disease, however universal screening is not available and population data is scarce.

Objective: This study investigates the prevalence of anemia within the rural Belkotgadi Municipality of Nepal.

Methods: A Nepali medical and public health team carried out an anemia screening intervention in 7 locations (wards) of Belkotgadi municipality from 05/25/23 to 06/05/23 using a handheld, point-of-care HgB screening tool. This study analyzes medical record data of 1659 patients using WHO definitions of anemia, describing demographic variables and hemoglobin values. Results: Of 1659 patients (66% female) screened 66% (avg HgB 11.4) were anemic with equal gender distribution. Anemia prevalence varied between wards from 59% to 73% (Wards 3 and 6 respectively). Prevalence in children 0-5 years was 63% (avg HgB 10.41); in children 5-18: 73% (avg HgB 11.23), in adults 18-65: 58% (avg HgB 11.77), and adults 65+: 61% (avg HgB 11.82). The lowest prevalence was in males 18-65 with 44% anemic (avg HgB 12.88). The highest was in males 5-18 with 85% anemic (avg HgB 11.25). Of 11 pregnant women, 5 were anemic (avg HgB 10.65)

Conclusion: Anemia prevalence in Belkotgadi is high. Future programs should determine the cause of anemia within these populations.

PERINATAL CARE QUALITY REVIEW IN RURAL DISTRICT OF NEPAL

Maximilian Brockwell, BS, Bibek Laminchhane, Bernhard Fassl, MD

The Sustained Development Goal 3.2 aims to reduce neonatal mortality below 12/1,000 live births globally, however as of 2021 Nepal's infant mortality rate remains 23/1,000 with inaccessible facilities and poor infrastructure representing barriers to care. In rural Nepal, birthing centers are often the most accessible option for delivery, but staff training and access to equipment remains a challenge. The objective is to investigate the infrastructure, equipment, and manpower needed for a rural birthing center and describe per. The study took place in Nuwakot, Nepal from June 2022 to June 2023. A team of Nepali community health specialists conducted standardized health facility surveys and household surveys in the catchment area of MHP, interviewing recently delivered women using validated survey tools. Survey data from medical records were transferred into an electronic database for analysis. Reporting of findings is descriptive. Surveys were approved by the NEOMED IRB and local authorities. One facility survey and 101 household surveys were completed. MHP had one Skilled Birthing Assistant and antenatal care, but lacked a staff doctor, delivery equipment, and postnatal equipment. Of women interviewed 99% received antenatal care at a health post. 44% delivered in a birthing center, 48% in a hospital, and 9% at home. 22% identified a health issue in the child. 16% of mothers faced complications during labor. 100% of children are alive and healthy, but only 38% saw healthcare workers within 6 weeks after birth, and none have been screened for anemia.

The Prevalence of Anemia in Children Admitted to the Child Malnutrition Treatment Center in Rural India

Milanya Thumma, Nirav Patel MD, Allison Judkins MD, Bernhard Fassl MD

52 million children below 5 years suffer from malnutrition worldwide. South Asia is home to more than 50% of children affected by severe malnutrition and wasting. Childhood anemia is an indicator of micronutrient deficiency and is associated with poor long-term cognitive, physical, emotional, and social functioning. Interventions commonly address caloric malnutrition but micronutrient deficiencies/anemia are not assessed routinely. Identifying anemia in malnourished children could guide treatment plans and lifelong dietary management.

To assess the prevalence of anemia in patients admitted for treatment of severe acute malnutrition (SAM) to a Child Malnutrition Treatment Center (CMTC) in Gujarat, India. This retrospective chart review took place in Mota Fofalia Community Health Center in May 2023 and includes children with SAM treated between 2021-2023. As part of a quality improvement initiative, the medical team included routine hemoglobin measurements and anemia treatment if applicable in addition to providing high-caloric nutritional supplementation. We performed a retrospective analysis on these admission data points to determine anemia prevalence and used WHO diagnostic criteria to classify anemia severity.

121 children were admitted to the CMTC between 2021 and 2023. Mean age was 33.85 months (8 - 86mo) and 47% were female. Mean hemoglobin values were 9.80 (range from 2.2 to 14). 9 children were severely anemic (5 female), 59 moderately anemic (27 female), 24 mildly anemic (13 female), and 29 were not anemic (12 female).

Anemia and micronutrient deficiencies are highly prevalent in children with SAM. Routine assessments for micronutrient deficiencies would be beneficial.

Clinical Investigations and Interventions

Referred Headache of Ophthalmic Origin

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Headache disorders impact patients of all populations and have been ranked as the second leading cause of years lived with disability worldwide. They are associated with impaired quality of life and high economic costs. Previous studies have demonstrated ophthalmic conditions, including refractive error and dry eye disease, can be associated with headaches. By treating ophthalmic conditions such as dry eyes, blepharitis, and refractive error in the setting of headaches, we hope to demonstrate through temporal and spatial response to treatment that headaches, not localized to the eye, may indeed be caused by these ophthalmic conditions. Patients who are referred to neurologists or eye care providers for headache management may then be able to obtain significant relief, precluding the need for neuroimaging, migraine prophylaxis, or chronic headache medications. This retrospective case-control study aims to determine the nature of ophthalmic conditions individually or cumulatively precipitating extra-ocular headaches.

359 patients, aged 9-89, who presented with headaches from 1999-2009 were reviewed. De-identified data, including duration of symptoms before first office visit and time to resolution, was recorded. Additional information regarding headache medication, location of headache, presenting ocular symptoms, SLE findings, treatments provided, and response to treatment was collected. Data regarding prescribed manifest refraction was also gathered in a subset of patients who presented with headaches.

Statistical analysis is currently ongoing, and a regression model will determine any relationship between these variables and headache onset, as well as resolution. By doing so, proper education, evaluation, and treatment may be delivered in order to relieve symptoms.

A Comprehensive Study of Heart Disease in Ohio

Sanjana Vivekanandan, M.S.

This research study seeks to understand the risk factors and prevalence of cardiovascular disease in Ohio. A comprehensive investigation on heart disease will be conducted, encompassing geographical distribution, prevalence and the policies and population health interventions aimed at addressing this growing public health concern.

The project encompasses various facets. Ohio's healthcare policies, particularly those related to access to care and the management of chronic diseases, will be examined with a specific focus on heart disease. A community assessment and a health systems proposal will be developed to understand the current medical landscape in regard to chronic disease management and prevention. An upstream/downstream approach will also be employed to explore how preventive healthcare processes can be delivered effectively. Extensive data analysis and policy reviews will help propose evidence-based strategies for enhancing health outcomes.

The results of this project will facilitate the development of targeted interventions and policies to reduce the burden of heart disease in the state, ultimately advancing the goal of promoting preventive medicine and improving the overall health and well-being of Ohio's residents.

Elements of a Pediatric Sickle Cell Disease Center

Prasad Bodas, MD¹, Sofia L. Arruda, MA

Evidence-based guidelines for treatments and prevention of sickle cell disease (SCD) complications are widely accepted by SCD providers and professional societies, yet there is poor implementation of guidelines and limited access to specialized care. This discrepancy highlights the need for an accredited program with comparable reach and impact as those for cystic fibrosis and hemophilia. Physicians have defined elements of adult and pediatric comprehensive SCD care, however patient and caregiver input was not elicited. We then asked patients' caregivers and community members to rate the importance of 41 pediatric SCD care center elements as defined by Hulbert et al. 2022. In structured interviews, a convenience sample of 7 community members and 22 patients' parents and caregivers rated the importance of the 41 elements as essential, optimal or suggested. Consensus was defined as 66% agreement on each element's categorization of importance. Community members rated 32 elements as essential and 9 elements as optimal, while parents and caregivers rated 39 elements as essential and 2 elements as optimal. There was broad consensus between patient caregivers/community members and physicians, especially regarding gaps in acute care and the need for transition programs, while physicians and caregivers/community members disagreed on elements regarding staff/team members and physical spaces. Pediatric comprehensive care is well defined and feasible, and having established elements of a pediatric SCD center with caregiver and community member input marks an opportune time to move forward with accreditation to implement guideline-based SCD care nationwide.

Evaluating the Viz Artificial Intelligence (AI) Application in Acute Ischemic Stroke (AIS).

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Acute ischemic stroke (AIS) must be treated under crucial time-constraints. Multiple previous studies with a smartphone system revealed a significant reduction in door to needle (DTN) time for tissue plasminogen activator (tPA) post implementation. The purpose of this project was to evaluate if the Viz smartphone application with AI could reduce door to be seen (DTS) and DTN in AIS, ensuring quicker effective treatment and improving patient outcomes. Viz utilizes AI to detect arterial occlusions and intracranial hemorrhages in a timely manner by creating a platform for mobile imaging and rapid notification of the stroke team.

Data for this study was obtained from two sources: EPIC CarePath, and the EMR used by Mercy Health Youngstown (MHY). Data before Viz implementation was considered Pre-Viz (n= 51); data after Viz implementation was considered Post-Viz (n=182). Process of care variables were recorded in a chronological manner, from Door to be Seen, Door to CT, Door to Lab, and Door to Needle in minutes. When appropriate, AIS patients receive tPA to lyse clots, promoting better tissue perfusion. Unexpectedly, DTN time increased after Viz implementation: pre-Viz, 48.3 \pm 28.2 minutes, and post-Viz, 59.0 \pm 33.5 minutes ($t = -2.06$, $p\text{-value} = 0.040$). Use of Viz.ai software was associated with longer DTN for TPA administration compared with neurology interpretation. Contrary to reported studies, our data suggests Viz may not decrease DTN time. Our data and literature reported outcomes suggest earlier, smaller studies exhibiting greater effects, may have influenced Viz app and AI adoption, overstating benefits.

“Cognitive Processes Contributing to Performance on Auditory Tasks in Adolescence and Young Adulthood”

Dr. Julia Huyck, John Wenger, Jordin Benedict, Sydney Streby, Leah Herbert

Hearing and listening are critical to how adolescents engage with the world. However, performance on auditory perceptual tasks takes a long time to become mature. Because few studies of auditory perception have centered on typically developing adolescents, little is known about the mechanisms underlying this immaturity. Listening effort and attention are thought to contribute to performance on perceptual tasks, and physiologic parameters such as blink rate, pupil size, and saccade amplitude are thought to reflect attention and engagement. Specifically, a decrease in blink rate, an increase in pupil size, and a decrease in saccade amplitude are expected when participants are more engaged in a task, indicating higher levels of listening effort. The goal of this study was to determine the extent to which attention and engagement reflect the variance in performance on basic auditory tasks among typically developing adolescents.

Participants of ages ten through twenty-three were asked to discriminate between slightly different frequencies and to detect gaps in sound. During the task, pupil size, blink rate, and saccade amplitude were used as proxies for attention and engagement. We also collected data on static cognition including verbal and nonverbal reasoning, auditory and visual working memory, processing speed, and sustained attention.

Preliminary data showed that the relative contributions of age, measures of static cognition, and measures of engagement to performance on the perceptual tasks varied between the two tasks.

Thus, it can be inferred that different tasks develop at different rates and that different cognitive processes are involved in different auditory tasks.

CHANGES IN B CELL RECEPTOR CDR3 PHYSIOCHEMICAL PROPERTIES ARE OBSERVED WITH TYPE 1 DIABETES (T1D) PROGRESSION

Brandon Petrovich, M.S., Daniel Moore, M.D., PhD, Rachel Bonami, PhD

Objective / Hypothesis: Autoantibodies predict T1D development. Various B cell receptor (BCR) physiochemical properties, which can be altered by somatic hypermutation, determine antigen specificity & affinity. We hypothesize that changes in BCR physiochemical properties will be observed with T1D progression but that changes in somatic hypermutation will not occur.

Approach: CD19+ B cells were isolated from n=6 Type 1 Diabetes TrialNet participants and the 10x Genomics platform was used to perform single-cell RNA-seq and BCR-seq profiling. Raw data was processed using 10x Cell Ranger and data were further processed, visualized, and statistically evaluated using a customized immune receptor analysis pipeline that incorporated IMG2 High/V-QUEST, Change-O, Shazam, and Alakazam.

Results: A decrease in CDR3 hydrophobicity was noted for IgG1 BCR between T1D stage 1 and 3 ($p=0.006$). For IgA in memory B cells, CDR3 charge increased between stage 1 and 2 ($p=0.025$). IgG+ plasmablasts showed increased somatic hypermutation ($p=0.049$) between stages 1 and 3.

Summary / Conclusions: Changes in CDR3 hydrophobicity, charge, and somatic hypermutation corresponded with T1D progression. More research is needed to evaluate BCR properties in T1D to discern useful biomarkers for tracking disease progression and responsiveness to immunotherapies.

KIDNEY REPLACEMENT THERAPY AND MORTALITY IN CHILDREN WITH INBORN ERRORS OF METABOLISM: A META-ANALYSIS

Bryce Pember, Kush Doshi, Rupesh Raina, M.D.

Introduction: Inborn errors of metabolism (IEM) are common etiologic bases for hyperammonemic disorders. Current therapeutic options for IEM disorders include peritoneal dialysis (PD), hemodialysis (HD), and continuous kidney replacement therapies (CKRT). Despite advancements in CKRT technology, overall KRT-associated mortality rates remain high in pediatric patients with IEMs. This meta-analysis aims to identify KRT-related mortality across a global cohort of children with IEM.

Methods: This retrospective study considered eligible pediatric patients diagnosed with an IEM and undergoing any KRT treatment modality. Fourteen studies met the inclusion criteria for survival analysis.

Results: A total of 231 patient with IEM were included. Pooled survival among children who received KRT was 63.4% (95% CI: 52.4%-73.7%) with no visual indication of publication bias. In seven studies with a mean/median age >0.7 years, our sensitivity analysis revealed a slightly lower survival rate of 59.8% (95% CI: 38.5%-79.3%) than the overall survival rate, 63.4% (95% CI: 52.4%-73.7%). This was also the case in five studies limited to only the United States, where the pooled proportion for survival was 59.2% (95% CI: 49.4%-68.5%).

Conclusions: There is a noticeable scarcity of clinical trials and cross-sectional studies that investigate and validate the effectiveness of newer CKRT modalities in comparison to existing treatments among IEM patients. Future developments should consider focusing on models to assess prognostic indicators for non-survival risk in pediatric IEM patients and optimize their intervention course for long-term positive outcomes.

Nirmatrelvir/Ritonavir in Patients with Moderate to Severe Chronic Kidney Disease and COVID-19: A Multicenter Study of 150,352 Patients

Omer S Ashruf, BS, Zara Orozco, BS, Imad Haq, BS, Razwana Khanam, MD, David C Kaelber, MD, PhD, MPH, Rupesh Raina, MD

Purpose: Chronic kidney disease (CKD) has been recognized as a key mortality risk factor for COVID-19, with moderate and severe stages correlated with poorer outcomes compared to other high-risk groups. An understanding of the efficacy of Nirmatrelvir/Ritonavir (Nm/r), the most effective oral antiviral combination drug for COVID-19, in moderate to severe CKD is needed to properly treat and counsel patients.

Methods: In this retrospective cohort study, we pooled patient data from an aggregated electronic health record platform. Severity of clinical outcomes and risk of COVID-19 rebound after Nm/r was analyzed in moderate-severe CKD patients (estimated glomerular filtration rate <60mL/min/1.73 m²). Cohorts were 1:1 propensity matched for demographic variables and comorbidities. Measures of association and Kaplan-Meier analysis were calculated to determine survival probability.

Results: Nm/r was associated with a risk reduction in all-cause ED visitation, hospitalization, ICU admission, and mortality at 30 days, 90 days, 180 days, and 365 days of Nm/r prescription. Our data suggests a 76.5% reduction in all-cause hospitalization and/or mortality associated with Nm/r use at 30 days compared to patients with COVID-19 and CKD not prescribed Nm/r. However, moderate-severe CKD patients incurred greater risk of COVID-19 rebound (OR 1.39, 95% CI 1.13-1.71) compared to other high-risk patients.

Conclusion: Nirmatrelvir/Ritonavir has shown promising results in hospitalization and mortality reduction in vulnerable patient populations; providers should counsel patients and monitor the progression of comorbid disease and risk of COVID-19 rebound in treated CKD patients. Further study is needed to determine drug-drug interactions in this patient population and efficacy in dialysis-dependent patients.

Low-Dose Atropine for Exotropia Control in Young Children

Tahir Kuraan, BS; Kayla Tucker, OD; S. A. Erzurum, MD

Purpose: Intermittent exotropia, a common pediatric ocular disease, lacks defined treatments. Suggested treatments such as part-time patching show results similar to observation, and over-minus therapy increases the risk of myopia. Often, physicians seek treatment to improve control until children are old enough for other viable options like surgery. Atropine has not been used for intermittent exotropia. This retrospective chart study assesses the effectiveness of 2 consecutive doses of 1% atropine per week for intermittent exotropia in children less than 5 years of age.

Methods: A database was queried for children diagnosed with intermittent, general, and monocular exotropia who were prescribed 1% atropine in the dominant eye for two consecutive days each week for a minimum of 6 weeks. Patients were included based on eligibility criteria

established from a recent randomized clinical trial for intermittent exotropia. Average control and alignment scores for pre-atropine and post-atropine treatment visits were recorded. Results: 29 eligible patients were identified for this study. Average pre-treatment control scores were 3.7 for distance and 1.7 for near and improved after treatment to 2.8 and 1.0, respectively (p-value <0.5). Furthermore, the average pretreatment distance ocular alignment was 22.1 prism diopters and improved to 18.6 prism diopters, and the average near ocular alignment was 13.5 prism diopters and improved to 9.4 prism diopters after treatment (p-value <0.5). Conclusion: Atropine, dosed at 1% two consecutive days of the week for 6 weeks, showed a statistically significant improvement in ocular alignment and control scores when compared to observation and part-time patching without the risk of myopia.

COMPARISON OF OUTCOMES & ADVERSE EVENTS FOR PERCUTANEOUS NEPHROSTOMY TUBE PLACEMENT VS. URETERAL STENT VS. LITHOTRIPSY IN ANTEPARTUM PATIENTS WITH KNOWN OR SUSPECTED NEPHROLITHIASIS

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Purpose: Nephrolithiasis is one of the leading causes of emergency department visits with an increased prevalence in pregnancy. Antepartum nephrolithiasis is typically managed conservatively with nearly 48-81% of cases involving spontaneous passage. Refractory cases may lead to serious complications such as preeclampsia, spontaneous abortion, UTI, pyelonephritis, urosepsis, and preterm labor. In these situations, ureteral stenting, percutaneous nephrostomy (PCNT) placement, and lithotripsy have been traditionally indicated for pregnant patients with definitive treatment delayed until the postpartum period. There is currently a lack of evidence on the comparison of these different therapies for antepartum nephrolithiasis.

Methods: A retrospective chart review will be conducted on pregnant patients at Summa Health System from the years 2021-2023 with diagnosed/suspected nephrolithiasis who received PCNT, ureteral stent, or lithotripsy. Outcomes including rate of infection, sepsis, pain, readmission; gestational age at time of procedure and delivery; rate of admission for preterm labor; mode of delivery; and intensive care unit (ICU) stay for patient or baby will be compared.

Results: We plan to statistically analyze the results of the chart review to generate guidelines for approaching pregnant patients with nephrolithiasis so that a continuum of care across Summa Health System's Urology, Maternal Fetal Medicine (MFM), and Interventional Radiology departments can be developed.

Conclusions: Our current practices at Summa Health System lack a standardized approach and are based on individual expert opinion. Ultimately, we hope to implement the best therapy by comparing each of their subsequent outcomes for both the patient and/or their baby to minimize risks and maximize patient well-being.

Sepsis Quality Improvement Project at Trumbull Regional Medical Center

Landry K Umbu MD, Ryan Egbert, Natasha Salmen

Introduction: Sepsis is a serious condition that results from the body responding to an infection. To identify early sepsis, several biomarkers found in the blood can be utilized, with blood lactate being the primary biomarker. Sepsis is associated with high mortality and costs. Artificial

intelligence is a computer-based machine learning that can be utilized in the detection of early sepsis.

Methods: This was a retrospective review of sepsis data from Trumbull Regional Medical Center from 2020-2022.

Results: The data from the project was obtained from 2020 to 2022. We collected data by utilizing clinical presentation, laboratory values, and physician clinical assessments. No AI was used to collect data for this project. Blood cultures were obtained before broad-spectrum antibiotics in 81 – 93% of the patients. Crystal fluid was only initiated on time in 34 – 59% of the patients. Repeat lactic acid was ordered in 72 – 88% of the patients. When patients needed to be started on vasopressor after adequate resuscitation with crystalloid fluids, only 16 to 40% of the patients were put on vasopressor in a timely manner.

Conclusion: AI is a rapidly evolving technology that assists clinical decision making. Despite some challenges with its use, AI can be beneficial in detecting early sepsis, which may allow earlier treatment, better patient care and better outcomes.

Ambiguous Definitions of Neonatal Abstinence Syndrome and Subsequent Misdiagnoses *Simran Chandawarkar, B.S, Prakash Nadkarni, MD*

Purpose: Opioid withdrawal is the commonest cause of Neonatal Abstinence Syndrome (NAS). The Finnegan Neonatal Abstinence Scoring System (FNASS), originally developed specifically for NAS, have long been considered the gold standard for NAS assessment. However, non-opioid neonatal withdrawal (NONW) etiologies of NAS, either alone or in combination with opioids, are frequent enough to present challenges in diagnosis, assessment, and treatment. Varying substance withdrawal calls for stricter diagnoses definitions to ensure proper care and prevent adverse events in neonatal treatment.

Methods: We conducted a literature search to organize diverse definitions of NAS and related terms, determine their use for NONW, and compared them to ICD-10 diagnostic entities. We additionally studied literature on NONW such as from SSRIs, ADHD medications, antipsychotic drugs, and benzodiazepines for differences in clinical presentation and treatments.

Results: Most notably, results showed that NAS has no defined meaning in terms of whether it relates to opioid, or simply any substance withdrawal. ICD-10 has multiple etiology-based codes for withdrawal in adults, but only one for neonates. In multiple publications, “NAS” described opioid withdrawal only: in others, it described polysubstance use prescribed medication withdrawal. Additionally, unclear etiology can cause wrongly treating NONW resulting in adverse consequences to neonate's health and development.

Conclusion: NAS is often incorrectly used to describe a multitude of withdrawals. Guidelines need to be devised that define the vocabulary in literature, clinical usage, and ICD-10. The lack of such guidelines leads to misdiagnoses and adverse events due to medication errors.

EVALUATING BALLROOM DANCE CURRICULUM: PILOT TESTING PROTOCOL FOR PARKINSON'S DISEASE PATIENTS

Shivani Agarwal, MPH, Amy Lee, M.D., M.P.H., MBA, Lyndall McPhail, Sheila Fleming, PhD, John Holden, PhD, Summer Aiti, MPH

Objective: Explore a new ballroom curriculum and investigate the use of mobility and social connectedness measurement tools.

Study design: Ten participants (>45 years old) were recruited, but one dropped out of the study. Participants had no prior ballroom dancing experience. They were taught rumba and American tango during a 10-week class. Social connectedness was measured using the De Jong Gierveld Loneliness Scale (DJ-LS), the UCLA Loneliness Scale (UCLA-LS), and the Social Connectedness Scale (SCS). The use of mobility tracking equipment was tested using motion capture (MOCAP) equipment. A five-point Likert scale evaluated the ballroom curriculum and measurement tools. Open-ended discussions gathered qualitative insights from the participants. Results: Surveying pilot test subjects showed they strongly agreed the ballroom curriculum was effective and impacted their everyday lives (N=9). They also showed strong agreement for the pace of the curriculum (N=8), effectiveness of changing partners (N=6), easy to complete dance patterns (N=7), easy to catch up on any missed classes (N=8), and likeness to dance outside of these classes (N=9). Little feedback was given about use of the mobility trackers. Participants also showed a preference for the UCLA-LS SCS scales.

Conclusion: Accommodations such as holding classes during daylight hours and making any reading materials in a large font should be made for the comfort and safety of future study subjects. These results are intended to be used to develop a research study on actual Parkinson's disease patients.

Using Artificial Intelligence to Predict Mortality in AKI Patients: A systematic review/Meta-Analysis

Rupesh Raina, Raghav Shah, Paul Nemer, Jared Fehlmen, Lena Nemer, Ali Murra, Abhishek Tibrewal, Sidharth Kumar Sethi, Javier A. Neyra, Jay Koyner

Acute kidney injury (AKI) is associated with increased morbidity/mortality. With artificial intelligence (AI), more dynamic models for mortality prediction in AKI patients have been developed using machine learning (ML) algorithms. The performance of various ML models were reviewed and stratified in their ability to predict in-hospital mortality (IHM) for AKI patients. A literature search was conducted through Pubmed, Embase, and Web of Science Databases. Included studies contained variables regarding the efficacy of the AI model (AUC, accuracy, sensitivity, specificity, negative predictive value (NPV), and positive predictive value (PPV)). Only original studies which consisted of cross-sectional studies, prospective and retrospective studies were included, while reviews and self-reported outcomes were excluded. A total of 8 studies with 37,032 AKI patients were included with a mean age of 65.3 years. The IHM was 18.0% in the derivation and 15.8% in the validation cohorts. The pooled (95% CI) AUC was observed to be highest for Broad Learning System (BLS) Models: [0.852 (0.820-0.883) and Elastic Net Final Model (ENF) [0.852 (0.813-0.891)] and lowest for proposed clinical model (PCM) [0.765 (0.716 - 0.814)]. Despite substantial variability, the pooled (95% CI) AUC of BLS and ENF did not differ significantly from other models except PCM [Delong's test $p=0.022$]. PCM exhibited the highest NPV, which supports this model's use as a possible rule out tool. Our results show that BLS & ENF Models are equally effective as other ML models, in predicting in-hospital mortality with variability across all models. Additional studies are needed.

Fun games, less pain?

Kate Jones, B.S., Henry Xiang, M.D. PhD, Megan Armstrong, MPH

Virtual Reality has been shown to be an effective mechanism of pain distraction for pediatric burn victims. We studied the effect of different VR conditions by age range and sex on patients aged 6-17 years (inclusive) with burn injuries. Prior to randomization, a researcher used a 100 mm visual analog scale (VAS) to assess expectations of helpfulness and need toward dressing changes. The Face, Legs, Activity, Cry, and Consolability-revised (FLACC-R) scale was used to assess pain during the burn dressings. Immediately following the dressing change, participants rated on a 100 mm VAS the following: time spent thinking about pain, degree of realism experienced in the VR environment, degree of pleasure/fun associated with playing the VR game, and perceived level of engagement with VR distraction during the procedure. Younger patients in the 6–9-year range reported higher mean expectations by helpfulness and need (Mean = 73.6, 94.5) than 10–12-year-olds (Mean = 55.7, 84.2) and 13-18 year olds (Mean = 68.6, 77.4). By both sex and age, engagement had a significant negative overall effect on overall pain score during burn dressing (coefficient = -0.45, -0.41), and time thinking of pain had a significant overall positive effect (coefficient = 0.38, 0.32). Younger patients had the highest expectations of VR helpfulness and necessity. Fun, realism, and engagement were not statistically different between age groups and sexes. Engagement and fun were correlated, with engagement decreasing pain scores, while time thinking about the pain increased pain scores.

Infective Endocarditis in the Era of the Opioid Epidemic: The Experience of a Large Urban Teaching Hospital

Jared Hinton, B.S., Daniel Redle, M.D., Abraham Saleem M.D., Michael Oravec Ph.D., Ottorino Costantini M.D.

Intravenous drug users (IVDUs) are at an increased risk of developing infective endocarditis (IE), a potentially life-threatening condition. The optimal treatment strategy for IE in this vulnerable population remains a subject of ongoing discussion, with limited clarity on whether surgical (valve repair / replacement) or non-surgical (antibiotic regimens) interventions offer the most favorable outcomes. Our study aims to profile recent infective endocarditis trends in IVDUs at Summa Health Hospital in Akron, Ohio — an urban facility with high intravenous drug use-related complication rates. We seek to determine complications of IE, surgical treatment rates, readmission rates, and overall mortality in patients treated surgically versus non-surgically.

Notably, patients who demonstrate a higher incidence of complications related to IE, including new valvular murmur, valve abscess/dehiscence, heart failure, conduction abnormalities, spine infection, and respiratory failure are significantly more likely to receive surgical intervention. Further statistical analysis is necessary to determine the recurrence of IE and mortality rates between surgical and non-surgical treatments given the confounding variables present within the surgical group. These insights offer valuable guidance for clinical decision-making in urban communities but necessitate further research with expanded cohorts to solidify trends and refine therapeutic strategies for this vulnerable population.

Timing Matters: The Impact of Initial Surgical Debridement Delays on Patient Health Outcomes in Necrotizing Soft Tissue Infections

Chloe Williams, M.D., Andrew Fiorentino, M.S., Camryn Hawkins, PhD, Brandon Radow, M.D.

Necrotizing soft tissue infections (NSTI) are life-threatening infections that require prompt diagnosis, early surgical debridement for source control, perioperative critical care, and frequent collaboration with multiple specialties and disciplines. NSTIs require significant healthcare resources and, as a result, are often transferred to tertiary and quaternary referral hospitals for definitive treatment. There are inherent limitations to interhospital transfers that may preclude timely surgical debridement, such as availability of critical care transport teams. Ultimately, this can lead to a delay in infection source control and potentially to worse patient outcomes. This study investigates the crucial factor of timing in the management of NSTIs by examining how the time elapsed between a patient's initial presentation and first surgical debridement affects various clinical outcomes. Specifically, we wish to evaluate how interhospital transfers affect clinical outcomes for NSTI patients by comparing patients who undergo immediate debridement upon initial evaluation to those who are transferred to our hospital prior to debridement. Through a retrospective analysis of medical records from patients who underwent surgical debridement(s) for NSTIs at University Hospitals Cleveland Medical Center (UHCMC), we assessed the relationship between time to surgical intervention and a range of clinical parameters. Short-term outcomes include intensive care unit (ICU) length of stay, inpatient mortality, hospital length of stay, time spent on a ventilator, total number of inpatient surgical debridements, instance of acute kidney injury (AKI), and other infectious complications such as pneumonia. Currently, we are awaiting finalized statistical aggregation to fully analyze the trends in our data.

Systematic Review of Extracorporeal CO₂ Removal in Chronic Obstructive Pulmonary Disease Exacerbation

Abaan Singh Saini, B.A., Abhijit Duggal MD, MPH, Omar Mehkri, MD, Sudhir Krishnan, MD

Purpose: Extracorporeal carbon dioxide removal (ECCO₂R) has been proposed as a potential therapy to either avoid or to help facilitate discontinuation of mechanical ventilation in patients with chronic obstructive pulmonary disease (COPD) exacerbations. The purpose of this systematic review is to evaluate the existing literature and to comment on the safety and efficacy of ECCO₂R in COPD exacerbations.

Methods: We performed a systematic review to look at the efficacy and safety of ECCO₂R in COPD exacerbation. After applying inclusion/ exclusion criteria we evaluated 20 full texts and identified 7 studies that reported on the use of ECCO₂R in patients with COPD exacerbations. The primary outcome of interest was the need for mechanical ventilation. Secondary outcomes included ICU length of stay, hospital length of stay, and mortality.

Results: 107 patients from the 7 included studies were evaluated. The pooled estimate for the need for mechanical ventilation was 12%, with a 95% confidence interval of 6-19%. The pooled estimate for ICU length of stay was 6 days, and the pooled estimate for hospital length of stay was 12 days. The overall mortality rate was 12%.

Conclusion: ECCO₂R is a safe and effective therapy for COPD exacerbations, with favorable outcomes in terms of ICU and hospital length of stay. However, the quality of the evidence is limited by the small number of studies and the risk of bias. Further studies are needed to confirm these findings and to identify which patients are most likely to benefit from ECCOR.

A Hospital Managed Urgent Dispatch Program: A Descriptive Evaluation of Year One of Program Implementation

Erin Simon, DO, Aditi Deshmukh, MSM, Cameron Marcus, MD, Jessica Krizo, PhD, Judy Welsh, MD

Study Objectives: Previously, the use of acute hospital-level care at home for chronically ill patients has led to decreased medical costs, sedentary time for patients, and hospital readmissions. Our healthcare system identified the need to develop a way to prevent frequent emergency department (ED) visits in this patient population. We addressed this by creating a home acute care program Urgent Dispatch (UD). The objective of this project is to characterize the implementation and effectiveness of the Urgent Dispatch program.

Methods: This was a retrospective cohort study of patients enrolled in the UD program from April 1, 2021, through February 28, 2022. We assessed encounters for patient demographics, referral source, reason for visit, number of at home visits, total number of days in the program, and determined if the patient had an ED encounter within seven and 30 days of participation in the program.

Results: A total of 2,218 orders were evaluated in the Urgent Dispatch program. The majority were elderly (mean age 75), white (70%), female (64%), and had Medicare (82%). The top three referral sources to the program were outpatient primary care, emergency department, and outpatient specialist. The top five referral complaints were heart failure, dyspnea, edema, UTI, and dehydration. Of patients enrolled in the program 665 (30%) had an ED visit within 30 days, of which 488 (22%) had a visit within seven days of program enrollment.

Conclusion: For patients enrolled in the Urgent Dispatch program, 70% did not visit the emergency department for at least 30 days.

Extrarenal Manifestations of Atypical Hemolytic Uremic Syndrome: A systematic review and meta-analysis

Abdel Rahem S. Yusuf, Kush Doshi, Rupesh Raina MD

Background: Atypical Hemolytic Uremic Syndrome (aHUS) is a thrombotic microangiopathy (TMA) resulting from excessive activity of the complement pathways due to either abnormal activation or regulation. Although renal vasculature is commonly targeted, aHUS can involve many organ systems. Our review investigates the incidence and clinical outcomes of aHUS patients with extrarenal manifestations.

Methods: The literature search was conducted through PubMed/Medline, Embase, Web of Science Core Collection, and CINAHL. The search criteria comprised terms such as 'aHUS', 'extrarenal', and various individual organ systems such as neurological, gastrointestinal, and cardiovascular. Clinical features specific to the patient were collected, including extrarenal involvement, laboratory values, genetic mutations, and adverse outcomes. The meta-analysis was completed using R software version 3.1.0.

Results: In 47 studies encompassing 890 aHUS patients (3 months to 66 years old), prevalent genetic abnormalities findings include factor H (CFH) mutations [12%; n=19 studies] and anti-FH IgG autoantibodies [27.1%; n=10 studies]. The predominant extrarenal manifestations were related to the central nervous system [28%, n=32 studies], with seizure being the most frequent CNS symptom. This was followed by the gastrointestinal system [31%; n=25 studies] and the

cardiovascular system [16%; n=23]. Kidney failure afflicted 13.2% of aHUS patients, as reported in 11 studies, while the mortality rate stood at 8.9% across 27 studies.

Conclusions: Extrarenal manifestations were present in approximately 20-30% of aHUS patients, with neurologic involvement recording the highest incidence. Studies infrequently report genetic findings due to cost and availability and are limited in population size, warranting larger multi-centered cohort investigations.

CHROMONAR DOES NOT INTERFERE WITH THE ANTI-CANCER EFFECTS OF DOXORUBICIN, BUT PREVENTS ITS CARDIOTOXICITY

Cayman Pearsall, M.S., Thomas Pucci, M.S., Karlina Kegecik, B.S., Mohanad Kaileh, M.S., Mason Covel, M.S., Tyler Nguyen, B.S., William Chilian, PhD, Vahagn Ohanyan, M.D., PhD

Doxorubicin is an anthracycline class chemotherapeutic agent that is used alone or in conjunction with other medications to treat various types of cancer. Doxorubicin works by slowing or stopping the growth of cancer cells due to its toxic effects mediated through redox cycling resulting in oxidative stress. A side effect of doxorubicin treatment, which restricts its use and efficacy, is a form of cardiomyopathy termed doxorubicin-induced cardiomyopathy (DiC). DiC typically presents with the morphological and functional abnormalities of dilated cardiomyopathy, with all four cardiac chambers being dilated. Our previous results indicated that DiC, which leads to cardiomyopathy, was related to inadequate myocardial perfusion. Pharmacological coronary vasodilation with Chromonar, to enhance myocardial blood flow, can halt and reverse the functional decline associated with doxorubicin treatment and improve cardiac function. The goal of this proposal is to test the hypothesis that Chromonar treatment will not interfere with the curative effect of Doxorubicin.

Methods: Four groups of C57Bl6 mice (Male, N=10) were injected with LLC (Lewis lung cancer cells). Group 1: untreated, Group 2: Chromonar treated, Group 3: Doxorubicin treated, Group 4: Doxorubicin + Chromonar treated. Tumor size was measured by ultrasound imaging weekly.

Results and Conclusion: Six weeks after cancer cell injection, all mice developed solid tumors. The Chromonar + Doxorubicin combination treatment significantly decreased the tumor size (80% smaller compared to the control and 60% smaller compared to the doxorubicin group). Taken together, our results indicate that Chromonar does not interfere with the chemotherapeutic effect of doxorubicin. Combination treatment with Chromonar potentiated the effect of doxorubicin.

MRI and Modern Diametric Magnet Cochlear Implants: A Systematic Review

Sidney Spencer, D.O., Quan Lu, B.A., Anita Jeyakumar, M.D

Introduction: The utilization of cochlear implants (CI) and MRI for diagnostic purposes is increasing. The review aims to examine the magnetic properties of CI with freely rotatable magnets, their safety, and the burden of artifacts during MRI scans.

Methods: The study was IRB-exempted. PubMed, Cochrane, and Web of Science databases were searched using MESH term “MRI” and phrases of “Med-El Synchrony (MS)”, “Advanced Bionics HiRes Ultra 3D (3D)”, “Cochlear Nucleus Profile Plus (PP)”, “rotatable magnet” “diametric magnet”, and “MRI-safe CI”. Additional studies were identified from reference lists.

Non-English, non-human, cadaveric, and non-implanted CI studies were excluded.

Results: 18 studies were included; 17 reporting on MS, 5 on 3D, and 2 on PP. 320 MRI scans were performed for MS, 25 for 3D, and 33 for PP, with more scans performed at 1.5T. Headwrap utilization was reported in 7 studies, while 13 mentioned no headwrap usage. 15 studies assessed for pain, with 2 reporting its occurrence: two cases for MS and one for 3D. Demagnetization did not occur in the 12 studies that reported on it. One implant displacement was noted with the 3D implant out of 16 reporting studies. No post-imaging sequelae were reported. Artifacts were reported across multiple studies, but the impact on image quality depended on the location of the lesions and the scanning protocols applied.

Conclusion: CI with diametric magnets may enable MRI usage with fewer safety concerns. However, clinical safety reports during MRI scans are sparse and contain incomplete data. MRI artifacts from CI still pose concerns.

Protocol-driven, multidisciplinary resident-run post discharge transition clinic to reduce hospital readmission in heart failure

Kimberly Howe, PhD, RN, Shyam Bhakta, M.D., MBA, Joseph Kessler, MS

The purpose of this study is to evaluate a comprehensive heart failure discharge program that includes heart failure education and care in a heart failure clinic by a multidisciplinary team. The goals of this study are to keep subjects optimized on their medical therapies, educated to detect any changes in their cardiovascular status, reduce all-cause and cardiac readmissions to the hospital, and improve quality of life. Patients admitted to the hospital with a diagnosis of heart failure are invited to join the study and are asked to complete the Minnesota Living with Heart Failure Questionnaire measuring quality of life over the past four weeks and the Atlanta Heart Failure Knowledge Test at bedside— both of which are followed up at subsequent visits to the Congestive Heart Failure Clinic, the first visit being within a week of discharge. Each patient will be seen post-discharge by a multi-disciplinary team consisting of a cardiologist, Internal Medicine resident, clinical pharmacist, dietician, certified exercise physiologist and a research nurse. The team will follow the patient for at least one-month post-discharge. 100 patients will be enrolled in this study with a current enrollment of 35 patients. The Seattle Heart Failure Model will calculate pre- and post-intervention survival rates for this study. As the project continues, low patient enrollment has been consistent with the patients' time-commitment, traveling, and number of physicians. Data is still being collected and analyzed but a quick overview is demonstrating improvements in our goals compared to baseline.

Rapid Outpatient Evaluation for Patients with HEART score 4/5 Safely Reduces Admissions

Lesh, Nicholas, MS4; Reyes, Michelle, DO; Jouriles, Nicholas, MD; Seaberg, David, MD; Reuter, Quentin, MD.

Background: Hospital overcrowding and Emergency Department (ED) boarding have become challenging issues in healthcare, particularly in the wake of the COVID-19 pandemic. Patients with moderate risk chest pain, as determined by HEART scores of 4 or 5, have traditionally been admitted for observation and further cardiology evaluation.

Objective: This study aims to assess the impact of an Outpatient Chest Pain Pathway (OCCP) for patients presenting to the ED with chest pain and HEART scores of 4 or 5 in terms of ED disposition and patient safety at 30 days as measured by AMI and death.

Methods: This is a retrospective, observational, non-inferiority study. Outcomes between patients evaluated in the pre-OCCP period (January to May 2018) and the post-OCCP period (January to October 2022) were compared. Data was collected via nonblinded chart review. Primary outcomes included admission and discharge rates before and after the implementation of this pathway, and AMI/Death rates in OCCP patients.

Results: After implementing the OCCP, the percentage of ED patients with HEART scores of 4 or 5 discharged increased from 15% to 26%. One out of 237 discharged patients experienced an AMI within 30 days, and there were no reported deaths within this period. Non-inferiority analysis demonstrated the safety of the OCCP with a 0.4% AMI/Death rate.

Conclusion: This study highlights the effectiveness of an OCCP in safely reducing inpatient admissions for patients presenting to the ED with chest pain and HEART scores of 4 or 5, thus aiding in mitigating ED and hospital congestion.

Mapping the Evolution of Existing Research in Robotic Cardiac Surgery:

A Bibliometric Analysis

Andrea Amabile MD, Irbaz Hameed MD, Tarik Whitham BS, Patrick Strzempek BS, Syed Usman Bin Mahmood MBBS, Sigurdur Ragnarsson MD, Wei-Guo Ma MD PhD, Madonna E. Lee MD, Arnar Geirsson MD, Markus Krane MD

Objective: We performed a bibliometric analysis to determine whether published literature in the field of robotic assisted cardiac surgery mirrors growing clinical practice.

Methods: We performed a bibliometric analysis of top-cited articles in robotic cardiac surgery published between 1998 and 2021. The Scopus database was queried. Articles were considered eligible if they had at least 20 citations and presented an original, clinical contribution about robotic cardiac surgery. Additionally, we performed a sensitivity analysis focused on 2018–2021. The same search strategy was applied, and articles with at least 4 citations were included.

Results: Of 562 articles retrieved, 69 and 23 original contributions met inclusion criteria for the main and the sensitivity analysis, respectively. Results are summarized in Table 1. In both timespans, robotic coronary revascularization and mitral surgery were the most represented topics, but the type of robotic procedures covered by manuscripts in the sensitivity analysis was more heterogenous. No significant correlation was found between number of authors per article and number of citations ($r=0.14$; $p=0.26$), not even after normalizing data to time since publication ($r=0.05$; $p=0.80$). Number of authors per article and impact factor of the publication were positively correlated ($r=0.25$; $p=0.03$). The proportion of retrospective versus prospective studies was 88% versus 12% in the main analysis, while all studies in the sensitivity analysis were retrospective.

Conclusions: Robotic cardiac surgery is a rapidly expanding field supported by a robust body of literature with its unique bibliometric footprint. The proportion of prospective versus retrospective studies has been decreasing over time.

Comparison of clinical outcome and hemostatic efficacy of Andexanet-alpha and four-factor prothrombin complex for reversal of Factor Xa oral anticoagulants in patients with severe acute brain injury

Madiah A Hepburn, M.D., Amber E Kerstetter-Fogle, Ph.D., Hunter J Landwehr, B.S.

Antithrombic-related intracranial hemorrhages constitute in-hospital mortality rates of 12.4% and 29% for traumatic and non-traumatic intracranial hemorrhage respectively. Four-factor prothrombin complex concentrate (4F-PCC), sold under the brand name Kcentra, delivers high amounts of Vitamin K-dependent factors to patients taking Vitamin-K antagonists which inhibits it. Regarding reversal of Factor Xa (FXa) inhibitors, Kcentra showed correction of coagulation in laboratory parameters, but this was inconsistent across all studies.

However, in May of 2018 a novel medication, Andexanet-Alfa sold under the name Andexxa, a FXa inhibitor reversal agent was approved under the FDA's accelerated approval pathway for treating FXa inhibitor reversal treatment. Andexxa utilizes molecular mimicry to bind with FXa inhibitors, reversing their anticoagulant property.

Currently, there is little research on the use of Kcentra vs. Andexxa in patients suffering from antithrombic-related intracranial hemorrhages. Therefore, the objective of this research will be to compare the effectiveness of Kcentra to Andexxa. This will be done via a retrospective indirect comparative study of patients taking anticoagulants who also received Andexxa or Kcentra. In-hospital and 30-day post-discharge mortality as well as change in intracranial hematoma size post-treatment will be compared to assess the effectiveness of treatment.

In conclusion, this is an ongoing study comparing the effectiveness of Kcentra vs. Andexxa in the reversal of antithrombic-related intracranial hemorrhages. The goal of this study is to provide data regarding patient outcomes post-reversal agents with hopes of modernizing current hospital protocols.

Epidemiology data on the cost and outcomes associated with pediatric acute kidney injury

Rupesh Raina, Sidharth Sethi, Varun Aitharaju, Ananya Vadhera, and Imad Haq

Hospitalized children with acute kidney injury (AKI) have not been extensively studied for clinical outcomes including hospital stay, need of mechanical ventilation, mortality rates, and healthcare utilization. We hypothesize significant financial cost and increased morbidity and mortality associated with pediatric AKI.

This is a retrospective study of pediatric patients (age <18 years) included in the Kids' Inpatient Database (KID) between January 1, 2016 and December 31, 2021. The results of the data analysis was utilized for comparative testing between the AKI and non-AKI cohorts. The study included 4,842 children [with AKI (n=2,424) and without AKI (n=2,418)]. The odds of mortality (p=0.004) and mechanical ventilation (p<0.001) were observed to be significantly higher among those with AKI as compared to those without AKI. Additionally, the median (IQR) duration of stay in the hospital (p<0.001) and total cost (p<0.001) were significantly higher among those with AKI versus those without AKI. AKI in children was associated with higher odds of mortality, longer duration of hospital stay, increased requirement of mechanical ventilation, and increased hospital expenditure. The scientific community can utilize this information to better understand the outcomes associated with this disease process in this patient population.

Comparison of Alternative Upper GI Bleeding Risk Assessments with Time to Scope and Mortality

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Upper gastrointestinal bleeding (UGIB) is a frequent emergency in clinical practice, with an incidence of 48-160 cases per 100,000 adults yearly and a mortality rate ranging from 3.1 to 15% [1]. Optimizing treatment methods and guidelines for upper gastrointestinal bleeding reduces poor clinical outcomes. An objective of this study is to determine if clinical scoring score for gastrointestinal bleeds (Rockall, GBS, AIM65) are better than clinical acumen and current standard of care regarding timing of endoscopy and subsequent clinical outcome.

This was a retrospective analysis including patients from Mercy Health Youngstown hospitals from 2021-2022. A clinical score was calculated for each patient who had been diagnosed with a GI bleed for risk stratification to determine need for urgent endoscopy, bleeding readmission, and mortality. Time to scope was also abstracted.

Seventeen percent of patients (n=50/289) had a history of bleeding in the last 12 months.

Baseline hemoglobin was 10.1 + 2.8 (range 3.4-17.0). Symptoms of melena, hematochezia, hematemesis, and syncope were prevalent, 43.3, 57.4, 11.1 and 5.9 percent, respectively.

49.8% (n=144/289) of patients were urgently scoped, with an average time to scope of 47+42 hours (range 5-323 hours). Stigmata of recent hemorrhage was noted on 42.4% (n=61/144) patients, with endoscopic treatment (clip, cautery, etc.) in 27.8% (40/144) patients.

Risk stratification modalities are not utilized. On average, patients who received less blood transfusions underwent endoscopic intervention in under 48 hours, while those who received 3 or more units underwent similar time to scope. Time to scope was 2.23 longer in non-survivors.

PROFILEPLASTY: COMPREHENSIVE FACIAL PROFILE MANAGEMENT ALGORITHM BASED ON 426 PATIENTS

Alvaro Reategui, MD; Hossein Jazayeri DMD; Alexa Mier BA; Connor J Peck, MD; Sarah Phillips MD; Joseph Lopez, MD, MBA; Derek Steinbacher, MD, DMD, FACS

Background: Profileplasty traditionally involves improving a nasal hump or an under-projected chin. However, this procedure can correct other facial defects like saddle nose or prognathism. To establish the best overall profile, the nose, the midface, and the chin should be considered altogether. This study aimed to describe typical facial profiles and propose an algorithm for targeted correction.

Methods: Patients who underwent rhinoplasty, with or without other facial procedures performed by the senior author were reviewed. Patients with pre- and post-operative photographs and clinical follow-up were included. Images were analyzed using Goode and Steiner analyses and E- and S-lines to assess and categorize nasal and facial profiles. A treatment algorithm for each sub-group was proposed based on expert opinion. Adherence to the algorithm was validated by reviewing patients' charts.

Results: 426 rhinoplasty patients were included, with 72 also undergoing orthognathic surgery, including genioplasty. There were two general groups of patients: Group 1) poor nasal profile with balanced facial profile and 2) poor nasal profile with an unbalanced facial profile. Group 1 included 1a) prominent (n=298) or 1b) flat (n=56) nasal dorsum. Group 2 included 2a) convex

profile (n=38), 2b) concave profile (n=32), and 2c) “pseudo-dorsum” (n=2). Proposed treatments for Group 1 involved balancing the nasal dorsum and nasofrontal angle, whereas Group 2 involved modifying the nasal dorsum and repositioning the maxilla/mandible. 98.6% of patients followed the proposed treatment algorithm.

Case Reports:

A Case Report: Forearm Both Bone Unstable Fractures with Chronic Fungal Infection. Should the Hardware Come Out?

Benoit Kindo DO, Timilehin Ogunjana MD, Cynthia Uzoukwu BS, John Gentile DO

Introduction: We report a patient with a chronic fungal infection following internal fixation of a both bone forearm fracture from a gunshot wound. This report shows the complexity of definitive treatment, rarity of one of the causative fungi, and difficulty curbing the infection despite prolonged suppressive antimicrobial therapy.

Case Report: A 27-year-old-male presented with a both bone forearm fracture after sustaining multiple gunshot wounds. He underwent an open reduction internal fixation with a bridge plating technique, but subsequently developed a chronic polyfungal infection, with cultures positive for *Candida Albicans* and *Acremonium* spp. He was started on IV Anidulafungin (Eraxis®) for empiric treatment and subsequently switched to IV Amphotericin B (Ambisome®). Despite treatment with different antibiotic regimens, infection persisted, and patient was readmitted multiple times for repeat excisional debridement. At eighth week follow-up, the patient still displayed features of fracture non-union. Although the patient is gaining some increased range of motion to the hand and wrist, he continues to undergo physical therapy.

Discussion: Unstable fractures in the setting of polymicrobial infections of hardware present a challenging dilemma to orthopedic surgeons. Additionally, persistent infection does not favor adequate bone union and fracture stabilization. We suggest that a multidisciplinary approach involving collaboration between the orthopedic surgery and infectious disease team would be useful, even though a clear and definitive approach to this issue remains elusive. More focus on an approach to managing these types of hardware infections needs to be highlighted, as the current focus of most available guidelines and case reports, are periprosthetic joint infections.

Non-Arteritic Ischemic Optic Neuropathy Associated with the use of Rhino 68, Extreme 50000, and Magnum 24K: A Case Report

Jovana Hanna, BS, Parker J. Williams, DO, Christopher Davis, MD, Faisal Ridha, MD

Purpose: An otherwise healthy 35-year-old male presenting with signs of unilateral optic neuropathy consistent with non-arteritic ischemic optic neuropathy (NAION) related to over-the-counter use of erectile dysfunction supplements.

Methods: The patient has been recommended to stop taking all performance enhancing drugs and to begin taking 0.2% Brimonidine twice a day for neuroprotection. Labs were ordered to rule out less likely causes. An MRI of the brain with and without contrast and orbits were also recommended to rule out infraorbital or intracranial compressive etiology. In addition, a fundus autofluorescence and ultrasound were also ordered. Unfortunately, the patient was lost to follow up after the initial first visit and was unable to be reached thereafter. All intended workup was unable to be completed.

Results: The patient's symptoms and labs make his diagnosis likely to be NIAON. Other diagnoses that were considered include: Glaucoma, Anomalous Nerve, and Drusen. We believe the diagnosis to be NIAON due to the vasodilatory effects of the PDE inhibitors and the likely decrease in optic nerve perfusion.

Conclusion: As more cases related to the use of ED over-the-counter supplements and NIAON arise, it is important that physicians do not neglect patient history, even in young males like our patient, who do not present with other medical conditions.

Laryngopharyngeal Edema - An Emerging and Serious Immune-related Adverse Event After Pd-1 Inhibition: A Case Report

Sonam Patel, MPH, MAS, Farhoud Faraji, MD, PhD, Robert Saddawi-Konefka, MD, PhD, Liza Blumenfeld, Philip Weissbrod, MD

Introduction: This case report describes immune checkpoint inhibitor (ICI)-related laryngopharyngeal edema with pembrolizumab in the treatment of HNSCC.

Methods: This case report is a descriptive study that details the course of HPV associated squamous cell carcinoma of the right base of the tongue and the associated immune-related adverse event (irAE), specifically laryngopharyngeal edema. The patient received six cycles of Pembrolizumab, an immune checkpoint inhibitor. After follow up seven months into treatment, we observed laryngopharyngeal edema.

Results: A 71-year-old male with a history of cT4bN1M0 p16-positive squamous cell carcinoma of the right base of tongue 13 months status post completion of definitive chemoradiotherapy presented with new onset dysphagia, dysphonia, vocal fold paralysis, cranial nerves X and XII palsy, and hypermetabolic foci in the right neck concerning for recurrent disease.

Immunohistochemical tumor evaluation demonstrated positivity for PD-L1 (combined positive score >1) and anti-PD1 immunotherapy with pembrolizumab was thus initiated. Seven months into pembrolizumab therapy (6 cycles), the patient presented with several weeks of worsening dysphagia, cough with swallow, and right neck stiffness. Videostroboscopic exam at this presentation demonstrated increased erythema diffusely within the larynx with notable increase in edema of the right aryepiglottic fold and arytenoid complex. Fiberoptic endoscopic evaluation of swallowing demonstrated worsening of penetration and aspiration score characterized by increase in pharyngeal residue more pronounced in the vallecula than the hypopharynx and worse with solids than with liquids.

Conclusion: ICIs like PD-1/PD-L1 and CTLA-4 have revolutionized the treatment of cancer and are now a mainstay of standard oncologic therapy. While ICIs have shown favorable results, they come at the expense of irAEs. Here, we showcase laryngopharyngeal edema induced by pembrolizumab immunotherapy as an emerging, but consequential irAE.

Cutaneous Reactions to COVID-19 Vaccine

Hafsa Hassan, B.S., Patrick Lee, Shannon, M.D.

In recent years, reports of cutaneous reactions following COVID-19 vaccination have emerged. We present a case of a 74-year-old male who sought evaluation for a pruritic rash on his arms, feet, and legs persisting for two months. Previous medical consultation had led to a prescription of 10mg prednisone twice daily and

over-the-counter hydroxyzine thrice daily. A comprehensive dermatological examination revealed leukocytoclastic vasculitis on the left lateral dorsal foot, seborrheic keratoses on the trunk, lentiginos on the face, and benign nevi scattered across his body. A 4mm punch biopsy confirmed leukocytoclastic vasculitis, and .1% triamcinolone acetonide topical cream was prescribed for a two-week regimen. At the follow-up two weeks later, the rash had markedly worsened, spreading extensively, with vasculopathy now evident throughout his body. The patient revealed that the rash had first appeared six weeks after receiving COVID-19 vaccinations a year earlier. Subsequent 3-week follow-up visits demonstrated further exacerbation of vasculopathy, prompting concern. This case underscores the need for heightened awareness and research of cutaneous reactions following COVID-19 vaccination. Furthermore, it raises questions regarding the mechanisms underlying these reactions and the long-term implications. In conclusion, this case report emphasizes the importance of vigilance in evaluating, monitoring, and managing cutaneous reactions associated with COVID-19 vaccination. Despite isolated incidents, a history of allergic reactions to specific substances should not discourage COVID-19 vaccination, particularly in the general population. However, individuals with immune dysregulation may require specialized selection and monitoring.

Cranial Nerve XII Palsy From Spontaneous Right Internal Carotid Artery Dissection

Michael F. Grasso, BS, Jonathon McCann, BS, Michael Kentris, DO

Internal carotid artery dissection is a dangerous condition caused by a separation of the intimal layers of the artery, potentially compromising blood flow distally to the dissection. This process can occur from mechanical forces, arteriopathies, or spontaneously without clear cause. Spontaneous rupture is a rare cause of ischemic stroke that most often affects those in the young to middle-aged population. Here, we report a case of an isolated cranial nerve XII palsy secondary to spontaneous internal carotid artery dissection with no known inciting cause. The patient described is a 40-year-old male presenting for evaluation of tongue weakness, difficulty swallowing, and a headache. Additionally, he was seen to have rightward tongue deviation on physical examination. CT head and neck were initially found to be unremarkable for any acute process. MRI brain with contrast showed dissection of the distal right cervical internal carotid artery. This case is being written to show the rare instance of internal carotid artery dissection causing ipsilateral, isolated cranial nerve XII palsy in a young patient without known risk factors for artery dissection.

Airway Management of a patient with Coffin-Lowry Syndrome: A Case Report

Shaarav Ghose, B.S., Bushra Abdul Aleem, M.D., Michael Leeds, M.D.

Introduction: Coffin-Lowry Syndrome (CLS) is a rare X-linked genetic disorder characterized by intellectual disabilities, facial dysmorphism, and cardiac abnormality. Anesthetic management of individuals with CLS can be complex due to difficult airway management. In this case report, we present a patient with CLS who underwent surgical intervention, highlighting the anesthetic considerations encountered throughout the perioperative period. We hope to analyze the difficulties involved in anesthetic management of rare conditions like CLS to improve clinical outcomes for affected individuals.

Case Report: A 17-year-old male with CLS and developmental delay presented with a right-sided neck mass for surgical resection. Given the patient's findings of retrognathia and an enlarged tongue, we anticipated difficulties with mask ventilation and tracheal intubation. Although the recommendation is an awake intubation, the patient's developmental delay precluded this approach. A fiberoptic intubation with the primary objective of maintaining spontaneous ventilation was planned. Pre-medication was administered with midazolam and glycopyrrolate. Once adequate sedation was obtained through intravenous dexmedetomidine infusion, mask induction was started with sevoflurane, ensuring the patient continued to stay spontaneous. Then a nasal fiberoptic intubation was performed. Once intubation was confirmed with capnometry, propofol, and rocuronium were given. The patient tolerated the procedure well. The patient was extubated awake and transported to the post-anesthesia care unit under close observation. Conclusion: This case report demonstrates the complexities involved in anesthetic management of individuals with rare genetic disorders such as CLS. We emphasize the necessity of customizing the airway management to optimize patient safety.

Erythroderma with waxy palmoplantar keratoderma: a classic presentation of type 1 pityriasis rubra pilaris (PRP)

Firdous Ali, Anthony P. Fernandez, M. D., Ph. D.

A 61-year-old man was seen in the clinic for evaluation of erythroderma (erythematous rash involving $\geq 90\%$ body surface area). The patient was referred over by his local dermatologist after his initial punch biopsy demonstrated areas of parakeratosis and psoriasiform hyperplasia along with a dermal perivascular lymphocytic infiltrate. Examination revealed erythroderma with orange-red plaques on the patient's back, chest, and bilateral upper and lower extremities with focal islands of sparing and diffuse scaling of the scalp. Additionally, the patient demonstrated thick, yellow keratoderma of his palms and soles with a waxy hue and pronounced thickening of his nails. Clinicopathologic correlation was consistent with a diagnosis of type 1 PRP. Type 1 PRP is a benign inflammatory condition that typically arises in adults and tends to gradually resolve within 3 to 5 years. Despite being self-limiting, PRP patients often have disabling symptoms throughout a variable disease course characterized by skin pain, pruritus, body temperature dysregulation, and psychological distress (Eastham, 2019). Overall, the symptoms related to PRP severely impact quality of life. Treatments include systemic retinoids, cyclosporine, and biologic medications such as TNF- α inhibitors and IL-17A inhibitors (Eastham, 2019). No treatment is effective in all patients, and combination systemic medication regimens are common. This case highlights the hallmark features of PRP, including islands of sparing and waxy palmoplantar keratoderma, that help distinguish it from other causes of erythroderma.

A Rare Case of an Emergent Third Valve in Valve Intervention

Mihail Paxos, MD, Ataul Qureshi, MD, Sara Godil, MD, Basharat Bajwa, MD, Cole Thompson, BS

Bioprosthetic valves are prone to structural valve degeneration and the typical lifetime is noted to be 10-15 years. We present a case of a 54-year-old male who underwent valve replacement twice and presented in obstructive shock requiring a third valve intervention.

This is a 54-year-old male with prior history of drug abuse and bicuspid aortic valve status post bioprosthetic aortic valve and aortic root repair at age of 15, aortic stenosis requiring repeat surgical bioprosthetic AVR (25 Magna Ease) in 2011 who presented in obstructive shock. Started on Levophed and dobutamine with no improvement. Emergently taken for right and left heart catheterization. Noted to have mild CAD but severe cardiomyopathy EF 15 to 20%. The aortic valve gradient was noted to be 80 mmHg. Emergent TEE showed no evidence of endocarditis. Impella CP and Swan-Ganz catheter were placed for hemodynamic support and monitoring. Patient subsequently underwent valve in valve TAVR with Medtronic CoreValve 26 mm. Post TAVR mean gradient on echocardiogram decreased to 10 mmHg and LVEF recovered to 55-60%.

Most common cause of transcatheter bioprosthetic valve failure is stenosis from calcification and thrombosis. Redo TAVR in recent studies has proven to be safe with favorable outcomes. Our young patient had already undergone two surgical valve interventions and now presented with critical bioprosthetic valve stenosis. Due to substance abuse, he was not a candidate for repeat surgical intervention and after a heart team approach, emergent Valve in Valve TAVR was deemed to be the best option.

Acetaminophen Absorption Test Mark to Assess Malabsorption

Balakrishna S. Brahmandam, BS, Michaelia Cucci, PharmD, Louis Nelson, DO, Darrick Emery, PharmD

The AAT has been shown to help be used as a diagnostic marker for graft rejection for small bowel transplantation (SBTX)¹. AAT was used in this case to evaluate if the patient would be able to absorb oral medications and nutrients from enteral feeds.

51-year-old male with a history of gastrointestinal hemorrhage presented to the Emergency Department (ED) for an evaluation of hematemesis. An esophagogastroduodenoscopy (EGD) showed large amount of blood throughout the stomach and a pulsatile vessel unable to be controlled endoscopically. So, he went to the operating room for an exploratory laparotomy (ex-lap). He was found to have an aberrant arterial supply to his liver. Given the patients on going bile leak and complex surgical anatomy there were concerns about whether patient was absorbing effectively. Therefore, an Acetaminophen Absorption Test (AAT) was completed to an oral medication and enteral feed. The AAT score was 7 ug/ml. The AAT score was on the lower end of the normal. After further surgeries including abdominal closure and skin grafting the patient was discharged to a long-term care facility.

The Acetaminophen Absorption Test can be used to assess GI function by measuring drug-absorption. The AAT has been shown to help be used as a diagnostic marker for graft rejection for small bowel transplantation (SBTX)¹. In this case, this test was clinically significant given the patient's ongoing bile leak and surgically altered upper gastrointestinal tract. AAT can be a surrogate to assess malabsorption in surgically altered GI tracts.

Quality Improvement

Factors Associated with COVID Vaccination Rates among Ohio Nursing Home Personnel

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Purpose: Ohio ranks 49th out of 50 in COVID vaccination rates among nursing home personnel with only 74% vaccinated. Nursing home personnel interact with a patient population that is at high risk for COVID complications, highlighting the need for personnel to be vaccinated.

Methods: In this study, we conducted a secondary data analysis using Centers for Medicare and Medicaid Services (CMS) data and data from the County Health Rankings matched by county of each Ohio nursing home to investigate socio-demographic variables that could be related to the reduction in COVID vaccination rates.

Results: We found that living in an Appalachian county and having higher rates of flu vaccinations was associated with higher rates of COVID vaccinations among nursing home personnel. Nursing homes within counties with higher percentages of uninsured residents and greater rates of segregation showed a decreased likelihood of COVID vaccination.

Conclusion: This information can be used to inform healthcare administrators of which socio-demographic variables are associated with lower COVID vaccination rates and which nursing homes to target for increased education on the importance of vaccination.

Bye-Bye HAIs: An Automated Hand Hygiene Monitoring System

Alexander P. Powell

Studies show that 1/32 of patients admitted to a hospital in the United States will develop a hospital acquired infection (HAI) and that 1/10 of these infections will be terminal. 70% of these occurrences were considered preventable. HAIs create financial strain within hospital systems across the United States, costing over 28 billion dollars annually. To combat HAIs, hospitals and regulatory agencies have set forth standards to encourage and track hand hygiene compliance. Our technology is a passive automated hand hygiene monitoring system that records hand hygiene upon entry to the room. The system also looks to involve patients in the hand hygiene process through a series of red or green lights. If the individual uses hand sanitizer before entering the room, a light above the door will illuminate green. If hand sanitizer is not used, the light will illuminate red upon entry.

We have completed 21 interviews for customer discovery and market validation. Market analysis demonstrated a growing 28-million-dollar market for hand hygiene monitoring systems related to continued increase interest in hand hygiene compliance, regulatory compliance, and overall patient safety.

The gold standard is the “secret-shopper method.” This system is labor intensive, costly, and does not provide a robust data set for significant analysis. Despite other devices on the market, there has not been an accepted product due to the cost or overall ineffectiveness of the system.

Training Video on How Healthcare Providers Can Create a Welcoming Environment for Latino/a Patients

Ricardo Velez, M.M.A.S., Amy Lee, M.D., M.P.H., M.B.A., David Ceraolo, B.S., Taeris Guzman, M.M.A.S.

The Pew Research Center reported in 2022 that about half of Hispanics surveyed state that less access to quality medical care is a major reason for worse health outcomes in their population. Just under half cite communication challenges in the health care settings. About 52% say they have had negative experiences in the health care system. Understanding how to provide a culturally welcoming environment will help providers create a positive experience for their Hispanic patients. The Consortium of Eastern Ohio Master of Public Health program has worked with Rita Aggarwal, co-director of Proyecto RAICES, an organization serving Latinx/Hispanic children and families of Summit County, to find out how providers can create a welcoming environment for patients in a healthcare setting. A spring MPH class aided in creating storyboards for video production from this work. Expanding on their work, we drafted a training video on best practices that healthcare professionals/medical teams can utilize to create this environment for Latino/a/x patients. We collected data via two Qualtrics surveys: one for healthcare professionals (n=8) and another for members of the Latino/a/x community (n=5) who were contacts of our team members. Results showed that 92.3% found the video scenarios aligned with real-life situations that Latino/a/x patients face in the medical system. Based on survey responses, "Hispanic community" was changed to "Latino/a/x community" to be more inclusive for our target audience. We also edited instructions on working with a medical interpreter and added the importance of providing culturally sensitive resources when closing visits.

Increasing Dietitian Referral Rates with Patient Education Handouts

Jakob P. Harmon, B.S., Zachary M. Bittinger, M.D., Candace L. Pumper M.S., R.D., L.D.

Diet and lifestyle modifications are the first step in management of many chronic health complications associated with obesity, but, at the Ohio State University Outpatient Care Upper Arlington office, referral rates to the dietitian are markedly low. We sought to increase the referral rate by creating an educational handout that provided information about the dietitian and their services. Patients with a BMI > 30 (obese) with obesity-associated comorbidities (hypertension, hyperlipidemia, Type 2 diabetes, etc.), a BMI > 35 (severely obese), or a BMI > 25 (overweight) with high-risk comorbidities (PCOS) were given the handout and questionnaire (pre- and post-handout) about the dietitian. Before the handout, patients had an average score of 3.6 on a Likert scale (1 = very unimportant, 3 = average importance, 5 = very important) on the importance of decreasing their BMI. Additionally, 63% previously considered talking with a dietitian. After the handout, 73% of the participants had more interest in seeking other dietary interventions with an average rating of 3.54 on a Likert scale (1 = very unlikely, 3 = indifferent, 5 = very likely) of how likely they were to visit the office dietitian. Despite the lackluster score on interest in seeing the dietitian, 45% of the patients asked their physician to be referred. This high referral rate and interest in seeking dietary interventions supports the use of the handouts in educating the office's most medically complex and at-risk patients about the potential benefits they can obtain from visiting the dietitian and improving their lifestyle.

Enhancing the Patient Portal Experience at Southwest General Health Center: A Survey-Based Approach

Angela Brkic, BS

This project aims to improve the patient portal system at Southwest General Health Center. The objective of this project is to enhance patient education on utilizing the portal system, strengthen patient communication with their physicians, and improve overall satisfaction with the system holistically. A survey was conducted among patients to measure the current usage of the portal system and satisfaction on the different factors of security, communication, and ability to manage healthcare information online.

The survey, which utilized a Likert scale ranging from 1 (Strongly Disagree) to 5 (Strongly Agree), yielded important insights into patient experiences with the patient portal system. Approximately 70% of respondents reported using the patient portal system, and among users, 80% accessed their health information at least once a month. While most users found the portal effective for communicating with their healthcare providers, some suggested improvements in the messaging system. Additionally, a considerable percentage of users indicated that they could easily manage their health information through the portal, but some encountered challenges with specific features, such as scheduling appointments online. Regarding security, 75% of users felt that their personal health information was adequately protected (rated 4 or 5 on the Likert scale), while 12% expressed concerns about the security of their data (rated 1 or 2). The results from the study were collected and then communicated with members of the Southwest General Health Center administration to augment their patient portal system for the future.

IMPROVING MAMMOGRAM COMPLIANCE AMONG WOMEN AGED 66-74: A TARGETED OUTREACH INITIATIVE AT MY COMMUNITY HEALTH CENTER

Adiaratou Ba, MMAS., MD Candidate, Richard Robertson, MD Candidate, Roger Musa, M.D.

Introduction: Mammography plays a pivotal role in the early detection of breast cancer, significantly contributing to improved treatment outcomes and reduced mortality rates among women. Despite its importance, the national mammogram compliance rate remains a critical concern.

Objective: This project aimed to enhance mammogram compliance among women aged 66-74 at My Community Health Center, a Federally Qualified Health Center (FQHC), with an initial compliance rate of 57.2%. Our primary objective was to achieve a 10% increase within a three-week period, focusing on 256 women identified as having a "Gap in Care" according to Azara Healthcare's database.

Methods: Daily patient outreach was conducted for 1-2 hours. Azara's data comprised active patients who had not undergone a mammogram in 27 months, excluding individuals with specific medical conditions or histories. We made three phone call attempts on different days and subsequently sent letters to unresponsive individuals. Success was evaluated by comparing data before and after the intervention. **Results:** Among the targeted group, 60 women agreed to schedule mammograms. The outcomes were as follows: 21 completed the mammogram, 59 declined due to various barriers, 2 refused to verify their information, 14 had already scheduled their mammograms before our intervention, 60 preferred their provider to order it, and 100 did not respond.

Conclusion: This initiative provided valuable insights into the barriers affecting mammogram compliance, emphasizing the effectiveness of targeted outreach in promoting preventive healthcare adherence. Further interventions and research are essential to effectively address the identified barriers and enhance compliance rates.

Enhanced Recovery After Surgery (E.R.A.S) for Laparoscopic Cholecystectomy: A Quality Project

Melanie Fernandez, BA, Tarun Bhalla, MD, MBA, FASA, FAAP, Lenore France, CRNA, MSN, Scott Boulanger, MD, Rami Karroum, MD, FASA

ERAS protocols have been used to improve patients' outcomes and satisfaction across a spectrum of different surgical procedures. We report the results of a Quality project where we implemented an ERAS protocol on our pediatric patients undergoing elective laparoscopic cholecystectomy. After obtaining an IRB exemption from our IRB, we conducted a retrospective chart review of a total of 234 patients who were scheduled for elective laparoscopic cholecystectomy from March 2020 to October 2022. 105 of those patients received conventional perioperative care (control group) and 129 patients received our implemented ERAS protocol. Primary end points were: Total length of hospital stay in days and total morphine equivalent usage in milligrams (mg). Secondary end points were: Procedure lengths, first food and out of bed (in minutes) and readmission to the hospital within 30 days. ERAS group had statically significant lower total morphine equivalent usage and shorter length of hospital stay then the group who received conventional care.

Reducing Time from Biopsy to Neoadjuvant Therapy and Time from Biopsy to Surgery in Breast Cancer Patients: A Quality Improvement Study

Jake Lininger, B.A.

Timely access to neoadjuvant and surgical intervention is critical for breast cancer patients, as delays in treatment can impact disease progression and overall outcomes. This quality improvement study aimed to evaluate and optimize the process of reducing the time from ultrasound guided breast biopsy to neoadjuvant chemotherapy as well as biopsy to surgical intervention. Electronic health records were analyzed for delays in care, identifying bottlenecks, and seeking areas for improvement at the Joanie Abdu Comprehensive Breast Care Center (JACBCC). Preliminary results demonstrate a mean biopsy to neoadjuvant therapy time of 41 days for patients being seen January-May 2023 compared to the previous year's mean of 85 days. Similarly, biopsy to surgery intervention mean time of 80 days in 2022 dropped to 61 days in 2023. While we have seen decreases in both biopsy to neoadjuvant therapy and biopsy to surgery times, continuous quality improvement aims to reduce those times further. We plan to implement strategies to streamline the referral process, as we see the greatest delay in care from new patients waiting to be seen by our providers. As new clinic procedures are currently being implemented, we hope to analyze new data from these later months to assess successful reduction of times.

Obstructive Sleep Apnea and Depression: How Screening Tools Can Aid in Proper Diagnosis & Management

Abbey Henderson, B.A.

In order to improve the health of an individual, medical professionals must be able to provide a proper diagnosis to effectively treat a given condition. Many conditions have overlapping symptoms, making proper diagnosis increasingly difficult. Two common conditions managed by family medicine physicians are obstructive sleep apnea and depression. These two conditions may present with similar symptoms including but not limited to: changes in mood, fatigue, poor concentration, restlessness, and anxiety. Prior research has demonstrated that major depressive disorder and obstructive sleep apnea have associated prevalence. Because of the overlapping symptomology and associated prevalence of these two conditions, simultaneously administering the Beck Depression Inventory and the STOP-BANG Obstructive Sleep Apnea Questionnaire can serve as an aid in differentiating between obstructive sleep apnea versus depression or obstructive sleep apnea accompanied with depression. These two screening tools were simultaneously administered to any patient with a previous diagnosis of either condition or to any patient with new onset of the symptoms listed above for a duration of four weeks. The goal of this quality improvement project was to increase awareness of overlapping symptomology and associated prevalence between depression and obstructive sleep apnea in an attempt to enhance effective diagnosis and treatment of these conditions. The recognition that these two conditions present similarly and a proper diagnosis of each will aid in a more effective treatment, enhancing the overall health of your patient.

Translational Models:

INCORPORATING CADAVERIC-SPECIFIC CT IMAGES INTO ANATOMICAL EDUCATION

Alison Pryor, B.S., Mason Covel, B.S., Marcus Julius, M.D., Erin Franks, Ph.D.

Gross anatomy is traditionally taught through cadaveric dissection. However, anatomical models and textbooks do not capture congenital or pathological variation of individuals, posing a challenge to student dissectors who are tasked with learning “standard” anatomy. Cadaveric-specific CT imaging has emerged as a tool to enhance anatomy education while highlighting inherent individual variation. We aimed to investigate how cadaver-specific CT scans could be incorporated into the Foundations of Medicine graduate program and, potentially, more broadly at NEOMED. Two cadaveric donors from the NEOMED Body Donation program underwent CT scanning at University Hospital Portage Medical Center (Ravenna, OH). We interpreted the scans using BeeDICOM software and then performed targeted dissections based on pathological regions of interest. For the first donor, we conducted localized dissections to visualize cancerous lesions of the apex of the left lung and brain parenchyma. Scans were also used as a guide in real time to determine accurate sectioning planes. In the second donor, the scans indicated a hiatal hernia. This enabled us to evaluate the extent of the pathology and develop a deliberate dissection plan. Overall, the CT scans allowed us to plan and conduct targeted dissections efficiently and accurately, while minimizing structural damage. There was also educational value in the practice of interpreting diagnostic images, a worthwhile skill for trainees as the prevalence of imaging within healthcare increases. Integrating CT scanning, traditionally a clinical tool, with

dissection augmented the learning experience while maintaining the value of anatomical teaching through dissection.

Effect of spectro-temporal characteristics of sound sequences and anesthesia on sound processing in the inferior colliculus

Nikhil Harish, Chun-Jen Hsiao, and Alexander V. Galazyuk

Background: To communicate, many species use rhythmic calls with short time intervals. Traditional research however has used long inter-stimulus intervals (ISIs) when studying the response properties of auditory neurons of mice under anesthesia. Our research aimed to investigate how neurons in the auditory midbrain process sound sequences with species-specific rhythmic structure in unanesthetized mice.

Methods: Extracellular recordings were conducted in the inferior colliculus (IC) of 6 adult CBA/CaJ mice with glass pipette electrodes. Responses from a single neuron to a sequence of pure tones was recorded. Each sequence contained 2,993 combinations of sound frequencies and sound levels presented pseudo-randomly. Each neuron was tested with four identical sequences presented at ISIs of 500ms, 300ms, 100ms, and 70ms. Frequency response areas (FRAs) were then constructed based on each's response. Two of these experiments were performed under ketamine/xylazine anesthesia.

Results: All seven IC neurons studied demonstrated similar FRAs at the four different ISIs. Half showed response enhancement when stimulated at short/behaviorally relevant ISIs. Nearly all exhibited much higher response thresholds. Furthermore, the diversity of FRAs typically observed in unanesthetized animals was greatly reduced in this anesthetized population.

Conclusions: Short/behaviorally relevant ISIs have little effect on sound processing in unanesthetized mice. Response enhancement in a selected group of IC neurons under short ISIs indicates that they should be used more broadly during assessment of the auditory system performance in sound processing. The effect of ketamine/xylazine anesthesia should be considered during interpretation of experimental results obtained at least under this type of anesthesia.

Motors for flight: Fine-scale dermal smooth muscle anatomy using contrast-enhanced microCT

Ishani Pandit, B.S., Tobin L. Hieronymus, Ph.D.

Birds achieve remarkably energy-efficient flight across a range of speeds, and a major contributing factor seems to be changing wing shape in flight. Maintaining muscle tissue in the wing's distal parts incurs an inertial cost, but birds retain intricate sets of autonomically-innervated smooth muscle in the distal wing for a purpose that is not currently well understood. One hypothesis is that these feather muscles play a role in fine-tuning wing configuration. Smooth muscle, unlike skeletal muscle, does not produce detectable voltage changes during contraction, meaning that electromyography (EMG) cannot be used to measure smooth muscle activity. Prior work by our group has led to knockdown approaches that locally, temporarily, and selectively denervate dermal smooth muscle for *in vivo* studies, but target regions for this approach remain poorly defined. To close this gap, whole wing cadaveric specimens from cockatiels (*Nymphicus hollandicus*) and coturnix quail (*Coturnix coturnix*) were stained with potassium iodide, a radiodense contrast agent that highlights both skeletal and smooth muscle.

Stained specimens were microCT scanned and segmented to reveal feather muscles *in situ*. Among the smooth muscle bundles that can be seen in our results, one prominent bundle forms a band that runs between proximal ends of primary feather follicles, positioned such that shortening would extend the flight feathers. Similar muscles are only currently known from distantly related rock pigeons (*Columba livia*). Our work is the first description of this muscle group for our study taxa, and provides a well-defined target for further *in vivo* work.

BONE REMODELING AND OSTEOCLAST DIFFERENTIATION VIA TRAPPC9 MODULATION

Gabrielle T. Robinson, BS, Alexander P. Powell, MS, Antoinette Holland, MS, Ernesto Solorzano-Zepeda, BS, Kennedy Nkachukwu, MS, Trinity A. Kronk, BS, Hope C. Ball, PhD, Fayez F. Safadi, PhD

PURPOSE: Approximately 6.5 million Americans suffer from some form of intellectual disability (ID). Non-syndromic autosomal-recessive intellectual disability (NSARID) is a form of intellectual disability which develops due to mutations in the trafficking protein particle complex subunit 9 (TRAPPC9) gene. Phenotypic presentations of NSARID include microcephaly, and skeletal abnormalities inclusive of an increase in bone mass, resulting in a denser cranium, limb deformities, and the loss of teeth.

METHODS: Osteoclast (OCs) functionality was assessed using *in vitro* cellular and biochemical assays of bone marrow-derived hematopoietic stem cells (HSCs) isolated from TRAPPC9 Wild-Type (WT) and TRAPPC9 Knock-Out (KO) mice. HSCs were utilized in the assessment of cell viability, proliferation, differentiation, and function *in vitro*. OC-related gene expression levels were assessed using qPCR analysis as well as assessing serum C-telopeptide of type I collagen (CTX) levels isolated from 8-week-old and 8-month-old TRAPPC9 WT and KO, respectively.

RESULTS: The osteoclast differentiation of the 8-week-old TRAPPC9 WT mice developed normally, while OCs from TRAPPC9 KO mice were larger in size with decreased function using resorption assay. We then analyzed serum from both ages of TRAPPC9 WT and KO animals. The eight-month-old WT animals displayed an increase in CTX levels compared to the eight-week-old TRAPPC9 WT mice. While the eight-month-old KO mice had decreased serum levels of CTX compared to 8-week-old KO animals. Suggesting a decrease in osteoclast activity in the TRAPPC9 KO mice with age.

CONCLUSION: Our data provides the first evidence of the potential therapeutic role of modulating TRAPPC9 expression and function in bone.

Mimicking In-Vivo Myometrial Cellular Phenotypes In-Vitro

Katelyn Sidloski, M.S., Beverlee Wood, M.S., Soma Chakravarti, B.S., Sarah Alserhaid, M.S., Sam Mesiano, PhD.

Once myometrial cells are extracted from the body via biopsy, they lose the capability to function as *in-vivo* human myometrial cells do. This loss of function entails a drastic downregulation of pregnancy-related genes including the Progesterone Receptor, as well as normal smooth muscle cell markers such as **H-Caldesmon**, **Alpha-Actin**, and **Connexin 43**. Such changes in cell behavior stem from a number of factors, the most impactful of which seems to be the composition of the culturing media. **Fetal bovine serum (FBS)** is an indispensable tool in cell culture protocols, providing the immortalized cell line with essential nutrients to

proliferate and grow. However, the FBS supplementation required for adequate growth and survival of these cells in-vitro seems to result in an ungovernable shift toward the **synthetic, proliferative phenotype**--a switch we aim to procure modulatory control over. The goal of this study is to examine various FBS concentrations and their effect on cell growth, morphology, and contractile smooth muscle cell protein markers over time in order to optimize the in-vitro environment to best mimic that of a human uterus. Additionally, methods used to effectively modulate the shift between a contractile and synthetic phenotype were examined and evaluated.

ANESTHETIZATION OF MANDIBULAR AFFERENTS SIGNIFICANTLY INCREASES JAW EXCURSION DURING INFANT FEEDING

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Purpose: Infant feeding is a complex process involving the integration of oral sensation to modulate feeding physiology. The inferior alveolar nerve and the mental nerves (CN V3) are an important source of oral sensation and provide sensation to the lower teeth and lip. Changes to some oropharyngeal sensory nerves alter the timing of the suck-swallow cycle, the effects of disrupting CN V3 afferents on feeding physiology are unknown.

Methods: We recorded six infant pigs using biplanar videofluoroscopy (100fps) while bottle-feeding on milk with barium, prior to and following injection of bupivacaine into the mandibular and mental foramina. Radiopaque beads were surgically implanted to visualize 3D oral kinematics using XMA Lab. Variables of interest included suck frequency and excursions of the anterior tongue, middle tongue, and jaw markers.

Results: Suck frequency did not change with anesthesia. Similarly, excursion of the anterior tongue was not significantly different following treatment. Excursion of the middle tongue decreased, though the effect size was small and the change was likely not large enough to be biologically relevant. However, jaw excursion did significantly increase after anesthetization with a large effect size.

Conclusions: By inhibiting afferent signals from CN V3 and subsequently observing a significant increase in jaw movement per suck, we show that motor outputs to muscles of the jaw are modulated by CN V3 afferents. Further research concerning this sensorimotor relationship is critical to developing sensory interventions for infants struggling to feed.

Histological Analysis of Lymphatic KRAS Mutation in Mouse Soft Tissue

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Complex Lymphatic Anomalies (CLAs) are rare conditions characterized by abnormal lymphatic vessel growth in soft tissue and bone causing massive destruction. In CLA diagnosed patients, a somatic activating mutation has been identified in the Kirsten rat sarcoma virus (KRAS) gene. KRAS gene encodes KRAS protein, which is part of a signaling pathway associated with cell proliferation. In this study, the KRASG12D mutation was induced in Prospero homeobox protein 1 (PROX1) expressing lymphatic endothelial cells (LECs) of mutant mice. Prior studies conducted have shown that hyperactivation of the KRAS gene causes abnormal lymphatic vessel growth, a key characteristic of CLAs. In this study, we determined whether abnormal lymphatic vessels invaded visceral organs. Soft tissue samples including kidney, heart, and spleen were harvested and stained using hematoxylin and eosin (H&E) and immunohistochemistry (IHC)

staining protocols. Through IHC staining, lymphatic invasion was assessed through Lymphatic Vessel Endothelial Receptor 1 (Lyve-1) staining. Lymphatic vessel invasion was not observed in the heart of the KRAS mutant mice via IHC staining. Additionally, a dark mineralization of the red pulp of the spleen and a reduction in size of the white pulp of the spleen was observed in KRAS mice. Images also showed brown staining in the medulla of the kidney of KRAS mutant mice (positive for Lyve-1), indicating abnormal lymphatic vessel growth. Overall, these studies clearly showed that KRAS overactivation mutation is linked to lymphatic invasion within visceral tissues. Future studies will be directed towards identifying/localizing factors (inflammatory) within the soft tissues in our mouse model.

PI3K γ Inhibitor Potentiates Anti-PD-L1 Checkpoint Immunotherapy Against Head and Neck Squamous Cell Carcinoma

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Introduction: Head and neck squamous cell carcinoma (HNSCC) is the sixth most common cancer worldwide. Identification of key treatment targets is imperative in improving HNSCC outcomes, as it can mitigate the common complications of surgical dissection for patients. Phosphoinositide 3-kinase (PI3K) mediates cell proliferation, survival and motility, and its upregulation in multiple forms of cancer presents itself as a possible target for modulation in HNSCC immunotherapy. Our group's previous studies have shown that PI3K γ inhibition upregulated programmed death-ligand 1 (PD-L1) expression in mouse models. Therefore, the objective of this study is to determine the efficacy of a novel PI3K γ inhibitor in HNSCC treatment in combination with PD-L1 checkpoint inhibitor in an HNSCC model.

Methods: We used an in vivo orthotopic HNSCC murine model in C57BL/6 mice using MOC2 cells. After two weeks of treatment, bone marrow, lungs, draining lymph nodes, spleen, and tumors were excised at terminal sacrifice for analysis.

Results: Our results show a greatly increased survival rate for the double-treatment group. In addition, a decrease in immunosuppressive cytokines IL-4, IL-10, and IL-17 was also seen in flow cytometric data, as well as increased CD8⁺ T-cell infiltration in the tumor from samples isolated from our dual-treatment mice.

Conclusion: Our study provides a novel approach for treatment of low immunogenic HNSCC. Further analysis needs to be conducted with histology and rt-qPCR of tumor, lymph node, and spleen tissue samples, as well as the analysis of our in vitro experiments to better elucidate the immunological mechanisms present in our therapy.

Determining Neuronal Densities in the Cerebellums of the Beluga (*Delphinapterus leucas*) and Bowhead (*Balaena mysticetus*) Whales

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Within mammals, echolocating whales (e.g., belugas and dolphins) are noted for having an exceptional brain size relative to body size, including the cerebellum. It is unknown how the cellular composition of the brain differs in taxa with exceptional brain size, specifically in the total abundance of cells and the proportion of neurons to glial cells. This study utilizes the preserved brains of an echolocating beluga (*Delphinapterus leucas*) and a non-echolocating

bowhead (*Balaena mysticetus*). Unlike belugas, the brains of bowheads are smaller, with a brain-to-body size ratio like that of terrestrial artiodactyls. We tested the hypothesis that the cerebellum of belugas contains a greater density of neurons and supportive glial cells than the bowhead. Subsamples of the cerebellum in both taxa were homogenized, stained to differentiate between nuclei of support cells (DAPI) and neurons (DAPI and anti-NeuN), and stained nuclei were counted. Results show the cerebellum of beluga whales has a greater cellular density, with greater counts of total cells and neurons. Combining these results with fossil data, we propose that the beluga-lineage underwent several evolutionary events that increased brain and cranial cavity size and densities of glial and neuronal cells. Our ongoing work utilizes histology to test for differences in the composition of the inferior and superior colliculus in both taxa to test for critical differences in their sensory systems.

The effects of ethanol on bile acid metabolism in Fgf15 intestinal knockout mice

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Fibroblast growth factor 15 (Fgf15, human homolog FGF19) is a gut-produced hormone with wide-ranging roles in embryogenesis. In adults, Fgf15 signaling is limited to the liver, where it reduces bile acid (BA) synthesis by indirect inhibition of Cyp7a1, the rate-limiting enzyme of BA synthesis. In human patients with alcoholic hepatitis, FGF19 is chronically elevated and bile acid synthesis is altered. Ethanol has also been shown to regulate BA synthesis, though these effects are dependent on whether ethanol is consumed in a chronic or a short-term period. In this study, we aimed to evaluate how chronic alcohol use affects BA synthesis in Fgf15 intestinal specific knockout (Fgf15 iKO) mice. Mice were subjected to 10 days of ethanol consumption via a liquid diet followed by an ethanol gavage 9 hours prior to termination. Predictably, the Fgf15 iKO control mice (receiving no ethanol) showed enhanced Cyp7a1 expression compared to the wild-type control mice. This effect was attenuated in Fgf15 iKO mice receiving ethanol. The quantity of BAs, however, showed no significant difference between the Fgf15 iKO control mice and the Fgf15 iKO ethanol mice in the liver and gallbladder. This could suggest that there was enhanced intestinal reabsorption of BAs to counteract the attenuated de novo synthesis of BAs in the ethanol receiving Fgf15 iKO mice. Further evaluation of intestinal reabsorption pathways and Cyp7a1 activity levels should be conducted to verify these findings and predictions.

ILC3s production of IL-10 maintains intestinal immune homeostasis.

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This project aimed to investigate the role of IL-10 production by group 3 innate lymphoid cells (ILC3s) in regulating intestinal immunity. While previous research highlighted the importance of both IL-10 and ILC3s in maintaining gut immune balance, the specific significance of IL-10 production by ILC3s remained unclear. The hypothesis suggested that IL-10 produced by ILC3s helps maintain intestinal balance by regulating inflammation. To test this hypothesis, we analyzed a single-cell RNA sequencing dataset from patients with ileal Crohn's disease to assess IL-10 transcripts in ILC3s. In mice, we created fluorescent reporter mice for IL-10 and ROR γ t to study IL-10 production by ROR γ t+ ILC3s both at baseline and during intestinal inflammation induced

by anti-CD40. Then, we generated mice with a cell-specific deletion of Il10 in ILC3s and studied their response to colitis induction.

The results showed that mice treated with anti-CD40 exhibited increased IL-10 in ROR γ t-expressing ILCs by day 7. When IL-10 production by ILC3s was specifically targeted in mice, termed Il10 Δ ILC3, these mice developed more severe colitis, primarily due to alterations in the phenotype of intestinal macrophages. Even in the presence of regulatory T cells, Il10 Δ ILC3 mice were susceptible to colitis, leading to the conclusion that IL-10 production by ILC3s plays a crucial role in maintaining intestinal immune homeostasis.

In summary, this research highlights the importance of IL-10 production by ILC3s in preventing inflammation and maintaining intestinal immune balance, as shown in the exacerbated colitis and increased susceptibility to colitis-associated cancer in mice lacking IL-10 production compared to their IL-10-sufficient counterparts.

O-GlcNAc transferase regulates vascular smooth muscle cell phenotypic switching

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Vascular smooth muscle cell (VSMC) de-differentiation, characterized by enhanced migratory and proliferative properties, contributes to the development and progression of atherosclerosis. Diabetic patients show increased propensity for VSMC de-differentiation from ‘quiescent’ contractile to ‘synthetic’ proliferative phenotypes. We previously showed a link between VSMC de-differentiation and O-GlcNAc Transferase (OGT) signaling, a key regulator of protein O-GlcNAcylation (a posttranslational modification), in response to hyperglycemia, characteristic of diabetes. We further reported that smooth muscle OGT deletion prevents hyperglycemia-induced atherosclerosis. The goal of the current study was to interrogate the role of OGT in VSMC phenotypic transition. For this, we developed conditional VSMC-specific OGT knockout mice (smOGT^{KO}) using VSMC-restricted Cre driver (*Itga8-CreER^{T2}*) mice, expressing VSMC-specific reporter gene (R26R-EYFP). For Cre recombinase activation, mice were injected with tamoxifen (40 mg/kg/day) at 6-wks-age. After a week’s washout, 8-wks-old wild-type (smOGT^{WT}) and smOGT^{KO} mice were placed on Western diet to induce hyperglycemia. Mice were harvested at 16-wks-age for blood and tissue collection. Immunoblotting of aortic lysates revealed significant reduction in OGT and O-GlcNAc protein expression in smOGT^{KO} mice, validating VSMC-specific OGT deletion. Aortic tissue sections co-stained with GFP and MYH11 (SM contractile marker) antibodies were used in immunohistochemistry. Confocal microscopy revealed increased YFP⁺-MYH11 expression in aortic vessels of Western diet-fed smOGT^{KO} vs. age-matched smOGT^{WT} mice. These data demonstrate that VSMC-specific OGT loss promotes SMC lineage switch to a contractile phenotype. Overall, our results suggest a regulatory role of smooth muscle OGT in VSMC phenotypic transition to de-differentiated state, which may contribute to atherogenic disease progression in diabetes.

DMSO exhibits a strong, Gram-dependent growth inhibitory effect on bacteria

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With bacterial resistance making bacterial infections more difficult to treat, accurate anti-microbial testing methods are imperative for mitigating patient mortality. Methods such as minimum inhibitory concentration (MIC) assays commonly employ polar aprotic solvents such

as dimethyl sulfoxide (DMSO) to solubilize hydrophobic lead compounds. While DMSO is non-toxic to human cells at concentrations up to 10% (v/v), there have been few investigations into this assumption with bacteria. Here, we demonstrate that DMSO exhibits a strong growth-inhibitory effect on bacteria and that this may lead to a significant overestimation of antibiotic efficacy. By measuring the half-maximal inhibitory concentration (IC_{50}) of DMSO with various bacteria, we observed that Gram-positive (IC_{50} , avg = $8.8\% \pm 0.7\%$) and Gram-negative (IC_{50} , avg = $5.7 \pm 0.4\%$) bacteria can withstand different concentrations of DMSO, indicating that even small amounts of DMSO can impede bacterial growth and alter antimicrobial susceptibility. Due to these findings, potential polar aprotic substitutes for DMSO (relative polarity¹, $rp=0.444$), were investigated. Dimethylformamide (DMF) ($rp=0.386$) was more toxic to tested bacteria than DMSO, indicating that decreased polarity likely significantly affects growth inhibition. Acetonitrile (MeCN) ($rp=0.46$), was less toxic than DMSO, with IC_{50} values of 13.1%, 8.4%, and 11.9% for *S. aureus*, *A. baumannii*, and *P. aeruginosa*, respectively. Our results demonstrate that solvent polarity is a critical factor affecting MIC assay results, and even low volume percentages can have significant effects on drug development. Therefore, we suggest routine reporting of solvent concentrations with antibiotic susceptibility assays.

The mechanics of arboreal stability in squirrel monkeys (*Saimiri boliviensis*) and rhesus macaques (*Macaca mulatta*)

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The need to maintain stability in narrow-branch arboreal environment is a primary selective pressure shaping primate locomotion. We test the hypothesis that grasping extremities in combination with gaits emphasizing contralateral fore/hind foot support improves stability by facilitating the production of opposing torques. Here, we measure the locomotor performance of a larger terrestrial monkey (rhesus macaques, *Macaca mulatta*, body mass; 5.1kg), and a smaller arboreal species (squirrel monkeys, *Saimiri boliviensis*, body mass; 0.5kg) on narrow supports. We predict that macaques will require increased opposing torques when walking on narrow supports to maintain stability.

We test this prediction using kinematic and kinetic data collected from two squirrel monkeys and two macaques moving on narrow poles (1.25cm, 2.5cm, 5cm, and 10cm in diameter; 23-40 strides/substrate). We use pkL_{sup} (peak whole-body angular momentum) to measure lateral stability. Macaques had significantly longer periods of total contact with the support ($p=0.011$), leading to an increase in their time spent in contralateral bipods ($p=0.027$). Increasing the amount of time spent in contralateral bipods theoretically permits cancellation between left and right limbs, but only if they are opposing torques. Indeed, pkL_{sup} decreased with the amount of time spent on contralateral bipods in both species ($p=0.029$), but macaques emphasized left/right torque cancellation more frequently than squirrel monkeys ($p=0.003$). Our results support our prediction that, due to their larger size and increased terrestriality, macaques require additional behavioral mechanisms to maintain stability on narrow supports.

THE EFFECTS OF SIMULATED GASTROESOPHAGEAL REFLUX DISEASE ON INFANT FEEDING PHYSIOLOGY IN AN ANIMAL MODEL

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Gastroesophageal Reflux Disease (GERD), the chronic movement of stomach contents into the esophagus, causes feeding difficulties among infants, impeding proper nutrient intake. Existing brainstem connections among the oral cavity, pharynx and esophagus may permit sensory signals from the esophagus to alter motor outputs to pre-esophageal structures. Yet, limited information exists regarding the role of esophageal sensation on oropharyngeal feeding physiology. We investigated how simulated GERD impacts oropharyngeal aspects of feeding in an infant animal model. To address this problem, we perfused 0.15N HCl into the esophagus of anesthetized infant pigs with an orogastric feeding tube. We then recorded infant pigs during bottle-feeding using biplanar videofluoroscopy (100fps). The three-dimensional positions of radiopaque markers in oropharyngeal structures were the basis of a kinematic analysis. HCl perfusion caused a slight decrease in swallowing frequency, although the suck rate did not change. We found small decreases in anterior and middle tongue excursions and a small increase in jaw movement, though these effect sizes were small. Two of five animals had a large increase in thyroid excursion, but there were no significant changes in hyoid excursion in any of the animals. The effects of HCl perfusion seen in were minimal, although a greater effect of perfusion might have been seen with an increased volume and/or concentration of HCl, or with chronic exposure to HCl. Our results also suggest that individuals may respond to reflux in variable ways.

The Aging Ultrastructure of GABAergic Modules in the Inferior Colliculus

Erin N. Beskitt, Aidan D. Wade, Andrew P. Ohl, Nick J. Tokar, Jeffrey G. Mellott

The downregulation of inhibitory and excitatory synapses in the aging lemniscal inferior colliculus (IC) likely contribute to presbycusis. In the non-lemniscal lateral cortex of the IC (IClc) there are modules that densely express GABA and process somatosensory input. We sought to determine if synapses in these GABAergic modules are lost with age. We assessed 3- and 28-month-old Fischer Brown Norway rats. We used immunogold transmission electron microscopy to characterize synapses. GABAergic synapses have symmetric synaptic junctions, pleomorphic vesicles, and are GABA-positive. Excitatory synapses have asymmetric junctions, round vesicles.

We analyzed 958 synapses. There was a 22% reduction of GABAergic synapses at 28 months; excitatory synapses were reduced by 13%. There was no loss of GABA-negative inhibitory (presumptively glycinergic) synapses at old age. The majority (~93%) of all synapses targeted dendrites. The average area of young GABAergic terminals was 0.73 μm^2 and increased to 0.89 μm^2 with age. The area of presynaptic excitatory terminals, the inhibitory and excitatory synaptic lengths and the size of the vesicle pools did not change with age.

As in the lemniscal IC, GABAergic synapses were reduced by roughly a quarter and the average terminal area increased in the IClc GABAergic modules. Unlike our previous report in non-modular IClc, excitatory synapses in the GABAergic modules were not markedly reduced, and increases to synaptic lengths, bouton size and the density of DCVs did not occur. Our data suggests that inputs to the IC from somatosensory nuclei may age differently than inputs from auditory nuclei.

The Role of Mir-21 in Regulating Coronary Blood Flow and Coronary Flow Reserve in Diet-Induced Diabetes

Amanda Osagie-Ogbeide, Yang Wang, Molly Enrick, Liya Yin

Studies show that dietary intake substantially impacts cardiovascular health, leading further research investigating the molecular basis and response to different diets. This study explores the effect of miR-21 expression on coronary blood flow (CBF) and coronary flow reserve (CFR) in two different experimental mice (wild-type mice, and miR-21 knockout) exposed to two distinct diets: a High-Fat-High-Sugar (HFHS) diet and a standard Chow diet. CBF was measured at 1% and 2.5% of the isoflurane at different time points after the HFHS diet treatment. In comparison, CFR was calculated based on the ratio of CBF during hyperemia (2.5% isoflurane) to baseline CBF (1% isoflurane, CBFH/CBFB). Additionally, the ratio of CFR was calculated by hyperemic and baseline velocity (Hyp vel/ B vel). CBF is critical to maintaining cardiac function. If the CBF can't meet the metabolic demands, cardiac function becomes abnormal. The results show that the wild-type mice on the HFHS diet demonstrated a decreased CBF compared to the wild-type mice on the chow diet, which explains the myocardial dysfunction in diabetes. CFR reflects how much CBF can increase under stress than at rest. CFR predicts the prognosis of cardiac events. The higher CFR suggests better recovery. The CFR calculated by the ratio of CBFH/CBFB showed the same trend as the CFR calculated by the ratio of Hyp vel/ B vel. The miR-21 knockout restored the decreased CBF and CFR in mice on the HFHS diet. Our preliminary data sheds light on the regulatory role of miR-21 in coronary microcirculation in diet-induced diabetes.

ROLE OF AUTOPHAGY IN AORTIC VALVE STENOSIS

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BACKGROUND: Aortic Valve Stenosis (AVS) is a condition where the left ventricular outflow tract is obstructed, leading to reduced blood flow to the body. Previous studies suggest that dysregulated autophagy under pathological conditions and aging is linked to the formation of calcific aortic valve stenosis in humans. Our study aims to investigate whether the deletion of CXCR4 in endothelial cells could result in compromised autophagy, potentially contributing to the development of AVS.

METHODS: CXCR4 endothelial cell-specific knockout mice (EC CXCR4 KO) were generated by crossing CXCR4^{fl/fl} mice with Tie2-Cre mice and the presence of AVS was confirmed with echocardiography. Western blotting was used to evaluate several proteins involved in the autophagy pathway in hearts of both control and EC CXCR4 KO mice including LC3-I, LC3-II, AMPK, phosphorylated AMPK (p-AMPK), AKT, phosphorylated AKT (p-AKT), and p62.

RESULTS: Compared with the CXCR4^{fl/fl} control mice, the EC CXCR4 KO mice showed a decrease of 27.3% and 42.7% in the ratio of LC3II/LC3I and p-AMPK/AMPK, respectively. On the other hand, the ratio of p-AKT/AKT increased by 183.9% in the EC CXCR4 KO mice. Additionally, the expression of p62 increased by 189.5% in EC CXCR4 KO mice when compared to control mice.

CONCLUSIONS: Our results suggest compromised autophagy in EC CXCR4 KO mice, which may play an important role in the development of AVS. Further investigation with a larger sample size is needed to confirm our hypothesis.

Preserving critical signals for hematopoiesis in ambient air through manipulation of calcium and DPP4 regulatory pathways

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The bone marrow (BM) niche (~1-4% low O₂) provides critical signals for hematopoietic stem and progenitor cell (HSC/HSPC) maintenance, self-renewal, and differentiation. Previous studies identified retaining HSC/HSPC in low O₂ retains stem cell number, phenotype, and function, which is blunted when HSC/HSPC are exposed to air (20% O₂). Despite this knowledge, most studies are performed in air (~21% O₂), leaving endogenous signaling mechanisms unidentified and HSC/HSPC phenotype/function diminished. Through isolating/sorting/analyzing HSC/HSPC in continuous low O₂, we previously generated the first reference landscape of endogenous phenotype/signaling/function. These studies demonstrated important roles for a serine peptidase (Dipeptidylpeptidase-4, DPP4) and cytosolic/mitochondrial Calcium (Ca²⁺) in the optimal regulation of HSC/HSPC phenotype/function in low O₂. Unfortunately, retaining HSC/HSPC in low O₂ for optimal clinical utilization is impractical as brief exposure to ambient air ablates the low O₂ enhancement in numbers, phenotype, and function. Our goals for the current study were to better understand the differential mechanisms regulating DPP4 and Ca²⁺ pathways to attempt to pharmacologically mimic the low O₂ HSC/HSPC phenotype, and function, in air. Mouse BM was harvested in low O₂ with pharmacological inhibitors of calcium influx channels and DPP4 activity (Verapamil, Diprotin A), left in low O₂ or split into air (60 minutes). Phenotypic analysis of HSC/HSPC markers (LSK, LSK CD150, DPP4) as well as cytosolic (FURA, MFI) and mitochondrial (RHOD, MFI) Ca²⁺ were performed via flow cytometry (FACSCORUS and Flow Jo). Pharmacological inhibition resulted in modification of phenotype and signaling in HSC/HSPC populations and further studies are ongoing to identify alterations to function.

Thrombospondin-1 promotes Vascular smooth muscle cell de-differentiation in Diabetes

Shreya Gupta, Amy Mathias, Jason Lallo, Neha Bhavnani

Diabetes is a major risk factor for atherosclerosis. Diabetic patients are prone to increased vascular smooth muscle cell (VSMC) migration and proliferation, hallmarks of VSMC de-differentiation. Thrombospondin-1 (TSP1), a recognized proatherogenic matricellular protein, is associated with diabetes and vascular pathology. However, the intricate molecular mechanisms by which TSP1 facilitates diabetic vasculopathy remain elusive. The study goal was to elucidate if smooth-muscle TSP1 (smTSP1) regulates VSMC phenotypic switch in diabetes. We generated conditional SMC-specific TSP1-knockout (smTSP1KO) mice by crossing TSP1^{fl/fl} mice with tamoxifen (tmx)-inducible Myh11-CreERT2 mice. For Cre-recombination, 5-wks-old TSP1^{fl/fl}Cretg and age-matched TSP1^{+/+}Cretg littermate mice were treated with 60 mg/Kg/day tmx i.p. for 5 consecutive days. To induce type-2 diabetes, mice cohorts were placed on western diet at 7-wks-age followed by streptozotocin (50 mg/Kg/day, i.p. x 5 days) at 16-wks-age and harvest at 20-wks-age. Immunoblotting of aortic lysates revealed significant decrease in TSP1 expression in tmx-treated TSP1^{fl/fl}Cretg, validating smTSP1KO mice. Lack of smTSP1 increased ACTA2 (SM-contractile marker) expression by 2-fold accompanied with 50% reduction in CDK4 (cell-cycle regulator) expression. Consistently, in murine aortic SMC (MASMC) primary cultures derived from smTSP1KO mice, smTSP1 deletion augmented (>65%) LMOD1 (SM-contractile marker) and SRF (transcriptional activator of SM contractile genes) expression coupled with diminished (45%) vimentin (SM-synthetic marker) expression in 25mM glucose-treated smTSP1KO cells. Further,

propidium-iodide staining revealed reduced S-phase and increased G0 -G1 cell distribution in glucose-treated smTSP1KO MASMC. Together, our data demonstrates a direct role of TSP1 in VSMC phenotypic transition and opens novel avenues for cell-specific TSP1-based therapies for treatment of diabetes.

Substrate Optimization for Patients with Melas and Leigh Syndrome Using Induced Pluripotent Stem Cell-Derived Cardiomyocytes

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Mitochondrial DNA (mtDNA) mutations increase the risk of health issues with overlapping clinical phenotypes. We propose that patient-derived induced pluripotent stem cells (iPSCs) can serve as surrogates for studying mitochondrial diseases, provided a standardized protocol is used to mitigate effects of mtDNA heteroplasmy. Accordingly, we reprogrammed peripheral blood mononuclear cells (CytoTune Kit) from mtDNA disease patients with epilepsy enrolled in clinical trials. After culturing the reprogrammed cells, six iPSC cell colonies were selected (Alkaline Phosphatase Live Stain) from each donor, pooled, and sorted by SSEA4+ marker at passage 6. Pluripotency was confirmed using OCT4 immuno-staining and RT-PCR for OCT4, NANOG, and SOX2 at passage 10. Because two of the patients (m.3243A>G MT-TL1, MELAS, and m.T8993G MT-ATP6, Leigh Syndrome) showed signs of improvement on drug therapy, we differentiated their iPSCs into cardiomyocytes (iCMs) and characterized them using immuno-staining (cTnT). We then screened the substrate utilization preferences of the iCMs using Phenotype MicroArray Mammalian assays (Biolog). The MELAS-iCMs failed to metabolize lactic acid, L-ornithine, and branched-chain amino acids, but performed better than control iCMs in the presence of arginine and glycerol phosphate. In contrast, LS-iCMs exhibited distinctly different substrate preferences and thrived in the presence of acetoacetic acid and α -keto-butyric acid with reduced oxidative stress (AmplexRed). The failure of MELAS-iCMs to survive in the presence of only lactic acid recapitulates a characteristic feature of MELAS, underscoring the potential of iPSCs for disease modeling. Our findings suggest that diverse outcomes to nutritional and pharmaceutical interventions must be tailored to each patient.

LIVING CELL, GAIN OF SIGNAL ASSAY SYSTEM FOR BROAD BASED ANTIVIRAL TESTING FOR SARS-COV-2

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The emergence of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), responsible for the global Covid-19 pandemic, has resulted in over 700 million cases and 6 million deaths worldwide (WHO 2023). Besides its continued circulation, SARS-CoV-2 has demonstrated the risk of reverse zoonosis, harboring the potential for future secondary zoonotic spillover infections (Yen et al., 2022). Consequently, the development of an improved antiviral screening method for CoV-2 is vital. In the past, highly effective antivirals have targeted both viral polymerases and proteases. CoV-2 encodes a highly conserved protease known as CoV 3-chymotrypsin-like Main Protease (Mpro), crucial for the formation of functional viral particles (Dey-Rao et al., 2021). HEK293T cells will undergo transfection with both the CoV-2 Mpro DNA expression plasmid, pGST-Mpro, and a Red Fluorescence Protein (RFP) biosensor. This

process will establish a live cell, gain of signal assay, specifically tailored to Mpro, facilitating comprehensive antiviral testing for CoV-2. Utilizing live cells will enhance the prediction of antiviral pharmacodynamics and offer a more accurate assessment of compound efficacy in a cellular context, measuring drug uptake, toxicity, and intracellular stability (Dey-Rao et al., 2021). Initially, HEK293T cells were transfected with the Red Fluorescence Protein (RFP) biosensor, displaying a gain of fluorescence signal. Now, the CoV-2 Mpro DNA expression plasmid, pGST-Mpro, will be stably transfected and expressed. Direct Mpro self-cleavage will produce the native wild-type mature form of the protease. Following cell line growth and expansion, the degree of inhibition of CoV-2 Mpro will be examined using two investigational drugs undergoing clinical trials.