WESTERN MICHIGAN UNIVERSITY
Homer Stryker M.D.
SCHOOL OF MEDICINE

41st Annual Kalamazoo Community Medical & Health Sciences

RESEARCH DAY 2023

Promoting Equity · Celebrating Research · Transforming Health

WMU Homer Stryker M.D. School of Medicine

W.E. Upjohn M.D. Campus

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KEYNOTE SPEAKER

Melissa B. Davis, PhD

Institute of Translational Genomic Medicine, Morehouse School of Medicine

Dr. Davis is the newly appointed director of the Institute of Translational Genomic Medicine at Morehouse School of Medicine, and Distinguished Investigator with the Georgia Research Alliance. She also serves as scientific director of the International Center for the Study of Breast Cancer Subtypes (ICSBCS), interim director of Health Equity for the Englander Institute of Precision Medicine and associate professor of Cell and Developmental Biology in the Department of Surgery at Weill Cornell Medicine in New York. She is also a Cancer Ethnicity Scholar, co-leading the PolyEthnic-1000 project at New York Genome Center.

Dr. Davis received her PhD in Molecular Genetics at the University of Georgia where she completed groundbreaking work on developmental functions of steroid signaling in model organisms. She completed postdoctoral training in Functional Genomics and Systems Biology at Yale School of Medicine (Human Genetics) and the University of Chicago (Human Genetics and Institute for Genomics and Systems Biology). Her work involved key elements of the ModENCODE project, showing the genome-wide and tissue-specific dynamics of hormone receptor binding, establishing the dynamics of these functions on a cellular level. Her postdoctoral training in Cancer Health Disparities at the University of Chicago at the Interdisciplinary Center for Health Disparities, led the current trajectory of her work to uncover the biological determinants of cancer health disparities and how they intersect with marginalization of minoritized population.

Dr. Davis has published groundbreaking findings that established a new lens to study associations of biological factors in cancer outcomes as related to genetic ancestry. Specifically, she has discovered links between African ancestry and tumor burdens that have a disproportionate burden in people across the African diaspora. Dr. Davis is a pioneer in the field of “disparities genomics,” with specific focus in breast cancer expanding into prostate and gynecological cancers in recent years. Her current findings involve utilizing quantified ancestry to unravel genetic vs. environmental influences in tumor biology among race/ethnic groups, including epigenetic cell signaling and immunological responses in the tumor microenvironment and systemic immune regulation. These novel opportunities to develop precision medicine applications in minority populations are part of a concerted effort to increase knowledge of genomic profiles of underrepresented minoritized and underrepresented cancer patients. Her work is a prime example of how inclusion of diverse ethnic groups can empower research designs for discovery of novel or unique tumor biology.

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The complete program including abstracts is available on the WMed website:
http://wmed.edu/researchday

CE CREDIT

In support of improving patient care, Western Michigan University Homer Stryker M.D. School of Medicine is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

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DISCLOSURES

For more information and credit types, visit:
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WELCOME

Dear Colleagues,

On behalf of the Organizing Committee Members, I am very pleased to welcome you to the 41st Annual Kalamazoo Community Medical and Health Sciences Research Day.

The commitment and participation of Western Michigan University Homer Stryker M.D. School of Medicine, its leadership, faculty, students and the Kalamazoo scientific community in "Research Day" continues on this day marking a 41st anniversary milestone. Overall, 124 research studies will be presented in various formats at our Research Day this year. We would like to thank the presenters, mentors, judges, and staff for their participation and support in making this event successful. We also thank our colleagues from Western Michigan University for their research collaboration with our school and for participating in the event.

In addition, it is my privilege to have worked with this year's Research Day organizing committee. This committee worked diligently over an extended period to bring you an exceptional learning and networking opportunity. Members of this year's committee are:

Adil Akkouch, PhD	Joseph Preziosi, BS	Nichol Holodick, PhD
Amy Shipley, PhD	Keith Kenter, MD	Parker Crutchfield, PhD
Catherine Kothari, PhD	Kevin Chen, BS	Pnina Rokhlin, BS
Consuelo Obaid	Krishna Jain, MD	Sandra Cochrane
Courtney Puffer, MA	Laura Bauler, PhD	Shamsi Berry, PhD
Elizabeth Stier	Laura Counterman	Steven Crooks, PhD
Geetha Dhateecharan, MD	Elizabeth Lorbeer, EdM	Tom Blok, MD
John Spitsbergen, PhD	Maureen Owens	Tom Melgar, MD

We hope this year's Research Day will inspire you to pursue your own research and to, as well, support the basic, clinical, and healthcare research of our Southwestern Michigan Community colleagues as well.

Adil Akkouch, PhD
Chair 2023 Research Day

ACKNOWLEDGMENTS

We extend our grateful acknowledgment to the following members of WMed and WMU professionals.

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Julie Hodge
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WMed W.E. Upjohn M.D. Campus First Floor

Entrance

TBL Hall 1

Lobby

Classroom 111

Auditorium

WMed W.E. Upjohn M.D. Campus Second Floor

TBL Hall 2

Classroom 211

PROGRAM

Wednesday, May 3		
4:30 p.m. – 5:00 p.m.	**Check-in** **Hors d'oeuvres Available**	1st Floor Lobby
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8:20 a.m. – 9:20 a.m.	**Keynote Address** Melissa B. Davis, PhD	Auditorium
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Failures, Modes, and Effects Analysis Exposes Failures in Prenatal Home Visitation Referral for Pregnant Persons
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ORAL PRESENTATION ABSTRACTS

5. The Analysis of Vitreous Humor: Enhanced Toxicological Testing Potential in Postmortem Examination

Jennifer Vosters, BS[1], Noelle Fukuda, BS[1], Tiffany Hangse, BA[1], Prentiss Jones, PhD[2]
[1]Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. [2]Western Michigan University Homer Stryker M.D. School of Medicine, Biomedical Sciences, Kalamazoo, MI

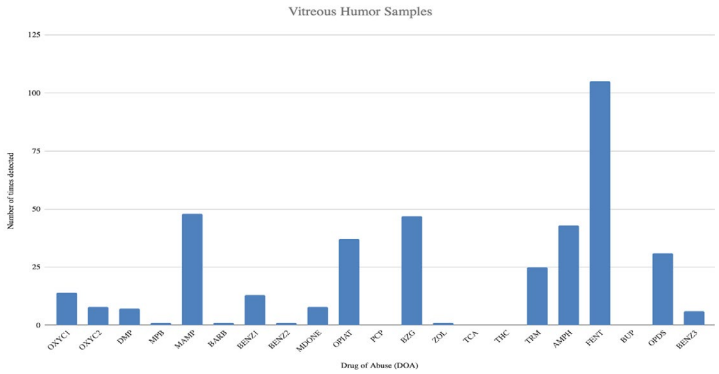
Introduction: Historically, whole blood (WB) has been one of the primary matrices used in postmortem drug screening. However, phenomena such as postmortem redistribution and contamination may limit its functionality. Therefore, determining an alternative specimen matrix in postmortem toxicology casework is extremely advantageous. Vitreous humor (VH) may serve as an alternative matrix for analysis, given its prolonged stability and protection from contamination. VH is a jelly-like substance found between the ocular lens and retina. Protected by the blood-retinal barrier, the mechanism by which various drugs of abuse (DOA) cross into the VH are not well understood. To better understand this, we used a Randox Drug of Abuse Ultra Whole Blood Immunoassay System to screen WB and VH samples from 111 postmortem cases for 21 DOA.

Methods: WB and VH from 111 postmortem cases were analyzed using Randox DOA Ultra Whole Blood Assay. In-house validation studies confirmed the accuracy of vitreous sample analysis.

Results: All 111 WB samples were positive for the presence of 1 or more analytes. The top 4 most frequently detected were fentanyl (97%), benzoylecgonine (45%), and amphetamines and methamphetamine (both 42%) (Fig 1). In VH samples, fentanyl (95%) was similarly the most detected drug, but the next most frequently detected categories differ from blood: methamphetamine (43%), benzoylecgonine (42%) and amphetamines (39%). Similar to the blood samples, neither phenylcycline nor buprenorphine were detected in vitreous samples. However, while cannabinoids were not found in any of the vitreous samples, 34 WB contained cannabinoids (Fig 2).

Conclusions: Given the unique properties that protect the integrity of VH, in addition to needing very little of it for testing, post-mortem toxicologic analysis of this substance has great potential. This is especially true regarding the preliminary observation in which fentanyl was strongly noted to be found in vitreous humor. Further determining the drugs more likely to be found in VH will increase its predictive power and streamline toxicological testing.

References: Bévalot, Fabien et al. “Vitreous humor analysis for the detection of xenobiotics in forensic toxicology: a review.” Forensic toxicology vol. 34 (2016): 12-40.



9. Pregnant, Postpartum, and Unnoticed During the Pandemic: A Literature Review

Shamanthika Shelkay, MD, Madhavi Nagalla, MD, Ruqiya Shama Tareen, MD
Department of Psychiatry, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

Background: The perinatal period starts with conception and lasts until the end of the first year following delivery. Women are twice as likely to get depressed during their reproductive age compared to their male counterparts in the same age group. Women are prone to become severely depressed, suicidal, and even psychotic during their pregnancy and postpartum period. In the past decade, there have been various advancements in perinatal mental health. However, the COVID-19 pandemic broadened the gaps in perinatal mental health care.

Methods: We conducted a focused literature review using the following terms: Emotional wellbeing AND pregnancy AND postpartum AND COVID; COVID AND Perinatal mood and anxiety disorders; COVID AND perinatal psychosis; COVID AND perinatal obsessive-compulsive disorder; COVID management AND psychotropics AND interactions. Articles were reviewed to identify the gaps and nuances in perinatal mental health care during COVID-19.

Discussion: COVID-19 had adverse effects on mental health in people with and without pre-existing mental health conditions. This is likely due to the uncertainty surrounding disease prevention and treatment, mandated government lock downs, and social/physical distancing. The decreased access to health care combined with diminished support from healthcare providers, family, and friends resulted in an increased duration of untreated symptoms and a subsequent worsening in prognosis. Furthermore, sociocultural practices and rituals were affected, further exacerbating symptoms and contributing to a poorer prognosis. However, not all aspects of the pandemic were negative. Some women highlighted the benefits of work from home and other visitation restrictions as a positive effect on their mental health. Our review also discusses how COVID 19 affected psychotherapy and psychopharmacology practices.

Conclusion: Implementation of perinatal depression screening at all levels of care is an important step which can help improve the outcomes for mothers and babies. Expanding the circle of care by including partners, family, or loved ones during the perinatal period is crucial. Transitioning care to telemedicine when needed may improve outcomes. Education is imperative for healthcare providers across specialties regarding the screening and referral processes for perinatal mood disorders.

29. FAIM Prevents Aggregation of Pathogenic Tau Protein Associated with Alzheimer's Disease

Allison Balaj, BS[1], Thomas Rothstein, MD, PhD[2,3], Hiroaki Kaku, PhD[2,3]
[1]Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. [2]Center for Immunobiology, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. [3]Department of Biomedical Sciences, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

Introduction: The pathology of Alzheimer's disease (AD) is characterized by aggregation of amyloid-β plaques and tau tangles. We recently found that Fas Apoptosis Inhibitory Molecule (FAIM) inhibits formation of amyloid-β oligomers/fibrils in Neuro 2A cells and in an in vitro cell-free system [1]. In this study, we sought to determine whether FAIM's isoforms, FAIM-short (FAIM-S) and FAIM-long (FAIM-L), can prevent formation of tau fibrils/aggregates in an in vitro cell-free system. If FAIM can prevent aggregation of tau in addition to amyloid-β, then there is great potential for it to be translated into a novel disease-modifying therapy for AD.

Methods: Tau protein was combined with either HSP27 (positive control), β-lactoglobulin (negative control), PBS (negative control), FAIM-S, or FAIM-L in a 384-well clear bottom plate. Heparin was added to induce tau fibrillization/aggregation. Tau aggregate formation was assessed by Thioflavin T (ThT) fluorescence. ThT is a dye that only fluoresces when incorporated into a tau fibril or aggregate. Fluorescence was detected by the Bio-Tek Synergy Neo2 Multi-Mode Microplate Reader. The experiment was repeated two times.

Results: We found that both FAIM-S and FAIM-L can prevent formation of tau fibrils/aggregates with fairly equal efficacy. The results of our positive and negative controls further support this finding. Tau fibrils/aggregates formed in the presence of PBS and β-lactoglobulin, as evidenced by significantly high ThT fluorescence, but did not form in the presence of HSP27, as previously described [2].

Conclusion/Clinical significance: There is currently no cure for AD and available treatments fail to modify disease progression because they only address the symptoms. The results of this study show that FAIM has great potential to one day be translated into a novel therapy that addresses the underlying pathology of AD and slows disease progression.

References:

[1] Kaku H, Ludlow AV, Gutknecht MF, Rothstein TL. Fas Apoptosis Inhibitory Molecule Blocks and Dissolves Pathological Amyloid-beta Species. Front Mol Neurosci. 2021; 14:750578.

[2] Baughman HER, Pham TT, Adams CS, Nath A, Klevit RE. Release of a disordered domain enhances HspB1 chaperone activity toward tau. Proc Natl Acad Sci USA. 2020; 117(6):2923-9.

30. Function of the Intrinsic Muscles of the Foot by Active Exercise and Electrical Stimulation

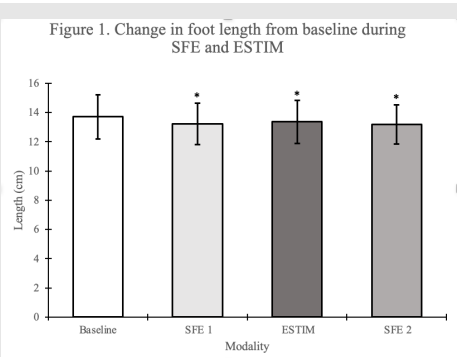
Samantha Dominguez, BA[1], Mark Holling, DPT[2], Jacob Baird[3], James Jastifer, MD[4,5]
[1]Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. [2]Armor Physical Therapy, Kalamazoo, MI. [3]Texas Christian University, Fort Worth, TX. [4]Western Michigan University Homer Stryker M.D. School of Medicine Department of Orthopaedic Surgery, Kalamazoo, MI. [5]Ascension Borgess Hospital, Kalamazoo, MI

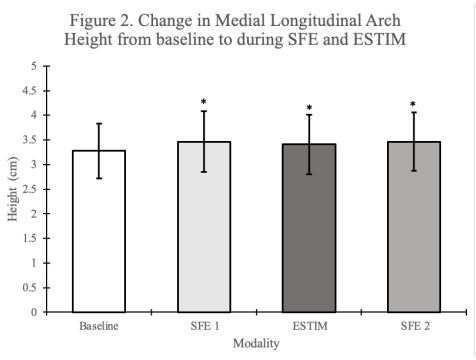
Introduction: The intrinsic muscles of the foot play an important role in foot posture and control during gait[1–3]. The contribution these muscles make to arch height, foot shape, and their correlation to targeted exercises have never been quantified[3]. In this study, we aim to utilize electrical stimulation to target the intrinsic foot muscles specifically and to measure the effectiveness of contraction of intrinsic foot muscles on changing medial longitudinal arch height and foot length.

Methods: 30 healthy volunteers underwent testing of the intrinsic foot muscles including foot length and arch height measurement. This was followed by activation of the intrinsic muscles (short foot exercise), followed by electrical stimulation, followed by a repeat of the short foot exercise. These weight bearing measurements were taken using validated digital imaging software.

Results: Foot length and height measurements were statistically significantly different between tests (both $p<.0001$). Pairwise comparisons were made utilizing the Bonferroni post hoc test that demonstrated a statistically significant difference between baseline foot length and height measurements and all other testing conditions (all $p<.05$) but no difference between short foot exercise and electrical stimulation for height or length (all $p>.109$).

Conclusion: This study demonstrates the intrinsic muscles of the foot contribute to arch height and foot length with weight bearing. Short foot exercise and ESTIM had similar effects on arch height and foot length confirming short foot exercise recruits intrinsic muscles similarly to electrical stimulation. Short foot exercise has a similar effect on foot shape as electrical stimulation and may be considered by the clinician to strengthen intrinsic muscles of the foot in athletes who have foot pain thought to be from intrinsic weakness or in flat footed patients.





References: [1] Fiolkowski P, et al. (2003). The Journal of Foot and Ankle Surgery. 327-333. [2] Mann RA, et al. [3] Soysa A, et al. (2012).

37. Is Use of Mesh Really Needed in Laparoscopic Hiatal/Paraesophageal Hernia Repair? Analysis of 30-day Outcome ACS-NSQIP Database

Clayton Wyland, DO[1], Saad Shebrain, MD[1], Alain Elian, MD[2]
[1]Department of Surgery, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. [2]Bariatric Surgery, General Surgery, Ascension Medical Group, Kalamazoo, MI

Background: Laparoscopic hiatal/paraesophageal hernia repair (LH/PEHR) has become the standard procedure for symptomatic paraesophageal hernia. Although mesh reinforcement had demonstrated early success at reducing short term recurrence rates, with the limited evidence of efficacy and known potential mesh-related complications, the use of mesh for hiatal hernia repair remains controversial. This study aims to evaluate the 30-day postoperative outcomes in patients who underwent LHH/PEH-R with and without mesh repair.

Methods: Patients listed in the ACS-NSQIP database over eight years (2010-2017) who underwent laparoscopic (HH/PEH) repair were identified and divided into group A [repair with mesh (CPT code = 43282)] and group B [repair without mesh (CPT code =43282)]. 30-day postoperative mortality, morbidity, length of hospital stay (LOS), operative time (minutes), return to the operating room (OR), and readmission rates were analyzed. Categorical and continuous variables were analyzed using the Chi-squared test, and parametric/non-parametric tests, respectively.

Results: A total of 24,488 patients underwent L-HH/PEH-R with mesh (n=9,170, group A) and without mesh (n=15,318, group B). Overall, 72% of patients (n=17,596 patients) were females. Both groups had similar demographic characteristics. However, patients who underwent repair with mesh had higher proportions of COPD (5.9% vs. 4.9%, p=.001), hypertension (52.4% vs. 48.8%, p<.001), and dyspnea (13.6% vs. 11.7%, p<.0001). Conversely, patients who had repair without mesh were younger (60.2 years vs. 63.2 years old, p<.001), and had higher rates of diabetes (10.0% vs. 8.5%, p<.001). No differences between groups A and B in 30-day outcomes, including mortality (0.5% vs. 0.6%, p=.921), serious morbidity (3.8% vs. 3.5%, p=.135), overall morbidity (6.4% vs. 6.2%, p=.468), and return to the operating room (2.7% vs. 2.7%, p=.825). However, patients who underwent mesh repair had increased readmission rate (6.4% vs. 5.7%, p=.047), increased operative time (160 ±75 vs. 136 ± 71 minutes, p<.001), and increased LOS (2.9 vs. 2.7 days, p=.002).

Conclusion: In this large ACS-NSQIP database, despite similarity of patient demographics, comorbidities, and majority of 30-day outcomes, laparoscopic HH/PEH repair with mesh was associated with increased LOS, operative time, and readmission rate. These findings support avoiding mesh repair in laparoscopic HH/PEH.

39. Errors Made by Emergency Medicine Residents During a Simulated Prehospital Pediatric Cardiac Arrest

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Background: Pediatric prehospital drug-dosing errors occur at high rates, with error rates of 60% for epinephrine. PGY 2 and 3 Emergency Medicine residents (EMR) in the XXX residency serve as EMS physicians and respond to all cardiac arrests in XXX County. We sought to determine error rates for weight estimation, epinephrine doses, dose administration mechanics and esophageal intubation (EI) recognition by EMRs at the end of the PGY-1 year, during EMS physician training summative testing.

Methods: Sixteen PGY-1 EMRs were observed during a simulated case: 5-year-old (Laerdal Sim Jr.) with an EMS EI in asystole requiring two doses of epinephrine administered by the EMR. All EMRs had completed PALS. Two observers scored performance. Scenarios were audio and video recorded. Each recording was reviewed by the observers and scoring was discussed. Any disagreements were resolved by consensus. If consensus could not be reached, the item was scored correct. Dosing error was defined as >20% difference from correct dose. Descriptive statistics with confidence intervals (95% CI) were utilized.

Results: All EMRs obtained correct weight with 15 (94%; 72.0%, 99.0%) using length-based tape (LBT) and one (6%; 1.1%, 28.3%) guessing. Four near miss errors occurred with the LBT. Seven (44%; 23.1%, 67.0%) and three (19%; 6.6%, 43.0%) of first and second epinephrine doses respectively, were incorrect. Five (50%) errors occurred using graduations on the preloaded syringe and five (50%) were due to air bubbles in the administration syringe. There were no ten-fold errors. Three (19%; 6.6%, 43.0%) EMRs took 3 attempts to assemble the preloaded syringe, six (38%; 18.5%, 61.4%) did not screw the preloaded syringe together correctly, seven (44%; 23.1%, 67.0%) had difficulty attaching a stopcock to the preloaded syringe and 14 (88%; 64.0%, 96.5%) did not prime the stopcock. One (6%; 1.1%, 28.3%) failed to recognize EI.

Conclusions: PALS-certified PGY-1 EMRs, were accurate estimating patient weight, had a high rate of epinephrine dosing errors and frequent difficulty assembling preloaded syringes. To address these errors, training will be developed that includes a checklist, length-based tape use, weight determination hierarchy, assembling epinephrine preloaded syringes, techniques for appropriate drug dose administration and recognition of EI.

41. Development of Antibacterial Mesh for Abdominal Wall Repair

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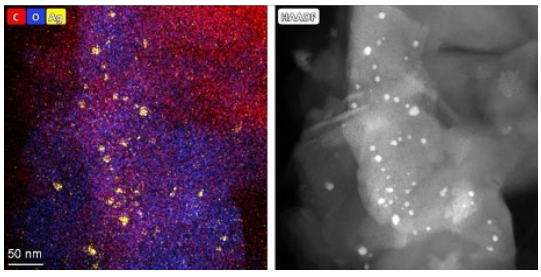
Introduction: Hernia repair is one of the most common operations in general surgery worldwide, and the use of synthetic mesh implants to prevent hernia recurrence have become a standard. However, persistent bacterial infection at the site of mesh implementation and subsequent biofilm formation has presented as a major drawback to the method [1]. In addition, mesh infection is associated with significant costs related to hospital re-admission, re-operations, and recurrences. Various design upgrades to the mesh have aimed to create an effective antibacterial environment at the site of repair. With the same goals, we fabricated a 3D-printed mesh with "smart" antibacterial functionality. The mesh is made by a combination of silver nanoparticles (AgNPs), graphene oxide nanosheets (GO) and biodegradable polycaprolactone (PCL).

Methods: We synthesized Ag-doped GO via solution synthesis using GO, AgNO3, and NaBH4 precursor. GO solution at 1 mg/mL was mixed with10−3 M $AgNO_3$ for 30 min. Subsequently, 10 mL of 3.35×10^{-3} M NaBH4 solution was added under stirring for 1 h. The solution turned dark yellow indicating the reduction in Ag^+ ions and the formation of AgNPs. The synthesized Ag-doped GO nanocomposites were washed and dried at 90°C. Transmission electron microscopy (TEM) combined energy dispersive x-ray spectroscopy (EDS) and dynamic light scattering were used to characterize the size and chemical composition of nanocomposites. For meshes fabrication, PCL at 1, 2 and 10% weight ratio to Ag-doped GO were prepared and printed using melt-electrowriting technology. Mechanical and surface properties were characterized using microscopy and water contact angle.

Results: TEM/EDS analysis showed the successful nucleation of AgNPs on the GO nanosheets. AgNPs were around 6.46 ± 3.4 nm in diameter. Increased amounts of Ag-doped GO (1 and 2%) resulted in higher peak force and tensile strength compared to pure PCL.

Conclusion/Clinical Significance: Nanotechnology-based antibacterial meshes can specifically address drawbacks of local antibiotics therapy administered after infections, as well as issues with antimicrobial coatings and bacterial resistance to antibiotics.

Figure: TEM images and chemical mapping of synthesized Ag-doped GO.



References: [1] Kao AM. et al. (2018) Plast Reconstr Surg. 149S-155S.

47. Altered Amyloid Beta 42 Aggregation in a Cerebrospinal Fluid Mimetic

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Introduction: Protein homeostasis (proteostasis) is essential for cell viability and organismal health. Dysfunction in pathways that control native protein folding, misfolded protein degradation, or removal of toxic protein aggregates can manifest as disease across disparate organ systems. The factors influencing these regulatory events can be both intracellular (intrinsic) or extracellular (extrinsic), and a focus of our research is to understand how these are integrated in the context of neurological diseases, including Alzheimer's disease and amyotrophic lateral sclerosis (ALS). Prior reports and our preliminary results have shown that solution constituents, heavy metals, and lipid substrates can dramatically alter protein aggregation state; however, these components are not routinely tested under conditions representative of the central nervous system. To address this, we evaluated the aggregation of amyloid beta peptide 42 (Aβ42), a component of brain plaques found in Alzheimer's disease patients, in a cerebrospinal fluid mimetic with altered heavy metal, protein, and lipid composition.

Methods: Aβ42 monomer (AnaSpec) was prepared in artificial cerebrospinal fluid (aCSF) and incubated at 37°C without agitation to induce aggregation. Experimental conditions were adjusted through the addition of metal chlorides, including $MnCl_2$, $CdCl_2$, $FeCl_2$, $FeCl_3$, $AlCl_3$, and $CoCl_2$, proteins (human albumin), and lipids substrates (extracellular vesicles) at the time of preparation. Aggregation state was monitored by native gel electrophoresis, thioflavin T fluorescence, and microparticle immunocapture followed by flow cytometry.

Results: Our results indicate that Aβ42 aggregation is influenced by the selection of incubation buffer, and that aCSF promotes aggregation beyond simple salt solutions. Metal chlorides largely promote the formation of higher order oligomers and very high molecular weight fibrils; however, this was not universal across the tested panel. The influence of added protein on Aβ42 aggregation was dependent on both the protein itself and its concentration. Direct comparison of methodologies to evaluate aggregation indicates that some are more accurate than others.

Conclusion/Clinical significance: The influence of cellular extrinsic factors on Aβ42 aggregation and assays thereof are highlighted by our results, and should be considered when evaluating clinical samples and during experimental design and analysis.

Acknowledgments: We would like to acknowledge WMed and NIH for funding support.

68. Findings in Neuropathologic Consultations Initiated for Seizure History

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Introduction: Forensic pathologists retain brains and their coverings for expert neuropathologic consultation for a variety of reasons, including a decedent's reported history of seizures. In the position paper regarding the certification of deaths in persons with epilepsy, the National Association of Medical Examiners (NAME) recommends an "extended" brain examination, ideally by a neuropathologist, following at least two weeks of formalin fixation [1]. A series cited in the aforementioned paper noted that abnormalities were found 7.5 times more frequently in formalin-fixed brains examined by a neuropathologist versus those examined in the fresh state [2]. We investigated the frequency at which contributory findings were noted on formal neuropathologic examination in decedents with a history of seizures.

Methods: The electronic neuropathology database was queried for all cases in which the WMed forensic pathologist indicated "seizure" and/or "epilepsy" as a reason for referral for consultation. The diagnostic lines of all reports were reviewed to determine if potentially contributory gross and/or microscopic findings were documented on examination.

Results: We identified 93 cases in which the brain (+/- dura mater) of a decedent was retained for neuropathologic consultation due to a history of seizures or epilepsy. A potential etiology for seizures was found in 45 cases (48%). Findings included remote contusions, neoplasms, and malformations.

Conclusion: Expert neuropathologic consultation following formalin fixation is recommended by NAME for decedents with a history of seizures, a practice that may be particularly useful when more subtle abnormalities, including medial temporal lobe pathology, are suspected. Others have reported neuropathologic abnormalities in 46% to 71% of epilepsy-related deaths, similar to the frequency found in our study [1]. It is known that decedents with a history of epilepsy, however, may lack neuropathologic findings. Forensic pathologists at WMed do not face some of the logistical challenges of referral that others might, as WMed has an in-house forensic neuropathologist.

References: [1] Middleton O, et al. (2018) NAME position paper: Recommendations for the investigation and certification of deaths in people with epilepsy. Epilepsia, 59(3), 530-543. [2] Black M, Graham DI. (2002) Sudden death in epilepsy. Curr Diagn Pathol, 8(6), 365-72.

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76. Damaged Peripheral Nerves Attenuate Myogenic Differentiation

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Introduction: Peripheral neuropathy can be caused by disease or injury and may result in pain, sensory abnormalities, weakness, and muscle atrophy. There are several treatment options for pain caused by peripheral neuropathy; however, there is a paucity of treatment options for muscle atrophy and functional recovery. This is in part due to our poor understanding of the molecular mechanisms implicated in neurogenic muscle atrophy. Our previous studies suggest that damaged motor neurons play an active role in neurogenic muscle atrophy by producing factors that modulate myogenic differentiation. Here, we build on our previous studies and hypothesize that damaged peripheral nerve axons also contain factors that inhibit myogenic differentiation and may be involved in muscular atrophy. We aim to determine whether damaged peripheral nerves produce factors that (1) inhibit myogenic differentiation and (2) modulate myogenic differentiation gene expression.

Methods: Murine sciatic nerves were harvested and subsequently damaged by crush injury. The damaged nerves were then seeded on differentiating muscle stem cells (MuSCs). MuSC differentiation was evaluated after 24 and 48 hours by visualizing and quantifying myotube formation with immunofluorescent staining of DAPI. Transcriptional changes of MuSC genes (Pax7, Myf5, Sca1) and myogenic progenitor genes (MyoD, Myogenin, MyosinHC) were assessed using qPCR. Protein levels of Pax7 were analyzed by western blot.

Results: Treatment with damaged murine sciatic nerves inhibited myogenic differentiation of MuSCs. Immunofluorescent staining and myotube quantification show that treated MuSCs formed fewer myotubes after 24 hours; this decrease in myotube formation is statistically significant after 48 hours (Figure 1). qPCR analysis revealed that treatment downregulated MuSC genes and upregulated myogenic progenitor genes, compared to control (Figure 2). Western blot analysis revealed that treated MuSCs have decreased Pax7 protein levels compared to control, which correlates with qPCR data. (Figure 3).

Conclusion/Clinical significance: Damaged peripheral nerve axons contain factors that attenuate myogenic differentiation by affecting myogenic cell lineage determination. Our work provides novel insight into a potential mechanism of muscle atrophy following peripheral nerve injury and may reveal new targets to reverse or halt muscle atrophy to improve structural and functional recovery after peripheral nerve damage.

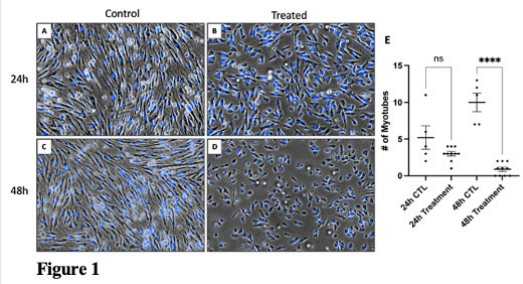

Figure 1

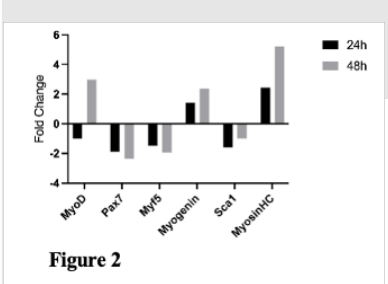

Figure 2

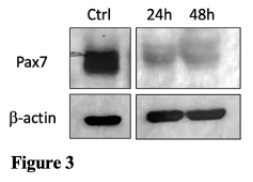

Figure 3

78. B Cell-Derived Natural IgM Maintains Retinal Homeostasis throughout Lifespan

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Introduction: The retina is an out-pocketing of the central nervous system (CNS) that contains neurons, including retinal ganglion cells and photoreceptors, that are responsible for the initiation and propagation of visual processing. Although the retina is immune privileged, lymphocytes may enter retinal tissue under certain circumstances, largely studied in ocular diseases. B cells have been previously identified in human retinal tissue. B-1 cells are a subset of B cells responsible for 80-90% of natural antibody production. Natural antibodies are present in the absence of infection and play an important role in homeostasis as well as in disease and infection prevention. Herein, we sought to better understand the role of natural antibody in the normal physiology of the murine and human eye during aging.

Methods: C57BL/6-*Ighm*^{tm1Che}/J mice are unable to produce the secreted form of IgM. Both male and female mice were used for these experimentations alongside aged-matched wildtype (C57BL/6) controls. Mice are maintained within our vivarium and used at either 3-4 (young) or 18-24 (aged) months of age. Enucleations were performed on euthanized mice. Mouse retinal tissue was isolated and used for flow cytometry, immunohistochemistry, H&E, and RT-qPCR.

Results: Consistent with previously published human reports, we found that B cells (B-1 cells specifically) are present in the murine neural retina compartment. Loss of IgM results in significant retinal degeneration, which is present in both the young and aged but intensified by the aging process. Blood-retina barrier (BRB) compromise is evident in secretory IgM-knockouts, as is supported by extensive multinucleation and vacuolation in the retinal pigment epithelium (RPE). Retinal degeneration is mediated by significant reactive gliosis by Müller glia and increased microglia infiltration. Moreover, loss of IgM is associated with a heightened pro-inflammatory cytokine profile and reduced anti-inflammatory molecules in the retina. These factors combined lead to increased retinal death by apoptosis.

Conclusion/Clinical Significance: Together, these data highlight a critical role for natural IgM in the physiology of healthy retinal preservation previously not described. A better understanding of intraocular maintenance may lead to the development of better therapeutics to support vision during the aging process.

82. Big Five Personality Dimensions in Ultramarathon Runners: Findings of the Ultrarunners Longitudinal TRAcking Study

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Introduction: Ultramarathon runners are described as mentally tough, and have been shown in studies to be goal oriented, and intrinsically motivated. It is otherwise unclear how the personality traits of this group compare to the general population. The purpose of this study is to report the personality traits and motivation for running of this unique patient population in order to help clinicians support their well-being.

Methods: The Ultrarunners Longitudinal TRAcking (ULTRA) Study is a large prospective, longitudinal study of ultramarathon runners. The most recent survey included questions on general health status, running behavior and performance, self-perception of physical and mental health, running motivation, as well as the validated Ten-Item Personality Inventory of the Big Five personality dimensions.

Results: 734 ultramarathon runners completed the inventory. This group exercised a median of 8 hours per week including running a median of 25 miles per week. Ultramarathon runners scored significantly lower in extroversion (3.76 vs 4.44, p<.0001), and agreeableness (5.11 vs 5.23, p=.0099) compared to a control population. They scored higher in conscientiousness (5.93 vs 5.40, p<.0001), and emotional stability (5.28 vs 4.83, p<.0001), while statistically similar in openness to experiences (5.34 vs 5.38, p=0.4174). 87% of ultramarathon runners report that they “agree” or “strongly agree” that they run to improve their physical and mental health. See Figure 1.

Conclusion/Clinical significance: The current findings suggest that ultramarathon runners have relatively low agreeableness (more competitive) and extroversion (able to stay within oneself), combined with relatively high conscientiousness (more organized, goal-directed), and emotional stability (stable in stressful circumstances), compared to a control group. These characteristics may help account for their capacity to withstand the demands of ultramarathon running. This study represents the largest known study of ultrarunners and the Big Five personality dimensions for this group. Appreciating these personality characteristics among this population will assist clinicians in developing interventions to support their well-being.

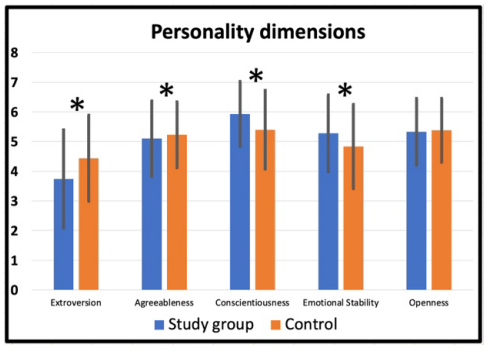

Figure 1: personality dimensions of the study group (blue) compared to control group (orange). Lines denote standard deviation, and * denotes statistically significant difference.

85. miR-200a Attenuates Osteoblasts Activity in Response to Low-Density Lipoproteins

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Introduction: Low-density lipoprotein particles (LDL) are known to cause inflammation within the body and contribute to an increased risk of cardiovascular disease. LDL levels increase with age and are negatively associated with bone marrow density and are correlated with increasing age-related bone loss. However, the signaling pathways involved in the dysregulation of bone metabolism and remodeling are unknown. MicroRNAs (miRNAs) are noncoding small RNAs with 19–23nt length. They can regulate gene expression by binding completely or partially to the 3'UTR of target gene related mRNA for posttranscriptional inhibition. Mir-200a is up-regulated in aged rats and elderly human keratinocytes [1]. We hypothesized that LDL particles inhibit the osteogenic potential of human osteoblasts through the activation of miR-200a.

Methods: LDL was oxidized using the Fenton Reaction. Saos-2 human osteosarcoma cells were cultured with increased concentrations of oxidized-LDL for up to 21 days. Cytotoxicity and proliferation were performed using lactate dehydrogenase, live/dead staining and Alamar Blue assay. Oil-red staining was performed to visualize the "oil-like" droplet formation and Alizarin red staining was performed to visualize calcium deposition. Expression of osteogenic (Osteocalcin, ALP and RUNX-2) and adipogenic (NKX1-2, PPARγ) markers was analyzed via qRT-PCR. Expression of a panel of miRNAs related to osteogenesis was analyzed via qRT-PCR. Statistical difference was determined by paired 2-tailed student's test. $P<0.05$ was considered statistically significant.

Results: Oxidized-LDL particles show an increase in cell proliferation at 12hr, then a decrease in proliferation after 3 days. There is a dose dependent decrease of proliferation starting at 25 µg/mL continuing to 200 µg/mL. At 3 days, LDL-treated osteoblasts show a decrease in osteogenic markers (ALP and osteocalcin), and an increase in adipogenic markers (PPAR-Y and NKX1-2). Oxidized-LDL particles treatment enhanced miR-200a expression which has been shown to inhibit osteogenic differentiation and to accelerate the progression of osteoporosis, while also promoting adipogenesis.

Conclusion/Clinical significance: We propose a novel path provided by oxidized-LDL particles and miR-200a in the connection between osteoporosis and osteoblasts transdifferentitation in elderly population.

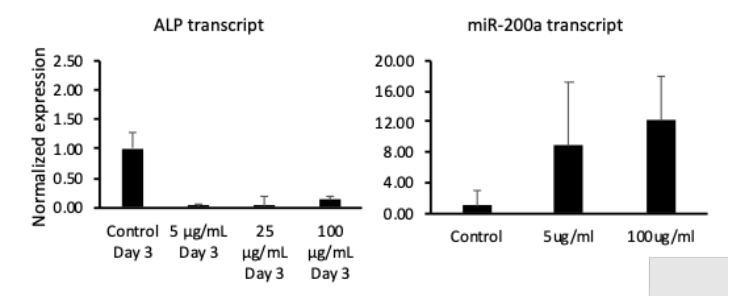

Figure: Expression of ALP and miR-200a 3- and 7-days post-treatment with oxidized LDL.

86. Failures, Modes, and Effects Analysis Exposes Failures in Prenatal Home Visitation Referral for Pregnant Persons

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Introduction: In Kalamazoo County, infants of color are dying at 4 times the rate of White infants; 53% of eligible birthing people get home visitation (HV) referrals and only 13% are enrolled. A Failure, Modes, and Effects Analysis (FMEA- Six Sigma tool) was used to map the current HV prenatal referral processes to identify gaps in the referral processes.

Methods: Researchers conducted two rounds of semi-structured interviews with stakeholders from 6 obstetric clinics (referral-generating) and 5 HV programs (referral-responding). From these interviews, common steps in the clinic-side and HV-side workflows were identified as well as the points of failure. Risk priority numbers (RPN: range 1-1000) for each of the identified failures were calculated- product of their severity, frequency, and detectability, where higher number indicates higher criticality.

Results: The clinical workflow begins with an intake appointment and ends with the patient receiving a curated list of resources or a warm hand-off, depending upon availability of time, and severity of needs. The HV referral process begins with the agency receiving a referral and ends with enrolling the patient into the program.

Multiple fail points were identified in both the processes. High-impact failures on the clinic-side included understaffing on the medical side (RPN 482) and CHWs (RPN 462), navigation burden falling on stressed patients (RPN 464), and lack of follow-up (RPN 427). On the HV-side, failures included inaccurate and missing contact information (RPN 559), insufficient administrative capacity to track referrals (RPN 518), and lack of HV-integration into care pathway (RPN 450).

Conclusion: The iterative quality improvement process will continue with developing and implementing plans to address the critical failures within both systems. This will be followed by generation of another set of RPN. Comparison of pre-, post-RPNs will aid in quantifying the change in the system post implementation thereby ensuring a continuous qualitative improvement of the processes and the system.

Acknowledgments: Special thanks to Stryker Johnston Foundation, Kalamazoo Health & Community Service Department, and United Way of South-Central Michigan, YWCA Kalamazoo, MDHHS, and Michigan Health Endowment Fund.

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87. ROS Separately Modulates Wound Healing and Regeneration Through a Threshold Mechanism

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Introduction: Reactive oxygen species (ROS), such as hydrogen peroxide, are highly conserved, well-established regulators of wound healing and regeneration. Millions are affected each year by inadequate wound healing or the inability to replace damaged tissues, causing non-functional fibrosis in both instances. Despite this healthcare burden, it is still not fully understood how the same ROS-mediated signaling regulates both wound healing and regeneration, further hampering therapeutic development. This study aims to elucidate the role of ROS in each process and identify differential ROS-mediated signaling. For this, we used the highly regenerative planarian model, where we can inflict wounds which only heal (W-wounds) and wounds which lead to stem-cell mediated tissue growth and functional adult regeneration (R-wounds). This ideal system allows us to distinguish the genes downstream of ROS that mediate both processes independently.

Methods: We used pharmacological inhibition of ROS (diphenyliodonium chloride, DPI) to investigate its potential role in wound healing and regeneration. To identify genes mediated by ROS that are injury-induced, wound healing only, or regeneration only, we conducted poly-A enriched bulk RNA-sequencing on decapitated (R-wound) and slit (W-wound) animals and compared differentially expressed genes to those in ROS-inhibited (DPI) decapitated animals (DMSO = vehicle control). Wound healing/regeneration roles of identified candidate genes are being validated by RNA interference.

Results: Our data indicate ROS accumulate at the injury site and are required for cytoskeletal-mediated wound closure and stem-cell directed blastema formation (regeneration). A dose-response assay revealed that threshold levels of ROS control wound healing vs. regenerative outcomes by modulating different downstream signaling targets (*jun-1* in healing and *hsp70* in regeneration). By manipulating ROS levels, we could functionally control repair outcomes: failure to close wounds (low ROS), wound healing only (moderate ROS), or full regeneration (high ROS). Lastly, RNA-seq analyses identified potential ROS-mediated gene expression that distinguishes W-wounds from R-wounds.

Conclusion/Clinical Significance: Our data demonstrate that differential ROS thresholds control injury-induced gene expression programs that result in chronic wounds vs. wound healing and functional tissue restoration. These data highlight that ROS modulation in vivo can potentially be used therapeutically to control wound repair and regeneration mechanisms in multiple contexts.

89. COVID-19 Infection in Ultramarathon Runners: Findings of the Ultrarunner Longitudinal TRAcking Study

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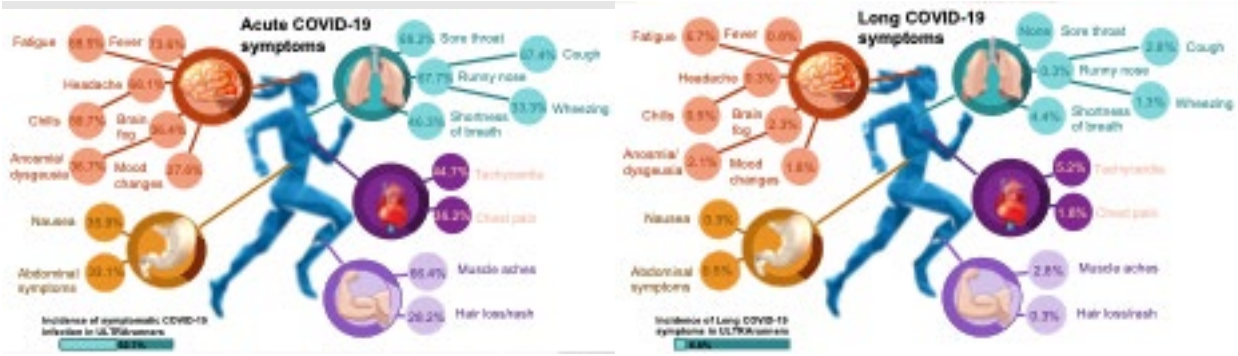
Introduction: Ultramarathon runners are a unique patient population who have been shown to be free of nearly all severe chronic medical conditions. However, the effect of COVID-19 infection on this population and their running behavior is unknown. The purpose of this study is to report the rates and impact of COVID-19 and Long COVID-19 infection on this population.

Methods: The Ultrarunner Longitudinal TRACking (ULTRA) Study is the largest known longitudinal study of ultramarathon runners. Questions on general health status, running behavior and performance, as well as COVID-19 infection were included in this IRB-approved study.

Results: A total of 734 ultramarathon runners participated in the study. This group exercised a median of 8 hours per week, including running a median of 25 miles per week. Of these runners, 52.1% reported ever being symptomatic from a COVID-19 infection, with 6.3% testing positive multiple times. Severe infection occurred in only 0.4% (3 patients), requiring a total of 4 days of hospitalization. Of those who were infected, 83.7% reported being fully vaccinated at the time of their infection. 67.4% of infections affected running for a median of 10 days. The most common symptoms reported were fever (73.6%), fatigue (68.5%), sore throat (68.2%), runny nose (67.7%), and cough (67.4%). Cardiovascular symptoms, which are of particular interest in the running population, included shortness of breath (46.3%), tachycardia (44.7%), chest pain (36.2%), and wheezing (33.3%). Additionally, 50 out of 734 (6.8%) of ultrarunners reported Long COVID (symptoms lasting more than 12 weeks).

Conclusion/Clinical significance: Severe COVID-19 infection is rare in ultramarathon runners, although symptomatic infection that affects running is common. These rates, along with the prevalence of Long COVID, are lower than reported in the literature for the population on average. In order to support the well-being of this group of highly active athletes, clinicians should appreciate that cardiovascular symptoms are common and that the long-term significance of these symptoms in runners remains unknown. Figure 1: Acute COVID-19 and Long COVID-19 symptoms.



92. Comparing Patient Characteristics and Mortality of Gram-Negative versus Gram-Positive Ventilator-Associated Pneumonia

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Background: Ventilator Associated Pneumonia (VAP) is a highly morbid occurrence within critical care units leading to increased ventilator days, ICU days, hospital stay, cost, and mortality. Starting effective empiric treatment early with an appropriate antibiotic regimen is paramount in reducing the impact on patients. Given that VAPs can be caused by both gram-negative (GN) or gram-positive (GP) bacteria, we hypothesized that clinical features of patients differentiate GN from GP VAP and suggest different empiric antimicrobial choices. Furthermore, we hypothesized that patients with GN VAP have a higher mortality overall compared to those with GP VAPs.

Methods: Data were compiled from 1996-2022 from surgical critical care patients treated for CDC-defined, culture positive, monomicrobial VAP. GN and GP VAPs were compared using univariate analysis, and logistic regression including patient age, sex, race, trauma status, transfusion status, APACHE II score, maximum white blood cell count (WBC), maximum temperature (Tmax), days from admission to diagnosis, and era (‘96-‘04, ‘06-‘14, ‘15-‘22) were used to determine predictors of GN versus GP VAP. A second model including similar variables plus GN or GP status was used to define predictors of hospital mortality.

Results: Among 847 VAPs, 602 were GN and 245 GP. Independent predictors of GN VAP included prior transfusion (OR 1.7 [95% CI, 1.1-2.7], $p = 0.013$) and days from admission to diagnosis (OR 1.02 [95% CI, 1.01-1.03], $p < 0.001$), with a C-statistic of 0.65. No difference in crude mortality was found when comparing GN to GP VAP (19.6% v 18.8%, $p = 0.78$). Independent predictors of mortality included age, APACHE II score, non-trauma diagnosis, high WBC, lower temperature, days from admission to diagnosis, shorter duration of therapy, and GP VAP (OR 1.7 [95% CI, 1.0-2.7], $p = 0.013$), with a C-statistic of 0.86. GN VAPs were treated longer than GP VAPs (13.1 ± 9.8 v 11.4 ± 7.8 days, $p = 0.016$).

Conclusion: Clinical characteristics poorly predict GN versus GP VAP and cannot be used to tailor empiric antimicrobial therapy. Although GN VAP is associated with prior transfusion and a longer hospital stay before diagnosis, after controlling for other factors, GP VAP is more deadly.

93. Pain Reduction after Periacetabular Osteotomy in Obese Patients

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Introduction: Periacetabular osteotomy (PAO) is performed to relieve symptomatic acetabular dysplasia by reorienting the acetabulum to provide adequate femoral head coverage. Potential complications include heterotopic ossification, nonunion, malunion, hardware failure, wound dehiscence, and deep infection. Previous investigations have demonstrated increased complications in obese patients (1-5). Some surgeons use obesity as a contraindication for surgery. However, we theorize obese patients will have similar reductions in their pain levels despite an increase in post-operative complications.

Methods: We performed a retrospective review of all patients who underwent a PAO in the last 12 years by the principal investigator to measure the incidence of postoperative complications and change in pain as assessed by the visual analog score (VAS). The incidence of adverse outcomes, defined as hardware failure, nonunion, deep vein thrombosis, reoperation, heterotopic ossification, deep infection, wound dehiscence, or superficial infection, and the change in VAS scores at 6 months follow up were then compared between obese patients and non-obese patients.

Results: 38 hips in 34 patients were analyzed. 13 hips were of obese patients at the time of operation and 25 hips were of non-obese patients. 61% of obese patients experienced a complication compared to 24% of non-obese patients. Obese patients rated their preoperative pain at an average of 5.77/10 (SD= 2.13), and non-obese patients rated their preoperative pain at 5.4/10 (SD= 2.0). Postoperatively, obese patients averaged their pain at an average of 2.31/10 (SD= 2.25); non-obese patients measured their pain at 2.18/10 (SD= 2.17). Obese patients had a mean reduction of 3.46 points in the VAS score (SD= 2.60), and non-obese patients had a mean reduction of 3.25 points in the VAS score (SD= 2.81). The difference between reduction in VAS scores was not significantly different between groups (p= 0.82)

Conclusions: The reduction in pain as measured by the VAS score was not significantly different between obese and non-obese patients despite the increased number of complications. Periacetabular osteotomy in obese patients will provide a significant reduction in patients' acetabular pain and subsequently improve their quality of life.

95. Assess the health of a community collaborative: Cradle Kalamazoo Social Network Analysis

Siobhan West[1], Hunter Burger[1], Daniel Wagner[1], Lauren Patrick[1], Vaishali Patil[1], Nia Evans[1], Oluwasomidoyin Bello[2], Kennedy Clark[3], Komal Razvi[3], Katie Corbit[3], Cathy Kothari[1]
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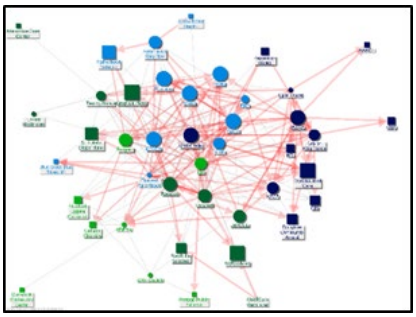
Introduction: Cradle-Kalamazoo is a multi-institutional, multi-sector collaborative working reduce racial disparities and infant mortality rates in Kalamazoo County. The effectiveness of organizational relationships is key. The goal of this study is to identify areas of strength and areas for future growth for the Cradle collaborative.

Methods: Sixty-three Cradle agency representatives completed a mixed-methods survey, combining Social Network Analysis (SNA) and open-ended qualitative questions regarding the Cradle-Kalamazoo collaborative. Node XL software produced network metrics and visualizations. Participants' open-ended responses were consensus-coded into themes and subthemes, before being further categorized into positive, negative, neutral. This analysis was conducted by two independent observers.

Results: As depicted in the SNA network graph, Cradle-Kalamazoo partner agencies are tightly connected (0.5199 graph density). Further, the backbone organizations are centrally located within the map (reflecting their high interrelationship scores) along with hospitals, public health department, doula organization, major funders, and other highly involved community organizations.

The majority (71%) rate Cradle effective, citing various measures of work conducted and/or outcomes improved. Most comments on leadership indicated that there are difficulties stemming from the 2019 transition (identified as top 3 theme, 5 out of 29 comments). Organizations were evenly split between negative and positive comments regarding their experience partnering with Cradle; the most common themes centering on collaboration, leadership, and appreciation. References to collaboration and appreciation were net positive responses while references to leadership were largely negative, serving as a call to action for Cradle leaders.



Conclusion: Similar to other multi-sector, grassroots-led initiatives, Cradle-Kalamazoo faces challenges organizing and aligning partners to tackle the complex, multi-pronged problem of high Black infant mortality. Despite these challenges, Cradle partners form a strong collaborative network that most feel is effective. The primary area for improvement lies in Cradle leadership – which has seen significant structural changes over time. Overall, partner experience within the collaborative have been mixed with a consistent call to action for leadership to provide more clarity. Additionally, the visual of Cradle as a network allowed better understanding of its partnership strengths and areas for opportunity.

100. Weak Magnetic Fields as a Tool to Control Tissue Growth via Reactive Oxygen Species

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Introduction: Accumulation of reactive oxygen species (ROS) regulates cell behaviors and tissue growth across various biological contexts, such as development, regeneration, and cancer. ROS is commonly manipulated pharmacologically, which (while effective) can come with complications such as off-target effects and drug toxicity. Excitingly, advances in quantum biology (and our own research) suggest the use of weak magnetic fields (WMFs, <1 mT) could be a powerful tool to control endogenous ROS levels non-invasively. However, the extant literature on WMF effects in biological systems indicates that changes in exposure field strengths do not follow typical pharmacological dose responses. Here we test hypotheses based on spin state theory and the radical pair mechanism, which outlines how magnetic fields can alter the formation of radical pairs. Our theoretical model suggests WMF exposures should both increase or decrease ROS levels in a binary (switch-like) manner based on the field strength used.

Methods: Custom-designed Helmholtz coils were used to generate WMFs and placed in a mu-Metal enclosure to block external fields. Detection of ROS was done with fluorescent indicator dyes: CM-H2DCFDA (general ROS), Peroxyorange 1 (hydrogen peroxide), and orange 1 (superoxide). Stem cell populations were visualized by in situ hybridization (piwi-1), and proliferation by immunohistochemistry (pH3). Blastema formation (normalized to body size) was quantified at 3 days.

Results: Previously, we demonstrated that some WMF strengths (peak at 200 microT) inhibit injury-induced ROS, reducing stem cell-mediated tissue growth at the wound site. As predicted by the radical pair mechanism, we found that other field strengths (peak at 500 microT) elevated ROS levels, promoting increased tissue regrowth. These data demonstrate WMFs can be used for the directed manipulation of new growth in a predictable, ROS-dependent manner for both loss- and gain-of-function. Furthermore, our results revealed that WMF exposures affect specific ROS, altering superoxide but not hydrogen peroxide levels after injury.

Conclusion/Clinical Significance: Our data reveal that field strength is a critical variable that must be considered when investigating the mechanisms by which WMFs interact with biological systems. These results highlight the potential of using WMFs to develop new and innovative approaches for cancer therapeutics and regenerative medicine.

115. Emotional Awareness and Well-Being Skills in the Clinic: Creating a Wellness Elective for Medical Students in Their Clinical Year

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Introduction: Emotional Awareness and Well-Being Skills in the Clinic is a longitudinal elective designed for the third-year medical student in clinical rotations. This elective is led by fourth-year students and is intended as a safe space for students to process situations they may encounter in clinical settings. The elective consisted of four in-person sessions that emphasized self-awareness, self-regulation, social awareness, and relationship management. Students were required to journal between sessions, read In Shock by Rana Awdish and Atlas of the Heart by Brene Brown, participate in a Balint group, and present a capstone project of their choosing. Reflections and feedback were collected at the end of the course.

Reasoning: This elective sought to fill a knowledge gap in medical student education. Understanding emotions is an important part of medical education for managing aspects of the patient-doctor relationship, retaining empathy, and protecting against burnout [1]. The short-term goal of this elective was to help students navigate challenging emotional terrain during initial clinical experiences while maintaining a sense of well-being, and the long-term goal was to engage students in developing well-being and resilience skills that will serve them throughout their clinical practice. A novel aspect of this training is delivery of the content by near peers, who can provide a unique perspective grounded in recent exposure to the clinic as a medical student.

Conclusion: Reoccurring themes in student reflections and feedback were centered around vulnerability, empathy, healing, and self-awareness. The most prominent theme and identified benefit from this course was finding connection and engaging with peers who are undergoing similar situations. Training in emotional awareness has demonstrated benefits to medical students, including increasing emotional intelligence and preserving empathy during medical education [2]. This elective was a valuable addition to third-year medical student learning and will continue to be a part of the WMed curriculum in the future.

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118. Similar Biomechanics between the Double–Cortical Button and Docking Techniques for Ulnar Collateral Ligament Reconstruction: A Cadaveric Evaluation

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Background: The docking technique is widely used to perform ulnar collateral ligament (UCL) reconstructions because of its high failure torque and reliable clinical outcomes. A double–cortical button technique was recently described, with advantages including the ability to tension the graft at the ulnar and humeral attachments and the creation of single bone tunnels. To compare the biomechanics between the docking and double-button UCL reconstruction techniques using cadaveric specimens. We hypothesized that there would be no difference in postoperative stiffness or maximum strength between the techniques.

Methods: Eight matched pairs of cadaveric elbow joints underwent controlled humeral valgus torsion cycles in a test frame, shown in Fig.1. Toe region stiffness, elastic region stiffness, and maximum torque were measured during a 4-step protocol: intact, injured, reconstructed (10 and 1000 cycles), and ramp to failure. Graft strains were calculated using 3-dimensional motion capture.

Results: After 10 cycles, intact ligaments from the docking and double-button groups exhibited mean ± SD elastic torsional stiffness of 1.60 ± 0.49 and 1.64 ± 0.35 N·m/deg (P = 0.827), while docking (1.10 ± 0.39 N·m/deg) and double-button (1.05 ± 0.29 N·m/deg) reconstructions were lower (P = 0.754). There were no significant differences in maximum torque between the docking (3.45 ± 1.35 N·m) and double-button (3.25 ± 1.31 N·m) groups (P = 0.777). Similarly, differences in maximum graft strains were not significant between the docking (8.1% ± 7.2%) and double-button (5.5% ± 3.1%) groups (P = 0.645). The groups demonstrated similar decreases in these measures after cyclic loading. Ramp-to-failure testing showed no significant differences in ultimate torque between the docking (8.93 ± 3.9 N·m) and double-button (9.56 ± 3.5 N·m) groups (P = 0.739). Results are shown in Fig.2

Conclusion: The biomechanical behavior of the double-button technique was not significantly different from that of the docking technique. Both reconstruction techniques restored joint stability, but neither fully recapitulated preinjury joint stiffness.

Clinical Relevance: With its procedural advantages, results preliminarily support the use of the double-button reconstruction technique for UCL reconstruction as a reliable single-tunnel technique for primary or revision cases.

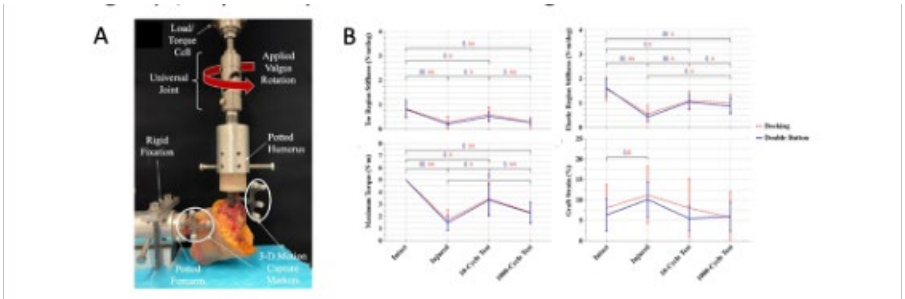

Figure: Photograph of an elbow during mechanical testing.

131. Tracking a Largescale Community Initiative, Cradle-Kalamazoo, Across Phases and Leadership Changes

Lauren Patrick[1], Dan Wagner[1], Oluwasomidoyin Bello[2], Siobhan West[1], Hunter Burger[1], Vaishali Patil[1], Nia Evans[1], Kennedy Clark[3], Komal Razvi[3], Katie Corbit[3], Cathy Kothari[1]
[1]Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. [2]Interdisciplinary Health Sciences, Western Michigan University, Kalamazoo, MI. [3]YWCA, Kalamazoo, MI

Introduction: Cradle Kalamazoo is a collective impact initiative focused on improving maternal-infant health and reducing racial disparities through system-wide multi-sector strategies. Launched in 2014, Cradle began with an awareness campaign, followed by strategic planning and implementation phases, undergoing significant changes in the backbone structure in 2017, 2019 and 2022. This study goal was to document trends in the partnership and performance of Cradle-Kalamazoo as the initiative matured and as the backbone structure evolved.

Methods: This was a prospective longitudinal survey of collective impact dimensions (communication, collaboration, trust and equity) among Cradle-Kalamazoo agency partners, conducted in 2017, 2019, and 2022. We analyzed survey responses of participants (n = 103) from 16 agencies that had completed all surveys across the three study periods. Using 4-point Likert scales, 16 items assessed on communication (5-items), collaboration (4-items), trust and engagement (4-items), and equity (3-items). Geometric means were calculated for each agency, each year. Generalized Estimating Equation (GEE) calculated the trend statistical significance with alpha=.10 (given the low n of 16 agencies).

Results: Overall, across time periods, Cradle consistently rated highest on Communication (89.0% positive ratings), followed by Equity (77.9%), Collaboration (77.3%) and lowest on Engagement/Trust (65.0%). Few items changed significantly over time. The one that changed for the better over time was: “People of different…backgrounds feel respected…” ($p = 0.056$). Those that changed for the worse over time were: “Engaging partners about the challenges and opportunities to improve birth outcomes” ($p = 0.007$), and “Cradle staff are dependable and follow through on promises” ($p = 0.095$). Two-way communication, transparency in decision-making and trust-building are significantly correlated to perception of Cradle effectiveness (from 0.474 r to 0.506 r, $p<0.01$).

Conclusion: Cradle has retained an overall positive impression among its partners, across growth phases and through significant structural changes. Cradle rates highly in communication, and transparency, critical to Cradle's success, while trust-building with partner is an area that needs to be shored up.

IRB number: WMed-2022-0925.

135. Opportunity in Chaos: A Review of Addiction Disorders During the COVID-19 Pandemic

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Background: By nature of illness the addiction disorders lead to many psychosocial problems in most patient's life. Depending on the nature of addiction it can cause many problem-like financial losses, serious medical issues, psychological problems, and downward spiral in every domain of social standing. Additionally, mistrust of the medical community, addiction-related stigma and structural barriers like lacking health insurance produce additional barriers for appropriate treatment and care. With the advent of COVID-19, this population faced additional risk factors most notably unstable housing, decreased access to food and social services.

Method: Literature review conducted using key terms: Harm Reduction, Addiction, COVID-19, Addiction treatment. Over 72 articles were curated. 48 were selected for the final review, rest were excluded because of less relevance to topic of interest. These risk factors also put this population at a higher risk of being infected with COVID-19 and having a problematic course of illness. The patients infected with COVID-19 may leave hospitals against medical advice for a variety of reasons such as seeking unregulated drugs (1), fear of financial consequences or simply due to mistreatment as a result of the stigmatization of their disease process.

Results:

1) Pandemic related Shift in Addiction Patterns: Lockdowns reduced access to safe use sites, needle exchanges, friends to monitor their use, patients reverted to use non-sterile equipment in isolation. (1, 2)

2) Social Patterns of Addiction: Social drinkers were drinking less due to not having the social opportunities. While others changed their drinking to a more isolated consumption that led to significant increase in their consumption. (3, 4)

3) Challenges to Treat COVID-19 in Substance Use Disorder Patients: Mistrust of the medical community, addiction-related stigma and structural barriers led to patients severely sick with COVID-19 leaving hospitals AMA with fear of financial consequences or due to mistreatment and stigmatization. (5)

Conclusion: Prior to the COVID-19 pandemic, we managed substance use disorder primarily with use of punitive measures through the criminal justice system. (10, 11) After pandemic, society started to deny the status quo and have created a wealth of information for researchers, public health officials and lawmakers to learn from.

139. Decreased Reoperation Rate Following Rotator Cuff Repair with Concomitant Biceps Tenodesis

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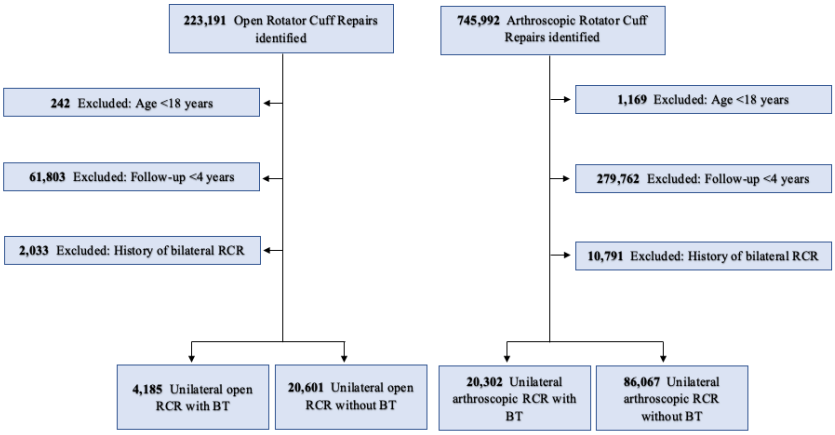
Introduction: Bicep's tendon pathology often exists concomitantly with rotator cuff pathology and both can be a significant source of pain. While the incidence of surgical management for these conditions is increasing, recent literature has suggested a higher reoperation rate in patients undergoing rotator cuff repair (RCR) with biceps tenodesis (BT) compared to patients undergoing RCR without BT. Therefore, the purpose of the study was to compare the reoperation rate between RCR with BT and RCR performed without BT.

Methods: A retrospective cohort analysis was conducted using the PearlDiver database. Current Procedural Terminology (CPT) and laterality-specific International Classification of Diseases (ICD) 10 codes were paired together to identify patients undergoing RCR with BT and RCR performed without BT. Demographic variables (age, gender, and comorbidities contained within the Elixhauser index) and 2- and 4-year reoperation rates were analyzed using X2 and Student T-tests where appropriate. Multivariate analyses were conducted using a logistic regression, controlling for demographics and comorbidities.

Results: We identified 131,115 patients undergoing RCR for our analysis. Of those, 24,487 underwent concomitant BT while 106,668 did not. After controlling for patient comorbidities and demographics, patients who underwent rotator cuff repair with biceps tenodesis were associated with significantly lower odds of requiring a biceps tenodesis reoperation (OR: 0.65; 95% CI: 0.55 – 0.76; p = <0.001) and any reoperation (OR: 0.77; 95% CI: 0.72 - 0.81; p = <0.001) in the ipsilateral shoulder within 4-years of index procedure compared to those who underwent rotator cuff repair without biceps tenodesis.

Conclusion: Contrary to the results of previous studies which suggested higher reoperation rates in patients who underwent RCR with BT when compared to RCR performed without BT, our study suggests a lower reoperation rate for patients undergoing concomitant BT.



POSTER PRESENTATION ABSTRACTS

1. Acute Emergence of Suicidal Thoughts Following Lemborexantinitiation: An Adverse Reaction Case Report

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This case report highlights the side effect of suicidal ideation with lemborexant, a novel agent approved for treatment of insomnia. A 22-year-old man received care at an outpatient psychiatrist for treatment of major depressive disorder, persistent depressive disorder, generalized anxiety disorder, social phobia and insomnia. Following numerous medication trials for depression and insomnia that resulted in partial remission of mood symptoms without improvement in sleep, he was initiated on lemborexant for insomnia. He had denied suicidal ideation when lemborexant was prescribed. The patient took the recommended 5 mg dose at bedtime for insomnia. The patient experienced drowsiness immediately following the dose, and awoke two hours later with new-onset suicidal ideation. The patient was brought to ED, and attempted suicide by hanging in the ED. Laboratory studies showed normal findings including CMP, CBC, TSH, B12 level, and UDS. Differential diagnosis includes acute reaction to insomnia, medication-induced side effect, and major depressive disorder. He completed trials for insomnia with zolpidem, hydroxyzine, quetiapine, nortriptyline, and trazodone before trialing lemborexant. Patient had no history of suicide attempts, but did experience suicidal ideation after trialing nortriptyline. In ED, lemborexant was discontinued and clonazepam was given for insomnia. After resolution of suicidal ideation and improvement in insomnia, he was discharged with outpatient psychiatry follow-up. This case highlights new-onset suicidal ideation with subsequent suicide attempt after use of lemborexant in a patient with major depressive disorder. This case is important given lemborexant is a new medication with limited information about efficacy and safety in major psychiatric disorders.

2. Waxing and Waning of Delirium or Manipulative Behavior?

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Introduction: Delirium is a complex syndrome characterized by disturbances in perception, sensorium, attention, and psychomotor behavior in the context of an underlying medical etiology [1]. A core feature of delirium is its waxing and waning course leading to fluctuation of symptoms. Borderline personality disorder (BPD) is characterized by long-standing, pervasive instability of affect, self-image, relationships, and impulse control [2]. Patients with BPD are often spoken of as being "manipulative" [3]. Both BPD and delirium can present with fluctuations in presentation, impulsivity, and behavioral and mood disturbances. Delirium is frequently misdiagnosed, leading to delays in care. The shared features of BPD and delirium leading to potential misdiagnosis of delirium has not been substantially discussed in the literature.

Case Presentation: In this poster we will discuss two cases where waxing and waning was mistaken for "manipulative" behavior. Evaluation by the psychiatry consult liaison team showed that both patients were experiencing delirium. The change in behavior towards the same staff at different times and between nurses in different shifts was mistaken to be "splitting". Hypervigilance was mistaken for "attention seeking behavior". These assumptions are much easier made in patients with a past diagnosis of psychiatric disorders.

Discussion: Through this poster, we hope to bring to light the healthcare provider stigma towards psychiatric disorders in general and especially borderline personality disorder which could result in under recognition and under treatment of delirium in clinical settings.

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3. Effect of Metronome Use on Medical First Responder Chest Compression Rate During Out-of-Hospital Cardiac Arrest

Michael Samborn, DO[1], Adam Peters, DO[1], Jason Helbig, DO[1], Sakibur Hasan, MS[2], Eric Hovda, DO[1], McKenzie, Titus MD[1], Alex VanWoerkom, DO[1], Joshua Mastenbrook, MD[1]
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Introduction: The American Heart Association recommends providing 100-120 compressions/minute during cardiopulmonary resuscitation. Locally, on-scene physicians have noted that first responders compress outside of this range at times. Manakin studies have demonstrated metronome use results in better compression rate compliance [1]. Many modern automated external defibrillators have a built-in optional metronome and record resuscitation data. In 2021, Kalamazoo County fire department-based Medical First Responder agencies upgraded their automated external defibrillators systemwide from the Philips FR2/FR3 to the Stryker CR2, which has a built-in metronome. We hypothesized that the use of a metronome during out-of-hospital cardiac arrests would improve chest compression rates to within the recommended range.

Methods: Compression rate data were abstracted retrospectively countywide from first responder automated external defibrillators, from the pre-metronome cohort in 2018 and 2019 and from the post-metronome cohort in 2021 and 2022. The average compression rates per arrest were recorded and then coded as either being within the recommended compression range or not. A two-sample proportion test was used to compare the ratio of average compressions within the recommended range between the two cohorts.

Results: Pre-metronome implementation data included 184 cardiac arrests while post-metronome implementation data included 307 cardiac arrests. Pre-metronome average compression rates were within the recommended range in 150/184 (81%) of arrests, as compared with 301/307 (98%) of post-metronome arrests, p-value < 0.01.

Conclusion/Clinical significance: Metronome use during out-of-hospital cardiac arrest resuscitation was associated with a statistically significant improvement in the percentage of cardiac arrests with an average compression rate within the 100-120 compressions/minute range. The authors recommend the continued use of a metronome within the local emergency medical services system during cardiac arrest resuscitation, and propose that further study is necessary involving other prehospital systems to improve generalizability.

References: [1] Kern KB, Stickney RE, Gallison L, Smith RE. Metronome improves compression and ventilation rates during CPR on a manikin in a randomized trial. Resuscitation. 2010; 81(2):206-210. doi:10.1016/j.resuscitation.2009.10.015

4. Don't Get Behind: Adenoma Detection Rates in 40–45-year Olds Undergoing Screening Colonoscopies

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Background: Although colorectal cancer is most frequently diagnosed among 65–74-year-olds, estimates show that 10.5% of new colorectal cancer cases occur in those younger than 50 years of age. In May of 2021, the US Preventative Services Task Force lowered the initial screening age for colon cancer in people of average risk to begin at 45 years old. The adenoma detection rate (ADR) is the proportion of screening colonoscopies performed by a physician that detects at least one histologically confirmed adenoma or adenocarcinoma. The nationally recognized minimum thresholds are 25% overall; 30% in men and 20% in women. Little is known regarding the ADR in ages 45-49. We aim to determine the ADR in patients ages 45-49 undergoing screening colonoscopies and compare this to the national recommended minimums to assure adequate colonoscopy quality in this age group.

Methods: This is a retrospective observational study utilizing the electronic health records in a single institution. Patients between the ages of 45-49 who were seen between 1/1/2022 and 6/20/2022 for a screening colonoscopy were included.

Results: Our study included 299 patients. 113 were found to have at least one histologically confirmed adenoma or adenocarcinoma. The calculated ADR was 37.79%; for males 41.84% and 34.18% for females. ADR by race was 37.1% for white patients [31.08 - 43.11%] and 48% for black patient [28.42 - 67.58%]. Patients with normal BMI had a ADR of 46.64% [32.09-61.24%], the overweight BMI rate was 34.07% [24.33 - 43.08%], and obese BMI rate was 37.89% [30.39-45.38%]. Smoking status revealed ADR of 27.78% in current everyday smokers [13.15 - 42.41%], 31.25% in current some day smokers [8.54-53.96%], 38.64% in former smokers [28.46 - 48.81%] and 40.25% in never smokers [32.63 - 47.87%]. There were no statically significant factors in our patients that predicted a higher chance of having an adenoma discovered on colonoscopy.

Conclusions: The ADR in our study was above the minimum threshold for ages 50-75. Colonoscopy remains an excellent screening tool for early detection of colorectal cancer and the ADR for ages 50-75 can be applied to the 45-49 age group. We may consider raising the expected ADR in this age group with additional data.

IRB: WMed-2022-0937

6. Prothrombin Gene Mutation as a Teaching Tool: An Autobiographical Case Report

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Introduction: This report presents the case of a patient with a heterozygous prothrombin G20210A factor II mutation who developed portal vein thrombosis after laparoscopic cholecystectomy. Only six cases of this rare complication have been reported in the literature, with only one other case associated with the prothrombin G20210A factor II mutation. The case is important to discuss as it presents various complications experienced by the patient due to the mutation and provides insight into strategies used to manage and prevent further complications. Moreover, it highlights the importance of contraception selection in these patients. Estrogen-containing modalities can act synergistically with this mutation to increase the risk of venous thromboembolism.

Case Presentation: The patient is a 47-year-old female with a diagnosed heterozygous prothrombin gene mutation. At 41, she had a slip-and-fall accident followed by an extended road trip. Upon returning home, the patient was diagnosed with deep vein thrombosis (DVT) and bilateral pulmonary emboli. She was treated with warfarin, and oral contraceptives were discontinued. Years later, in September of 2021, she underwent a laparoscopic cholecystectomy. Her surgeon administered low-molecular-weight heparin before the surgery to manage potential thrombosis. Ten days after the procedure, the patient developed a left occlusive portal venous thrombosis and a non-occlusive thrombus in the right portal vein and was treated with unfractionated heparin and long-term anticoagulation with rivaroxaban (Xarelto).

Discussion: Antithrombotic prophylaxis for patients with inherited thrombophilia undergoing surgery is complicated. Guidelines exist for perioperative management of thromboprophylaxis in patients with thrombophilia, but post-operative instructions are lacking. One study examining patients who underwent laparoscopic colorectal surgery showed that continuing anticoagulation postoperatively decreased the risk of venous thromboembolism with no increased risk of bleeding1. This warrants further discussion and investigation of the possible benefits of post-operative thromboprophylaxis in patients with thrombophilia.

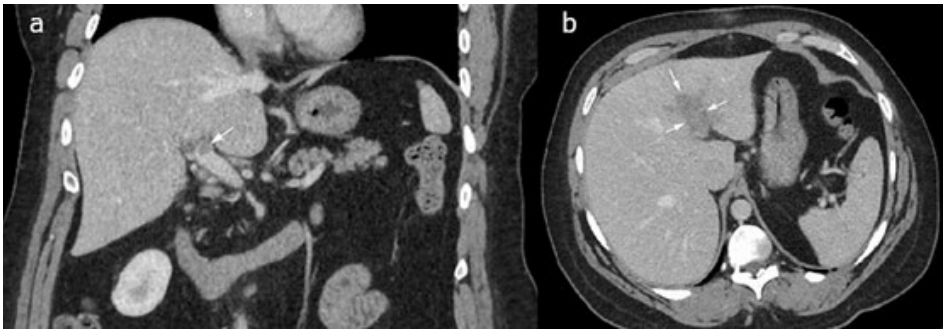

Figure 1: CT scan with contrast at portal venous phase revealed extensive thrombus extending from the main portal vein bifurcation (coronal CT, Figure 1A) into the left portal vein with periportal edema (axial CT, Figure 1B)

7. Identification of Difficult Topics in Medical Gross Anatomy and a Peer-to-Peer Intervention to Increase Confidence and Performance on Practical Exams

Mallory Ruvina, BS[1], Tucker Morris, BA[1], Carolyn Cooper, BS[1], Noelle Fukuda, BS[1], Dan Wagner, BS[1], Hunter Berger, BS[1], Sara Allison, PhD[2], Jade Woodcock, MS[2]
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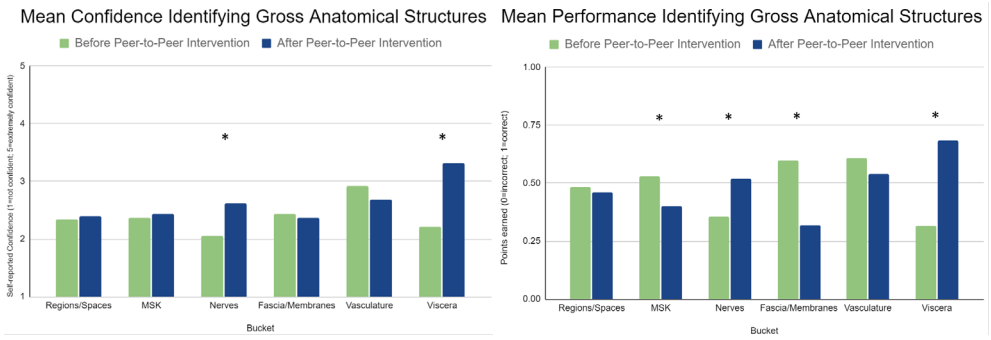
Introduction: Peer-to-peer teaching has a positive impact on medical student confidence and performance in gross anatomy. This study aimed to identify challenging topics in a gastrointestinal (GI) course and use a peer-to-peer intervention to improve confidence and performance in the subsequent endocrine/reproductive (END) course.

Methods: To identify challenging anatomical topics, 30 tagged structures on a GI practical were grouped into six buckets: nerves, vasculature, viscera, musculoskeletal, fascia/membranes, and regions/spaces. During the practical, students were asked to identify each structure and rate their confidence on a numerical scale from 1 (not at all confident) to 5 (extremely confident). MANOVA revealed lower confidence and performance on nerves and viscera. A one-hour peer-to-peer intervention was held on these topics where students worked in groups to identify a pre-selected list of nervous and visceral structures. Students indicated if they attended the intervention during the END practical. Performance and confidence data were collected for each of the items. All procedures were carried out according to the protocol approved by the WMU Homer Stryker MD School of Medicine IRB (IRB 2022-0950).

Results: Forty-two (56%) students participated in the GI practical. MANOVA showed significantly lower confidence in nerves (M = 2.06) and viscera (M = 2.21). Significant differences were also found in performance with students performing significantly worse on nerves (M=35%) and viscera (M = 31%). Fifty-four (72%) students attended the intervention. Forty-three (58%) students completed the END practical, 41 (55%) of which attended the intervention. These 41 students were included in the statistical analysis. Students who attended the intervention improved significantly in both nerve and viscera categories with average performance and confidence increasing to M = 66% and M = 3.25 for viscera and M = 49% and M = 2.53 for nerves. All two-sided p-values were <0.001.

Conclusion: The study found low confidence and performance on nerve and viscera topics in the GI course. A peer-to-peer intervention improved performance and confidence in the END course. Future research should examine student performance on non-mock practicals to further elucidate the impact of peer-to-peer instruction on both confidence and performance. * = p <0.001



10. Barriers to Advancing Population Health from the Perspective of Healthcare Anchor Institutions

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Introduction: United States hospitals are recognizing the importance of addressing social determinants of health (SDOH) that influence the communities they serve. Many institutions overtly pursue "anchor missions" by making a commitment to intentionally apply place-based economic power and human capital in partnership with community. However, little is known about how hospital-community partnerships are developed and implemented or whether they truly impact SDOH and population health. We conducted a qualitative analysis of anchor mission leads from health system members of a national "anchor institution" network to understand barriers and facilitators during implementation of hospital-community partnerships that aim to improve population health.

Methods: We used qualitative analysis of responses to open-ended items on an electronic, cross-sectional survey to explore the ways in which hospitals with anchor missions address SDOH. We administered the survey to the anchor mission leads of healthcare systems participating in the Healthcare Anchor Network (HAN), a national network of hospitals with explicit goals to address SDOH and improve population health. All study activities were reviewed and approved by Northwestern University's Institutional Review Board (#STU00214462).

Results: Responses from 16 organizations were included in this analysis. Two predominant themes emerged: 1) healthcare systems faced many demands, which competed with prioritization of the anchor mission, and 2) engagement of senior leadership was critical for impact of the anchor mission and efforts to address SDOH and population health. Several strategies to engage leadership were identified, such as peer networking and providing repetitive education on community health inequities to hospital leaders.

Conclusion/Clinical significance: Although there is enthusiasm about population health and addressing social determinants generally, even health systems committed to an anchor mission are constrained by competing priorities. These barriers limit the implementation of strategies to address SDOH and the impact these institutions can have on population health. We also found that healthcare system leaders play an essential role in operationalizing anchor missions. It is possible that without external encouragement (in the form of quality metrics, payment incentives, or other policy changes), health systems will continue to have limited engagement with communities and limited ability to address social determinants of health.

11. The Effects of Sedentary Aging and Exercise on Endplate Area and Morphology in Female Rats

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Introduction: Glial cell line-derived neurotrophic factor (GDNF) is an important neurotrophic support factor for the motor nervous system. Previous studies from our laboratory showed that with aging, there was a decline in GDNF content in skeletal muscle and alterations in size and dispersion in motor endplates in male rats. We believe that decline in levels of GDNF concentration may play a role in the increased dispersion in motor endplates. However, little is known about GDNF expression in skeletal muscle and endplate morphology in female rats.

Methods: Previous work in our lab shows that there is an increase of GDNF content in skeletal muscle in female rats during development, followed by a decline with age, but with exercise GDNF content is restored. Because we have seen this relationship between exercise and GDNF concentration in skeletal muscle, we wanted to investigate how aging and exercise are impacting the nervous system by looking at size/dispersion of endplates. We hypothesize that endplate size/dispersion in female rats will remain stable prior to reproductive senescence and decline thereafter, and that exercise will inhibit that decline. To determine if exercise has neuroprotective effects, we took hindlimb skeletal muscle from sedentary and exercised rats between the ages of 4-week to 78-weeks. We stained acetylcholine receptors at the neuromuscular junction with α-Bungarotoxin, viewed slides on Nikon Eclipse E750 confocal microscope, and analyzed the images using ImageJ software.

Results: The average area of endplates significantly increased from 4-weeks (84.132 ± 5.054 μm2) to 52-weeks (362.464 ± 21.955 μm2) with a significant decrease at 78-weeks (269.673 ± 24.270 μm2). There was a decrease in endplate dispersion from 4-weeks (35.75% ± 1.06%) to 78-weeks (5.82% ± 0.71%). Exercise in 78-week female restored dispersion to levels observed in sedentary 52-week female rats.

Conclusion: The morphology and dispersion of the endplates from exercised 78-week females were similar to that of 52-week sedentary females, suggesting that exercise is reversing the negative effect of aging. Exercised 78-week endplate dispersion was significantly higher than that of age-matched sedentary controls, which suggests that there is a negative correlation between endplate dispersion and aging in sedentary female rats, and that exercise can help mitigate those effects.

12. Biomolecular Condensates Defined by Activator of G Protein Signaling 3 Exhibit Distinct Properties and Regulation

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Introduction: Activator of G-protein Signaling 3 (AGS3) is a receptor independent activator of G-protein signaling. AGS3 oscillates among different subcellular compartments in a regulated manner, which is intimately related to the functional diversity of the protein. AGS3 also exhibits an inherent and apparently regulated propensity to form biomolecular condensates (BMCs). BMCs are non-membranous, micron-scale compartments where a specific subset of molecules sequestered from the rest of the cytoplasm and are engaged in a wide range of biological and chemical events within the cell.

Methods: To further address the properties and regulation of AGS3 BMCs, we asked initial questions regarding a) the distribution of AGS3 across the broader BMC landscape with and without cellular stress, and b) the core material properties of these punctate structures.

Results: Cellular stress (arsenate treatment) induced the formation of distinct stress granules and AGS3 BMCs as determined by fluorescent microscopy. In contrast, AGS3 colocalized with processing (P) body BMCs and this colocalization was disrupted by cellular stress with the generation of distinct AGS3 BMCs. Immunoblots of fractionated cell lysates indicated that cellular stress shifted AGS3 to the membrane pellet fraction, whereas the protein markers for stress granule and P-body BMCs remained in the supernatant. These data suggest that AGS3 BMCs may define a distinct type of BMC. To further address this hypothesis, we characterized the AGS3 BMCs by a) analysis of cell lysates under non-reducing gel electrophoresis and b) through examination of AGS3 diffusion dynamics in specific BMCs using fluorescence recovery after photobleaching (FRAP). Stress-induced AGS3 BMCs migrated as higher order structures as determined by immunoblots following non-reducing gel electrophoresis and the stress-induced properties of AGS3 BMCs were reversed by co-expression of the AGS3 binding partner Giα3. Results from a series of FRAP experiments indicated differences in the diffusion dynamics of AGS3 in AGS3-DVL2 BMCs versus stress-induced AGS3 BMCs as well as AGS3 BMCs generated by changes in phosphorylation status.

Results: These data indicate that AGS3 BMCs, the formation of which is regulated by both cellular stress and the signaling proteins Giα3 and DVL2, define a new type of BMC that may serve as previously unappreciated signal processing nodes.

14. Tendon Repair Using Biodegradable and Bioactive 3D Poly (Glycerol Sebacate) Scaffolds

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Introduction: One of the more prevalent clinical complications from sports and daily activities are tendon injuries due to overuse or strain. Tendon injuries can result in pain, reduced quality of life, and disability. Some of the most common tendon injuries are rotator cuff tear, Achilles' tendon tear, lateral epicondylitis, and patellar tendonitis. Tendon tissue engineering with 3D scaffolds has emerged as a promising approach to treating tendon injuries, as the technique allows integration into the host tissue [1]. However, the healing process is complicated due to the lack of cellular orientation which results in poor regenerative capabilities. Indeed, selecting the appropriate biomaterials and fabrication technology for scaffolds remains a challenge. Poly (glycerol sebacate) (PGS), and polycaprolactone (PCL) are biocompatible polymers used in tissue engineering [2]. This study aims to develop a composite scaffold made by PGS/PCL using melt electrowriting for tendon repair.

Methods: We first synthesized PGS using a poly-condensation reaction of glycerol and sebacic acid under nitrogen at 120 °C. PGS was mixed with PCL at 10, 25 and 50% weight ratio and melted in a microwave. Composites were loaded and printed using the Axo-A3 3D bioprinter (Axolotl Bio). Mechanical and wettability of the 3D-printed composites were analyzed. Scaffolds were observed under scanning electron microscope and filament size and distribution were noted. Tenocytes were used to test cell adhesion, proliferation, and orientation.

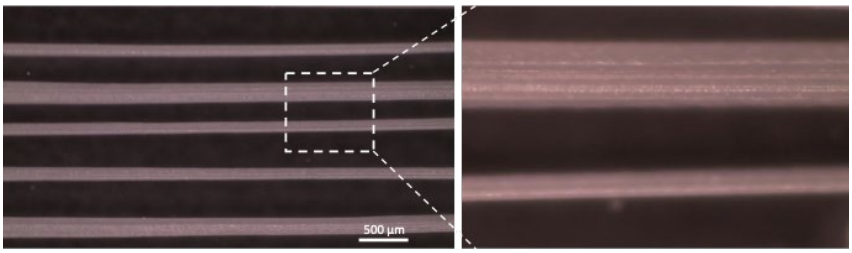

Figure: 3D printed aligned fibers using melt-electrowriting.

Results: PGS was successfully synthesized using a poly-condensation reaction. PGS/PCL well-oriented filaments were successfully printed using melt-electrowriting. The filament size was 30 µm in diameter. Surface wettability and mechanical properties were determined by the percentage of PCL in the scaffold. The fabricated composite is non-cytotoxic and effectively improved tenocytes adhesion and orientation.

Conclusion/Clinical significance: The use of well oriented and elastic PGS/PCL scaffold may provide a more effective and long-lasting solution by promoting the growth of healthy tendon tissue. Improving the effectiveness of the treatment can lead to reduced recovery time and improved outcomes for patients.

References: [1] Kacarevic et al (2019) Int J Artif Organs, 69-86. [2] Luis-Alonso et al. (2020) J Control Release. 2021; 333:448-486.

15. Use of a Checklist and Metronome during Simulated Cardiac Arrest by Medical Students Trained as Medical First Responders.

John Hoyle, MD[1], Neil Hughes, MD[2], Bill Rantz, PhD[3], Maureen Ford, MD[1], Phil Pazderka, MD[1], Judy Wheeler, MPM[1], Bryan Harmer, MA[1], Josh Mastenbrook, MD[1], William Fales, MD[1], Mark Williams[4]

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Introduction: Research has shown the utility of checklist use during a crisis in medicine, including cardiac arrest. The impact of checklist and metronome use by Medical First Responders (MFR) has yet to be studied.

Methods: The first-year medical students at Western Michigan University School of Medicine participating in a MFR course were recruited for this study. 84 students were split into 16 squads of 4-5 students each. Eight squads were trained in the usual fashion according to the national MFR curriculum. Eight received additional training to use a checklist and metronome during cardiac arrest. One month later, the students were presented with a simulated cardiac arrest scenario and their performance was recorded using video recording and Laerdal ALS Manikin LLEAP software. Two study staff recorded performance with a data form. Videos were reviewed and items were scored by consensus. Any items not resolved by consensus were scored as correct. Analyzed metrics included time to defibrillation, compression rate, time to airway interventions and critical item completion.

Results: In the experimental (E) group, the average time to initiate compressions from the start of the simulation was 52.38 seconds vs 40.25 seconds in the control (C) group (P = 0.0.01). The average time to defibrillation was 122.38 seconds and 93.9 seconds in the E and C groups, respectively (p = 0.02). The average time to insertion of an oropharyngeal airway was 84 seconds (E) versus 127.75 seconds (C) (p = 0.16). Both groups transitioned from oral airway to an IGel supraglottic airway in similar timeframes. The average compression rate was 118 (SD 3.62) and 115 (SD 7.36) compressions per minute C and E groups, respectively (p = 0.18). Checklist use resulted in significantly higher rate of critical item completion (OR= 4.12).

Conclusions: The use of a checklist by MFR students during a simulated cardiac arrest resulted in a significant higher rate of critical item completion, good quality basic life support, but with delays to compressions and defibrillation of uncertain clinical significance. Checklist revision to improve time to compressions and defibrillation is indicated.

16. Unusual Lung Morphology Associated with Clinical Diagnosis of "Trapped Lung"

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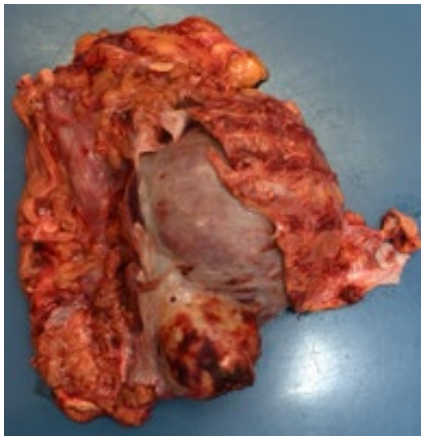
Introduction: Trapped lung is the inability of lung expansion due to a fibrotic pleural layer that restricts normal apposition of the visceral and parietal pleura. This diagnosis has been described in association with various inflammatory sequalae[1] and malignant pleural effusions[2]. We report a case of unusual lung morphology in a decedent with a history of trapped lung and respiratory failure due to COVID-19.

Case Presentation: A 60-year-old male with a past medical history of hypertension, chronic obstructive pulmonary disease, pulmonary hypertension, and illicit drug use was found dead at home. He was previously hospitalized with respiratory failure, during which he was diagnosed with COVID-19 pneumonia/pneumonitis. Chronic right pleural effusion with suspected trapped lung was noted in his records. Complete autopsy revealed a markedly abnormal right lung that was collapsed and atelectatic, with only two apparent lobes and no diaphragmatic surface (Figure 1). The right parietal pleura was thickened, fibrotic, and focally hemorrhagic. The right pleural cavity contained 1000 mL of serous fluid, and the right visceral pleura was focally adherent to the parietal pleura and pericardium. On cut surface, the right pulmonary parenchyma was dense and firm; microscopic examination revealed fibrotic parenchyma with thickened vessels, scattered pigment-laden macrophages, and foci of giant cells containing foreign material and cholesterol clefts. Cause of death was certified as combined toxic effects of methamphetamine and gabapentin, with his natural disease as contributory factors. (IRB: WMed-2023-0998)

Discussion: Trapped lung typically presents with chronic pleural effusion. Chronic atelectasis and restriction of the visceral pleura are two typical causes of trapped lung. A patient may undergo multiple thoracenteses if this condition goes undiagnosed, which can lead to discomfort and worsening of the underlying condition[1]. This case highlights the gross lung abnormalities that may arise with "trapped lung" diagnosis.

Figure 1: Right lung upon removal from pleural cavity, with associated adjacent and adherent soft tissue, including parietal pleura, posterior view.



References: [1] Upadrista P.K. et al. Trapped Lung. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. [ES2] [AF3] [2] Petrov, Danail, et al. "Malignant pleural effusions and trapped lung." AME Medical Journal [Online], 5 (2020).

17. CD39 Expression in the Glioblastoma Microenvironment Does Not Affect T Cell Exhaustion or Survival

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Department of Neurological Surgery, San Francisco, CA

Introduction: Glioblastoma (GBM), the most common malignant brain tumor, is notable for its dysfunctional T-cells. The initial optimism of immune checkpoint inhibitors has been tempered as these agents have not been successful in treating GBM. CD39 is the first enzyme in the breakdown of ATP to adenosine and is highly upregulated in GBM. CD39 is also thought to contribute to T-cell exhaustion [1]. However, inhibiting the CD39 ATP breakdown pathway did not improve survival in mice, even with PD-1 inhibition, leading to uncertainty about whether non-enzymatic functions of CD39 give it a role in T-cell exhaustion in GBM [2].

Methods: We performed intracranial injections of SB28 and GL261 GBM cell lines into CD39 global nulls (KO) and C57BL/6J (WT) mice and measured survival. Another cohort of mice were similarly injected and sacrificed after 2 weeks. These tumors were analyzed for T-cell exhaustion markers using flow cytometry.

Results: There was no survival benefit seen in either cell line when compared to wild type mice. The immune cell profile was not found to be statistically different between KO and WT mice. Next, expression of known exhaustion markers such as PD-1, TIM3, and LAG3 on tumor infiltrating lymphocytes (TILs) were analyzed. Expression of TIM3 and 2B4 were found to be increased in CD39KO TILs compared to WT ($p < 0.01$). Additionally, numerous exhaustion markers such as LAG3, TIGIT, and CTLA4 were decreased on TILs compared to peripheral blood T-cells in tumor-bearing mice ($p < 0.01$).

Conclusion/Clinical significance: These results suggest that CD39 lacks a direct impact on GBM outcomes but may affect the expression of other exhaustion markers. Further studies will continue to investigate the interaction between immune checkpoint molecules in GBM.

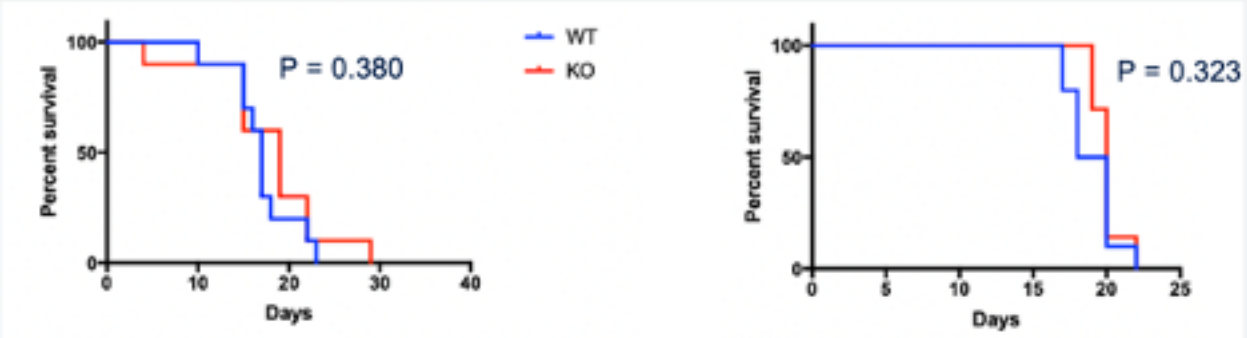

Figure 1: There was no significant difference in survival between CD39KO mice vs C57BL/6J WT mice after intracranial injection of two GBM cell lines: SB28 on the left, and GL261 on the right.

References: [1] Woroniecka et al. (2018) Clinical Cancer Research, 24(17) 4157 – 4186 [2] Ott et al. (2020) JCI insight, 5(17):e134386

18. Violence Against Emergency Medical Services Personnel: Tracking Incidence and Characteristics of Aggression in the Field

Marie Freudenburg, 2nd year Medical Student, Noelle Fukuda, 2nd year Medical Student, Eric Wolatz, Resident, Mallory Ruvina, 2nd year Medical Student, Gillian Erickson, 2nd year Medical Student, Rebecca Kusko, Resident, David Overton, MD, Joshua Mastenbrook, MD
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Introduction: Emergency Medical Services (EMS) personnel experience high levels of violence. Across the US, 69% of EMS survey respondents reported at least one violent incident within 12 months [1]. However, most studies investigating this issue are retrospective with significant recall bias challenges. The authors seek to evaluate the incidence and characteristics of violence faced by paramedics and emergency medical technicians in Kalamazoo County and establish a near real-time data collection system that could be standardized broadly.

Methods: These researchers developed a REDCap survey to gather information including whether a violent incident occurred (verbal, physical, or sexual), incident characteristics, and prior employee de-escalation training. The survey was trialed on a subset of paramedics and feedback was incorporated. IRB approval was obtained prior to launching the survey on March 8, 2023. Data will be stored anonymously on a secure WMed server for 12 months. After each 911 response, providers may access this survey by scanning a QR code, copies of which are found in Pride Care and Life EMS ambulances and stations. A brief informational video was created and distributed via intra-agency communications. Furthermore, EMS providers were informed of a randomized Starbucks gift card give-away among ambulance associates that would occur if survey completion benchmarks are met.

Results: Preliminary data are pending. Participation will be assessed at 3-month intervals by comparing survey completion to the number of 911 emergency scene responses completed in Kalamazoo County by the two ambulance agencies. After 12 months, analysis will provide the incidence of violence and characteristics for these incidents.

Conclusion: Unlike other studies, data will be collected in near real-time by scanning accessible QR codes, limiting retrospective bias. These data could more accurately guide proposed interventions and recommendations for further studies. Furthermore, this model of data collection could be replicated by researchers in other communities.

Acknowledgements: Special thanks to Juli McCarroll with WMed Library Services; Theresa McGoff, Maureen Owens, Christine McNett, Mara Jessup; and the WMed Student-Initiated Research Project Grant.

References: [1] Gormley, M. A. et al (2016). A National Description of Violence toward Emergency Medical Services Personnel. *Prehospital emergency care*, 20(4), 439–447. https://doi.org/10.3109/10903127.2015.1128029

20. Hypoxia-Induced Reprogramming of Breast Cancer Cells

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BACKGROUND: A small fraction of cells inside the solid tumor environment, known as cancer stem cells (CSCs), flourish in the tumor hypoxic environment. Tumorigenesis, growth, progression, and low patient survival are all resulting characteristics of the hypoxic tumor environment. Although little is known about the causes and processes involved in tumor hypoxia, it is known that CSCs formed in this environment are more aggressive, immune-evading, and tumorigenic. We seek to develop an in vitro model of tumor reprogramming with the breast cancer cell line E0771 into CSC using hypoxia stimulation. With this model, we can identify the reprogramming biomarkers, cellular activity, and behavioral alterations resulted from hypoxia treatment.

OBJECTIVE: We aim to determine effects of hypoxia vs. low O2 levels and time ranges on gene expression, proliferation, cell migration, and cell cycling in the E0771 breast cancer cell line.

METHODS: To determine the effects of hypoxia on cellular behavior, E0771 cells were exposed to 1%, 3%, or 5% hypoxia for 12h, 24h, 48h, and 72h. Western blot and qPCR were utilized to measure hypoxia inducible factor (Hif-1α) and Yamanaka factor expression (KLF4, Oct-3/4, SOX2 and c-Myc) to assess reprogramming. We also evaluated the proliferation with MTT and cell migration with a spheroid invasion assay. Epithelial to mesenchymal markers were assessed to verify E0771's metastatic capabilities. Single cell sequencing (scRNAseq) was utilized to demonstrate genome-wide changes associated during hypoxia treatment.

RESULTS: Preliminary data showed that 5% hypoxia treatment significantly increased E0771 cell proliferation by 48h and 72h with MTT (Figure 1). The spheroid invasions assay revealed that 1% hypoxia increased the migratory behavior of E0771 by 48h (Figure 2). Reprogramming evaluation is under investigation, and we expect to obtain data from scRNAseq analysis.

DISSCUSION/CONCLUSION: Our results suggest that hypoxic conditions can promote cellular behavior changes in E0771 cells that may course the reprogramming CSCs as well as increase the tumorigenic potentials.

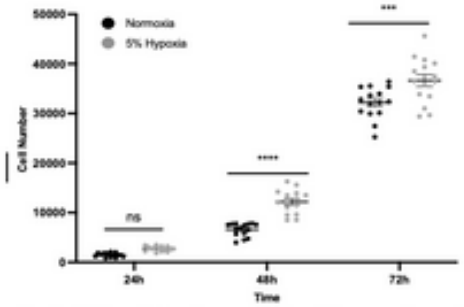

Fig. 1. Cell proliferation analysis with MTT showed increased cell number with 5% hypoxia by 48h and 72h compared to normoxia control (21% O_2). Data represents 3 biological replicates. ns = significant. ***P<0.001.

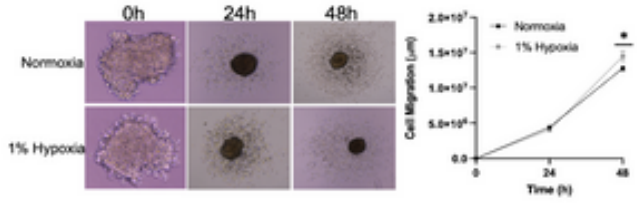

Fig. 2. Spheroid invasion assay with 1% hypoxia treated indicated increased migration in E0771by 48h compared to normoxia control (21% O_2). Data represents 3 biological replicates. **P<0.05.

21. Myogenic and Vasculogenic Responses to Hypoxia in a Novel Coculture Model of Muscle Cells and Endothelial Cells

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Introduction: A key variable promoting tissue growth and survival is angiogenesis. It is well known that hypoxia stimulates cell migration and proliferation (1). The objective of this experiment is to construct an in vitro composite tissue model composed of muscle and endothelial cells. The ability of the combined tissue to survive and develop a circulatory network will then be examined. Our goal is to describe the alterations brought on by hypoxia in a novel co-culture of muscle and endothelial cells.

Methods: C2C12 myoblasts were exposed to hypoxia (5% O2) for 24, 48, or 72 hours, with an ELISA assay to measure VEGF levels. F2 myocytes were incubated in hypoxia or normoxia (20% O2) for 24 and 48 hours, and their media was transferred to plates of human umbilical vein endothelial cells (HUVEC) cells which were incubated with the conditioned F2 media before imaging by light microscopy. For co-culture, F2 myocytes and HUVECs were cultured independently and then combined in a 10:1 ratio respectively; they were incubated in either hypoxia or normoxia before RNA extraction or immunofluorescent imaging. qPCR was performed to measure the expression of the myogenic and vasculogenic markers.

Results: At 0 hours of hypoxia in the C2C12 culture, VEGF concentration was 33.47±.016 pg/ml. This increased to 274.098±0.082 pg/ml at 72 hours (Fig. 1). HUVECs incubated in media from muscle cells exposed to hypoxia showed increased vascular tube formation compared to media from muscle cells in normoxia (Fig. 2). Successful co-culture showed increased proliferation in hypoxia. Upon analysis with qPCR, F2 cells alone in hypoxia significantly increased the expression of MYHC-7 (Fig. 3A), and cocultured F2/HUVEC cells showed increased expression of CD31, HIF-1, Ki-67, MYHC-7, and VEGF (Fig. 3B).

Discussion: There are 2 primary outcomes from our research. First, muscle and endothelial cells are able to be included in a successful culture system in vitro; second, hypoxic preconditioning of co-cultured cells promotes the proliferation of both muscle and endothelial cells, potentially enhancing muscle graft and angiogenesis. Therefore, future in vitro research on muscle compounds can be done using our model system.

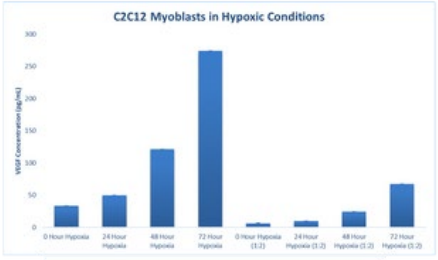

Fig 1. *Muscle cells produce VEGF in hypoxia*

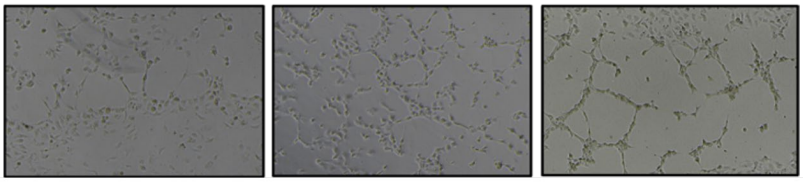

Fig 2. *HUVEC cells form vascular tubes when incubated in hypoxic muscle cell media.* From left to right: HUVEC cells in normoxia media, media from muscle cells exposed to hypoxia for 24h, and media from muscle cells exposed to hypoxia for 48h.

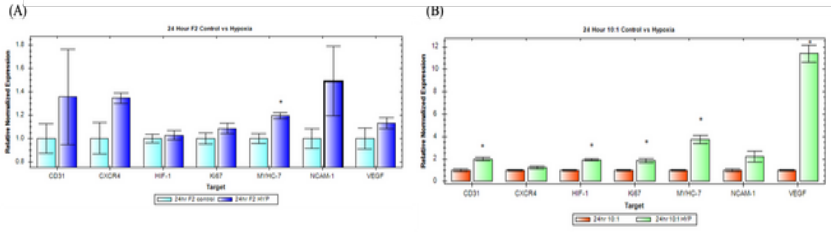

Fig 3. *Identification of co-culture system by qPCR analyses in both hypoxia and normoxia.* (A) F2 cells alone in culture. (B) 10:1 F2:HUVEC cell co-culture. *P < 0.05

23. Retinal Cell Population Differences after Treatment with an α7 Nicotinic Acetylcholine Receptor Agonist Detected by Flow Cytometry

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Introduction: Previous studies from this lab have reported that the selective α7 nicotinic acetylcholine receptor agonist, PNU-282987, induces neurogenesis in the adult mammalian retina. This study was designed to examine changes in different retinal populations as a result of PNU-282987 treatment.

Methods: Male and female 129/SvJ adult wild-type mice were used for this research. Animals were treated bilaterally daily for 7 or 28 days with PBS eyedrops containing 1 mg/mL BrdU and 1 mM PNU-282987 in experimental groups. After treatment, the retinas were removed, cells were isolated and processed for flow cytometry analysis using antibodies against Ki67 and BrdU. The average percentage of each retinal population before and after PNU-282987 treatment was calculated using FlowJo v10 and shown as mean±SD. Averages were compared using a two-tailed unpaired T test with Welch's correction with an n=2 for all experiments.

Results: Thy1.2+ RGCs increased from an average of 15.5% ± 0.35 retinal cells under control conditions to 28.3% after 7 days of treatment, to 34.6% after 28 days of treatment. Similarly, vimentin+ Müller glia cells increased from an average of 5.86% ± 0.08 retinal cells to 23.3% after 7 days of PNU-282987 and to 15.8% after 28 days. PNU-282987 had no significant effect on photoreceptor numbers after 7 days of treatment, but the total percentage of rhodopsin+ photoreceptors significantly increased by 33.4% after 28 days of treatment. In other experiments, Thy1.2+ BrdU+ RGCs increased from an average of 1.72% ± 0.42 cells after 7-days of treatment to 7.73% after 28-days. Thy1.2+ Ki67+ RGCs increased from an average of 3.31% ± 0.21 cells at 7 days of treatment to 5.57% after 28 days. Vimentin+ BrdU+ Müller glia cells increased from 3.40% ± 0.82 total cells at 7-days of treatment to 7.15% at 28-days. The average percentage of vimentin+ Ki67+ Müller glia cells was 10.10%±0.04 of cells after 7 days of treatment compared to 6.56% after 28 days. Rhodopsin+ BrdU+ photoreceptors increased from an average of 3.31% ± 0.06 cells after 7 days treatment to 5.90% after 28 days of treatment.

Conclusion: This study supports the hypothesis that PNU-282987 is capable of inducing neurogenesis in the adult mammalian retina.

24. Efficacy and Safety of 561 nm Laser Pan-Retinal Photocoagulation Treatment for Retinal Vascular Disorders

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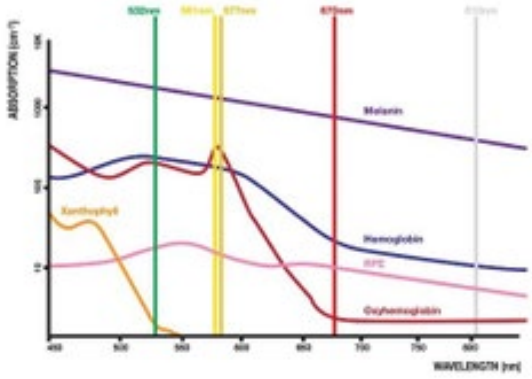
Introduction: Diabetic Retinopathy, a retinal vascular disorder, is a critical complication of diabetes that affects blood vessels in the retina and can cause retinal neovascularization leading to vision damage and blindness. The presence of neovascularization is an indication for treatment with laser photocoagulation. Pan-retinal photocoagulation (PRP) was introduced in the Diabetic Retinopathy Study (DRS) in 1976 as an effective treatment to decrease the risk of severe vision loss in patients with Proliferative Diabetic Retinopathy (PDR) and the use of 532 nm (green) PRP has since been the first-line treatment for PDR. Given the scarcity of literature describing the safety and efficacy of alternative PRP laser wavelengths, this study provides an analysis of the outcomes in patients with retinal ischemia after treatment with a 561 nm (yellow) laser.

Methods: We analyzed 47 eyes from 36 patients suffering from retinal ischemia, secondary to diabetic retinopathy or renal vein occlusion, upon being treated with the yellow laser. The mean age of the patients was 64, and the participant pool consisted of 18 males and 18 females. In addition to the PRP treatment, 36 eyes received intravitreal injections to inhibit retinal vascular proliferation, while 11 did not receive injections. The study was performed by collection and analysis of medical records that documented the treatment given to patients, along with an assessment of the treatment outcomes using the yellow laser.

Results: We considered the measures of visual acuity (VA) after PRP treatment and the occurrence of PRP-related complications during follow-up visits. The improvement in mean decimal VA following yellow PRP treatment was statistically significant with 99% confidence. We observed no adverse effects to patients from the utilization of the yellow laser.

Conclusion: The statistically significant improvement of visual acuity after receiving PRP treatment with yellow laser was consistent with the expected outcomes from using the traditional green laser. In this retrospective study, we have demonstrated the safety and efficacy of the yellow laser in the routine clinical treatment of retinal vascular disorders.

The study protocol was reviewed by Pearl IRB Committee and this study was performed after **IRB approval (#22-LIGH-101).**



25. Thirty-Day Postoperative Outcomes Following Laparoscopic Adrenalectomy for Functional Adrenal Tumors

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Background: Functional adrenal tumors (FATs) are rare, and if left untreated, there is a substantial risk of morbidity and mortality due to uncontrolled excess hormone secretion. The three most common FATs are cortisone-producing tumors (Cushing's syndrome, CUSH), primary hyperaldosteronism (Conn's syndrome, PACS), and pheochromocytoma (PHEO). The study aims to evaluate demographic characteristics and 30-day outcomes after laparoscopic adrenalectomy for FATs.

Methods: Patients who underwent adrenalectomy for FATs were selected from the ACS-NSQIP database (2015-2017). Preoperative demographics/medical comorbidities, and 30-day postoperative outcomes were analyzed using the chi-squared test, ANOVA, and Kruskal-Wallis.

Results: Of a total of 2410 patients who underwent laparoscopic adrenalectomy, 345 (14.3%) patients had FATs, of which PACS was present in 199/345 (57.7%) patients, CUSH in 110/345 (31.9%), and PHEO in 36/345 (10.4%) patients.

Compared to PACS and PHEO groups, patients in the CUSH group were younger (47.8 [± 14.7], vs. 51.6 ± [11.7] vs 53.5 ± [16.1]), had a higher proportion of females ($p<0.001$), had a higher BMI (34.6 ± [7.7] vs 31.0 ± [6.7] vs. 26.0 ± [6.3]), had a higher proportion of DM ($p=0.004$), and had a higher proportion of white ethnicity ($p<0.001$). Compared to CUSH and PHEO, the PACS group had a higher proportion of Black ethnicity ($p<0.001$) and a higher proportion of HTN requiring medication ($p<0.001$).

Thirty-day postoperative outcomes: compared to CUSH and PACS, the PHEO group had a higher rate of serious morbidity ($p<0.001$), overall morbidity ($p<0.001$), and higher readmission rates ($p=0.9$). There were three deaths: 1 in the PHEO and 2 in the CUSH groups. No reported return to OR in any group. Operative time, in minutes, was longer in CUSH compared to PACS and PHEO (157 ± [81] vs. 121 ± [55] vs. 137 ± [70]). Median LOS was higher in CUSH and PHEO compared PACS ($p=0.014$) and ($p<0.001$).

Conclusion(s): FATs show distinct variations in patient demographics. While almost all patients with PACS have HTN, patients with CUSH have higher BMI and diabetes. Patients with pheochromocytomas have higher overall and serious morbidity, especially cardiovascular events. Both CUSH and PHEO have longer LOS. Preoperative optimization is essential.

26. Children of Quarantine: A Post Covid-19 Mental Health Dilemma

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Background: The COVID-19 pandemic has affected the way of living as we have known for all strata of society. While disease containment measures imposed by governmental agencies have been instrumental in controlling the spread of the virus, it has had profound collateral impacts on all populations. However, the disruption caused in the lives of one segment of population has been far more damaging than most others: the emotional wellbeing of our child and adolescent populations. This impact was even more pronounced in children who already suffered from neurodevelopmental or psychiatric disorders. In particular, school closures have not only led to profound social isolation, but also negative impacts on normal developmental opportunities and interruptions in mental health services obtained through school systems. It is too soon to understand the full impacts of quarantine, isolation, stress of social detachment and fear of pandemic, but we have started to see the devastating impact on C&A already. This review intends to shed light on the current understanding of psychiatric wellbeing of C&A during COVID-19 pandemic.

Method: Literature search utilizing key words COVID-19 and children, quarantine and children, social isolation, Loneliness, pandemic stress and children, and mental health of children, disease containment measures was carried out. Over 200 articles were identified, out of which 81 articles were included in this review article.

Results: The disruption caused by COVID-19 in the lives of C&A is much more damaging and its impact is far reaching. The C&A ED visits for possible suicide attempts have jumped to 22.3% in 2020 and 39.1% during 2021. One study utilizing T1-weighted structural images, computed the thickness of cortical and subcortical structures including amygdala, hippocampus, and nucleus accumbens. The Peri-COVID group showed reduced cortical and subcortical thickness and more advanced brain aging compared to pre pandemic studies.

Conclusion: Mental health resources for C&A remain under funded, neglected, and inaccessible to population that needs it most. Children with ongoing mental health disorders were impacted worst, along with those with predisposed biopsychosocial risk factors.

27. First Aid Fanatics: Educating the Girl Scouts of Michigan

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Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

Introduction: Since 2019, Girl Scouts Heart of Michigan has partnered with Western Michigan University Homer Stryker M.D. School of Medicine to host First Aid Fanatics, a medical-student-led program that enables Girl Scouts to earn first aid badges through virtual and in-person education. Despite positive verbal feedback, program efficacy has never been formally evaluated. Multiple studies have shown that teaching first aid to youth leads to longitudinal retention of knowledge and overall positive perceptions of first aid.[1] Further, future career goals are positively impacted when youth are exposed to real-life contexts at earlier ages.[2] Given this impact, it is imperative that First Aid Fanatics is analyzed for its ability to teach retainable first aid knowledge and skills.

Methods: Investigators followed the PDSA model (Plan, Do, Study, Act). The study focused on "Study and Act", as physical implementation of the First Aid Fanatics program had previously been executed. Investigators created a survey targeting first aid knowledge, perceptions of science/healthcare, and educational gaps. Surveys were administered to Girl Scouts, levels Brownies through Ambassadors, following program completion. Investigators analyzed the data to determine the effectiveness of the program.

Results: Preliminary results include a sample size of 64 Girl Scouts. Following program participation, 65.6% of participants felt comfortable calling 911 in an emergency and 81.3% felt confident in their CPR knowledge. Further, 73.4% of participants reported knowing how to use a first aid kit. Of all topics covered, knowledge using an automated external defibrillator and bag-valve-mask were the lowest, with 34.4% and 54.7% of participants feeling confident in their ability to use them, respectively. In regards to interest, 79.7% of participants felt more interested in science after the session while only 34.4% felt more interested in a healthcare career.

Conclusions: This study shows that First Aid Fanatics is effective in educating participants in first aid knowledge and improving interest in science. However, this study highlights gaps in the curriculum, indicating the necessity to improve education to administer a comprehensive first aid program in the future.

References: [1] Reveruzzi B. et al. (2020) J Safety Res.75:32-40 [2] Huang B. et al. (2022) Front Psychol.13:903252 IRB#: WMed-2022-0964

31. Hyperglycemia rather than Hypoglycemia: Beckwith-Wiedemann Syndrome Pediatric Patient with New-Onset Type 1 Diabetes Mellitus (T1DM)

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Introduction: Beckwith-Wiedemann Syndrome (BWS) is the most common overgrowth syndrome with up to 50% of infants found to have hypoglycemia which has been believed to be related to hyperinsulinemia. However, our case report highlights a patient with the unusual presentation of concurrent BWS and T1DM along with the discussion of genetic factors that may contribute to the pathogenesis.

Case Description: We present the case of a 4-year-old African American female with a past medical history of BWS, twin gestation, prematurity, omphalocele, and patent ductus arteriosus. Her BWS had been diagnosed at birth via genetic testing which found a loss of methylation on the maternal chromosome at imprinting center 2 (IC2) on chromosome 11. During her newborn period, she did not have hypoglycemia. She presented with 2.4-kilogram weight loss, new-onset headaches, polyuria, and polydipsia for three months - had a viral respiratory infection one week ago. Her twin sister did not have similar complaints. Her physical exam including vital signs was reassuring. With the concern for diabetes, further work-up showed elevated serum glucose level of 681 mg/dL, and hemoglobin A1C of 12.4%. She was admitted for new-onset diabetes. Further labs on admission also showed elevated transglutaminase IgG and positive glutamic acid decarboxylase 65 (GAD65) antibody (level: 444 nmol/L, normal: =<0.02 nmol/L). Notably, no acidosis was detected in the initial investigations. She was started on a basal-bolus insulin regimen with the diagnosis of new-onset T1DM without ketoacidosis.

Discussion: BWS does not have T1DM as a known characteristic. Hypoglycemia secondary to hyperinsulinemia rather than the opposite, such as our case, is associated with BWS. Due to this, our case is rare, and we found a case report from Europe describing a similar phenomenon. Our patient also had a viral infection prior to the diagnosis of T1DM which may have triggered autoimmunity. Further, IC2 loss of methylation present in our patient regulates the expression of CDKN1C which has been previously reported to be associated with diabetes. Further studies will be required to identify the possible case of T1DM in a patient with BWS.

32. Gender Differences in Biomarkers and the Effects of Cannabinoids in Psychotic Illnesses: a Review of the Literature

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Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

Introduction: Gender has long been understood to influence the rates and presentations of psychiatric disorders including psychotic disorders. Contemporary research has investigated linkages to biomarkers and endogenous hormones as well as use of exogenous substances, including cannabinoids. Our review aims to evaluate the results of studies focused on these topics.

Methods: We performed a review of the psychiatric literature from 2017 to 2022 in the PubMed database using the search strings “Gender differences psychosis” and “Gender differences psychotic symptoms”, with inclusion criteria of (i) English-language peer-reviewed publications; (ii) that examined gender or sex differences in psychosis-spectrum illnesses as defined by the DSM-5; (iii) where the gender or sex difference was analyzed and discussed as a focus of the paper. We used cross-referencing to identify additional studies fulfilling inclusion criteria. We excluded all articles that were not: randomized clinical trials, meta-analyses, or review articles.

Results: Prolactin levels are higher in first-episode psychosis patients compared to non-psychotic individuals. First-episode psychosis in women results in higher prolactin levels than men. Prolactin appears to have a protective effect on females, but a deleterious effect on male cognition. Male childhood-onset schizophrenia patients have increased likelihood of carrying X-linked gene variants compared to unaffected fathers. Aberrant connectivity in schizophrenia is left-lateralized in males, particularly to Broca’s area, compared to right-lateralization in females, especially the orbital-frontal center. There is decreased white matter volume in the left cingulate gyrus in males with schizophrenia compared to females. Brain derived neurotrophic factor (BDNF) levels are elevated in female patients with schizophrenia compared to controls or males with schizophrenia. Cannabis use correlates with decreased level of function in males but increased functionality in females. There is no significant gender difference in age of onset of cannabis use. There is disagreement about whether earlier onset of cannabis use correlates with earlier age of onset of psychotic symptoms in females.

Conclusion: Neuroanatomical differences, genetic variants, and hormone levels vary significantly by gender in individuals with psychotic illnesses. Gendered impact of cannabis use on schizophrenia onset remains controversial. Further research is needed to explore whether these differences correlate with presentation or treatment response.

33. Mitochondria as a Key Player in Stress-Induced Tolerance of Muscle Stem Cells

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Introduction: Cell transplantation has tremendous potential as a therapeutic in cases of extensive damage to skeletal muscle tissue as well as muscle related disorders such as muscular dystrophy. Success of the treatment is conditioned by the ability of muscle stem cells (MuSC) to resist rejection at the implantation site. Hypoxic or Cobalt chloride (CoCL2) pretreatment of stem cells can trigger an adaptive response called hypoxia-induced tolerance, which markedly increases the ability of these cells to survive and regenerate in the host environment, leading to enhanced therapeutic effects in muscle regeneration. This likely is due to up-regulation of hypoxia-inducible factor-1alpha (HIF-1α) which promotes angiogenesis, and changes mitochondrial oxidative metabolism. Furthermore, mitochondria play a key role in cellular responses to internal and external stressors. Our hypothesis is that mitochondria play a key role during tolerance induction of MuSCs.

Methods: For this proposal we used the established C2C12 myoblast cell line and mouse MuSCs as an in-vitro model system, and induced cellular stress by culturing cells under hypoxic conditions (5% oxygen, compared to normoxia at 21% oxygen) or CoCL2 treatment. Cells were harvest at 12, 24 and 48 hours for protein analysis. Western blot was performed using antibodies against mitochondrial pro-survival proteins X-linked Inhibitors of Apoptosis Protein (XIAP), B-cell lymphoma 2 (Bcl-2) family and mitochondrial Oxidative phosphorylation (OXPHOS) complex proteins.

Results: XIAP expression increased during 48hrs of hypoxia treatment, whereas Bcl-2 expression peaked at 12h. Similarly, CoCl2 stimulation led to the expression of XIAP and Bcl-2. Interestingly lower levels of mitochondrial complex I, II, and III protein were detected in the C2C12 myoblasts, indicating an altered mitochondrial respiration in hypoxia-induced tolerance.

Conclusion/Clinical significance: Hypoxia treatment increases XIAP and Bcl-2 protein, while reducing mitochondrial respiration in muscle cells in vitro. Our results suggest that XIAP, probably through Bcl-2, prevents apoptosis and could promote survival, possibly by avoiding over-production of reactive oxygen species. Identifying the mechanism underlying induction of cellular tolerance in MuSCs will have great significance and application in cell therapies aimed at treating muscle dystrophy disorders.

36. Gender Differences in Presentation, Outcome, Social Functioning, and Trauma Experiences in Psychotic Illnesses: a Review of the Literature

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Introduction: Gender differences are known to exist in the rates and typical presentation of psychotic disorders. Recent trends in this literature include how gender impacts prodromal timeline, initial presentation, treatment outcomes and side effects, social outcomes, and the influence of trauma experiences on psychosis.

Methods: Using the Pubmed database, we performed a review of the psychiatric literature from 2017 to 2022 using the search strings "Gender differences psychosis" and "Gender differences psychotic symptoms". The inclusion criteria included (i) English-language peer-reviewed publications; (ii) that examined gender or sex differences in psychosis-spectrum illnesses as defined by the DSM-5; (iii) where the gender or sex difference was analyzed and discussed as a focus of the paper.

Results: When looking at the effects of gender on prodrome, there is evidence that an earlier age of onset in males correlates with longer duration of untreated psychosis and poorer long-term outcomes. However, disagreement exists on whether there is a greater incidence of depressive symptoms, disorganized communication, or loss of baseline function between genders. The influence of traumatic life experiences on the course of psychotic disorders has been shown to increase the severity of psychotic symptoms in both men and women, but has been shown to cause an earlier onset in women only. With regards to treatment outcomes, women appear more responsive to antipsychotic medications, requiring lower dosages for efficacy, but carry a higher adverse effect burden. A notable exception may exist with tardive dyskinesia perhaps being more prevalent in males. Differences in mental health outcomes between men and women favor women as measured by reduced number and length of psychiatric hospitalizations, but when measured by cognitive functioning over the long term, this difference is not sustained. With social outcome measures such as relationship engagement, educational attainment, and employment, females tend to fare better than males.

Conclusions: The impact that gender plays on various aspects of psychotic disorders is a continually evolving field. Continued effort to disentangle these differences can lead to more individualized care and perhaps improved outcomes. Studies evaluating sex and gender identity separately are needed.

39. Errors Made by Emergency Medicine Residents during a Simulated Prehospital Pediatric Cardiac Arrest

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Background: Pediatric prehospital drug-dosing errors occur at high rates, with error rates of 60% for epinephrine. PGY 2 and 3 Emergency Medicine residents (EMR) in the XXX residency serve as EMS physicians and respond to all cardiac arrests in XXX County. We sought to determine error rates for weight estimation, epinephrine doses, dose administration mechanics and esophageal intubation (EI) recognition by EMRs at the end of the PGY-1 year, during EMS physician training summative testing.

Methods: Sixteen PGY-1 EMRs were observed during a simulated case: 5-year-old (Laerdal Sim Jr.) with an EMS EI in asystole requiring two doses of epinephrine administered by the EMR. All EMRs had completed PALS. Two observers scored performance. Scenarios were audio and video recorded. Each recording was reviewed by the observers and scoring was discussed. Any disagreements were resolved by consensus. If consensus could not be reached, the item was scored correct. Dosing error was defined as >20% difference from correct dose. Descriptive statistics with confidence intervals (95% CI) were utilized.

Results: All EMRs obtained correct weight with 15 (94%; 72.0%, 99.0%) using length-based tape (LBT) and one (6%; 1.1%, 28.3%) guessing. Four near miss errors occurred with the LBT. Seven (44%; 23.1%, 67.0%) and three (19%; 6.6%, 43.0%) of first and second epinephrine doses respectively, were incorrect. Five (50%) errors occurred using graduations on the preloaded syringe and five (50%) were due to air bubbles in the administration syringe. There were no ten-fold errors. Three (19%; 6.6%, 43.0%) EMRs took 3 attempts to assemble the preloaded syringe, six (38%; 18.5%, 61.4%) did not screw the preloaded syringe together correctly, seven (44%; 23.1%, 67.0%) had difficulty attaching a stopcock to the preloaded syringe and 14 (88%; 64.0%, 96.5%) did not prime the stopcock. One (6%; 1.1%, 28.3%) failed to recognize EI.

Conclusions: PALS-certified PGY-1 EMRs, were accurate estimating patient weight, had a high rate of epinephrine dosing errors and frequent difficulty assembling preloaded syringes. To address these errors, training will be developed that includes a checklist, length-based tape use, weight determination hierarchy, assembling epinephrine preloaded syringes, techniques for appropriate drug dose administration and recognition of EI.

40. Autologous Blood Clots Improve Wound Healing

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BACKGROUND: The use of biomaterials as a delivery system for skin wounds has great potential for enhancing tissue repair and regeneration. However, current delivery systems aim for individualized treatments and lack versatility in wound healing applications. A composite system capable of precise release of factors to treat a wide variety of skin wounds has yet to be found. We will investigate the use of autologous blood clots as a vehicle for delivery for wound healing. With composited blood clots with antibiotics and mesenchymal stem cells, we aim to prevent infection and improve skin wound healing.

OBJECTIVE: We aim to determine whether an autologous blood clot is an effective vehicle of delivery for preventing infection and improving skin wound healing.

METHODS: To determine maintenance time of antibiotics in blood clots (BCs) and their toxic potential to host stem cells, murine mesenchymal cells were treated with vancomycin and gentamicin of concentrations up to 5.0mg/mL. The duration of antimicrobial activity of the composited BC were also monitored. To evaluate the progression of wound healing, levels of VEGF were measured by ELISA.

RESULTS: The results showed no toxicity of vancomycin and gentamicin to pig and murine mesenchymal cells within a one-week duration in the BCs. Composited murine and pig BCs were also found to functionally prevent bacterial growth for up to 7 days with increasing levels of VEGF measured for more than 7 days in vitro.

CONCLUSION: Our results suggest that the use of autologous blood clots as a delivery system could be an effective and easy method to deliver antibiotics and possibly other drugs to prevent infection and accelerate healing of skin wounds.

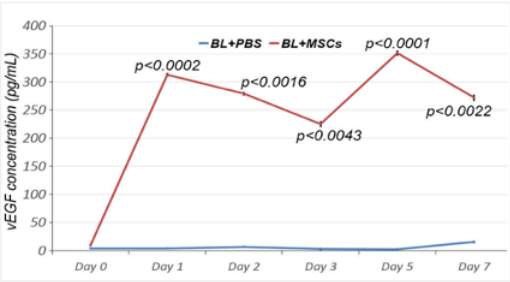

Fig 2. The vEGF release from the blood clot compounds by using ELISA tests. Our results suggested that the clots compounded with murine MSCs release consistently higher vEGF over more than seven days in vitro.

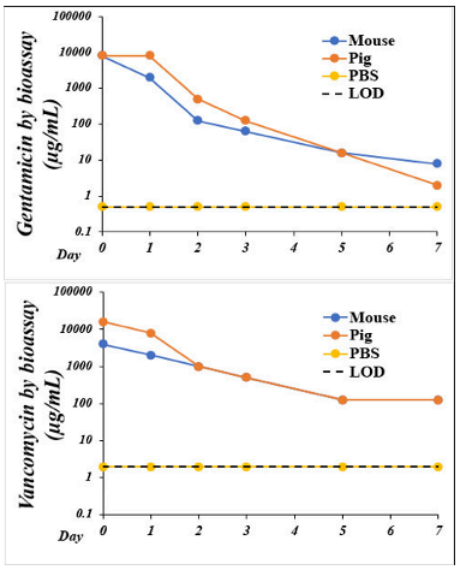

Fig 1. The released antibiotics from the conjugated blood clots for up to 7 days from composited murine (blue) and pig (red) blood clots.

42. Visualization of DNA G-Quadruplex Structures and PKD1 in Human Kidney Cells and Polycystic Kidney Disease

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Introduction: Polycystic kidney disease (PKD) is one of the most common inherited genetic disorders. It causes fluid filled cyst to form in the kidneys that ultimately lead to impaired kidney function and kidney failure. Autosomal dominant PKD (ADPKD) is the most common form and is largely due to genetic inactivation of the PKD1 gene (~85% of cases). At least 10-15% of patients with ADPKD have no family history, suggesting a high rate of de novo mutations at this locus. Our bioinformatic analysis of the human PKD1 gene revealed widespread sequence motifs capable of forming four-stranded structures known as G-quadruplex (G4 DNA). This alternative DNA conformation is known to promote site specific genetic instability. Therefore, the goal of this project was to visualize G4 DNA in human kidney cells and test the model that G4 DNA forms at the PKD1 locus. Our hypothesis is that G4 structures within PKD1 lead to do novo mutations that could lead to gene inactivation and cyst development.

Methods: Immunofluorescence microscopy was performed on human embryonic kidney (HEK293) cells, as well as normal kidney tissue sections and kidney tissue from patients with PKD using a monoclonal antibody against PKD1 and a G4-antibody raised against G4 DNA structures. G4-stabilizing compounds were also assayed in cultured kidney cells to determine if G4 formation within PKD1 impacts gene expression.

Results: G4 DNA was visualized within human kidney cell nuclei, and qPCR results indicate that G4 formation decreases PKD1 mRNA levels.

Conclusion/Clinical significance: Our data support the model that DNA quadruplexes form within PKD1 and in human kidney cells, which provides a molecular rationale for the high rate of genetic instability at the PKD1 locus.

43. The Effects of Immune Modulation on the Recovery Rate of Zebrafish Olfactory Glomeruli after Deafferentation

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Introduction: Brain damage has devastating consequences in humans who have experienced injury or disease. Full recovery after neuronal damage is elusive for many organisms partially due to limited neurogenesis in adulthood. Zebrafish, however, are renowned for persistent neurogenesis and neuroplasticity. Chemical lesions damage sensory neurons in the olfactory epithelium and disrupt neuronal organization in the olfactory bulb, but recovery occurs in about one week. Although the brain's primary immune cells, phagocytic microglia, are active in pro- and anti-inflammatory functions, their role in zebrafish injury response and neuroplasticity is unclear. Modulating microglial populations with L-clodronate, a drug that specifically targets phagocytic cells for apoptosis, illustrates the contribution of these cells on recovery rate. Comparing morphology of three neuronal structures (glomeruli) in the olfactory bulb from treated and untreated fish over recovery time will help characterize the role of microglia in neuroplasticity.

Methods: Detergent was applied to the right olfactory epithelium to damage sensory neurons, preserving the left side as an internal control. Treated fish received L-clodronate injections in the brain 12 and 24 hours prior to lesioning and baseline fish were lesioned without immune modulation. Glomerular structures were visualized in whole brains with confocal microscopy using antibody-labeled sensory axons. Glomerular structures were assessed 4 hours to 7 days post-lesioning for level of damage and compared to control tissues.

Results: Previous work demonstrated full recovery of lesioned fish in 7 days. A delayed recovery after reducing microglial populations was expected; however, clodronate-treated fish appeared to recover morphology in all three glomerular structures by 4 days, significantly faster than baseline. It is unclear if drug mechanism or injection timing affected the rate, thus future projects will include additional pre-treatment, concurrent treatment, and immune-stimulating treatment groups.

Conclusion/Clinical significance: The activity of microglia after neuronal damage can vary dramatically during recovery. As Covid-19 infections have demonstrated, macrophage activation can result in a "cytokine storm" of hyperinflammation or in viral clearance. Zebrafish is a model system that can demonstrate how conserved immune system features promote complete recovery in the nervous system of adult mammals, leading to potential treatments for brain injury and disease.

44. Common Elements of Motor Vehicle Homicide and Suicide in Southwest Michigan: A Retrospective Case Series

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Western Michigan University Homer Stryker M.D. School of Medicine, Department of Pathology, Kalamazoo, MI

Introduction: Retrospective studies estimate that suicidal behaviors underlie approximately 2% of all motor vehicle accidents, and that the phenomenon is likely under-reported [1]. Despite the high prevalence of motor vehicle accidents precipitated by suicidal and or homicidal intent, a dearth of these cases has been reported in existing forensic pathology literature. This relative lack of literature may stem from the difficulties in assessing intentionality upon autopsy of victims involved in motor vehicle fatalities. In order to facilitate more efficient and accurate recognition of intentionality in motor vehicle fatalities, this case series identifies unique and shared features of 18 vehicular suicides and 4 vehicular homicides that occurred in Southwest Michigan between 2011 and 2023.

Case Presentation: Eighteen18 cases of vehicular suicide and four4 cases of vehicular homicide were identified by the using Michigan's Medicolegal Death Investigation Logthe Medical Examiner's Office using their web-based case management system of all reported deaths. In each case, an autopsy was conducted, and the manner of death was determined to be either suicide or homicide. Further analysis of each case reveals that shared features are often present in cases of vehicular suicide and vehicular homicide. Victims of suicide involving a motor vehicle frequently experience acute stressors leading up to the incident, leave a record of electronic communication, and present with psychiatric comorbidities and/ or a history of substance abuse. On the other hand, victims of vehicular homicide tend to be in the driver's seat at the time of the incident and present with documented histories of interpersonal conflict with the perpetrator.

Discussion: Given the relative dearth of literature, forensic pathologists may experience difficulties in ascertaining intentionality in cases of suicide and homicide involving a motor vehicle. To facilitate more accurate and efficient assessment in such instances, this case series discusses both common and unique features of eighteen 18 vehicular suicides and four 4 vehicular homicides across Southwest Michigan between 2011 and 2023.

48. Atypical Coronary Artery Disease: An Easily Missed Diagnosis

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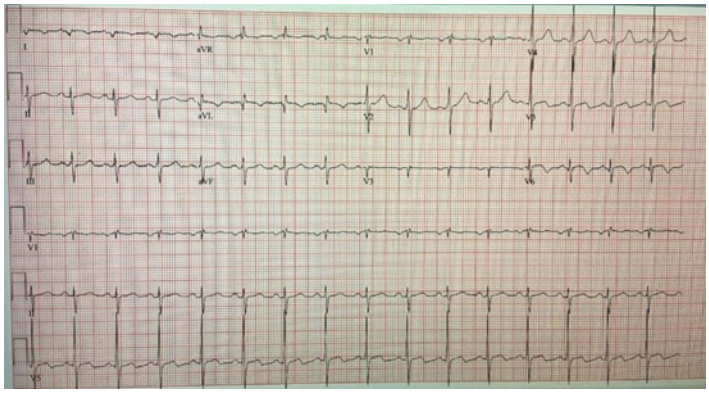
Acute coronary syndrome is a common differential diagnosis seen in the emergency department with complaints of chest pain. Less common is the diagnosis considered with abdominal complaints where acid reflux, cholecystitis, pancreatitis, and diverticulitis are higher on the differential [1]. Despite this, acute coronary syndrome can present with a myriad of symptoms other than chest pain and are categorized as atypical. Examples of atypical presentations include back pain, dyspnea, or epigastric abdominal pain and are seen more frequently in elderly females [2]. Here we report 60-year-old African American women who presents to the emergency department with burning epigastric abdominal pain. Initial triage placed the patient into an abdominal pain workup. Subsequent lab work prior to evaluation were unremarkable which include basic labs and urinalysis. Upon initial evaluation, cardiac workup was initiated due to patient prior history of coronary artery disease with last testing performed one decade prior. Initial ECG showed T wave inversions and biphasic T waves in lateral lead with initial troponin critically elevated. Patient was admitted to the hospital as a non-ST segment elevation myocardial infarction where a greater than 95% occlusion of the mid ramus treated with drug eluted stent placement. Over the subsequent day, patient was noted to have shortness of breath with subsequent ECG showing ST elevations in anterolateral leads considered to be reperfusion injury. Echocardiogram was performed showing a decreased ejection fraction from 55% to 35-40%. Patient was given Lasix with improvement in symptoms and discharge the following day. This case portrays the importance of including acute coronary syndrome in the differential diagnosis of multiple complaints besides chest pain. Although atypical symptoms are less common, it stills presents the opportunity to avoid major adverse cardiac events if caught early in disease progression. Further research is required to fully understand the full scope of atypical acute coronary syndrome including correlation with specific vessel of occlusion such as mid ramus occlusions versus multi-vessels occlusions.



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49. Impact of Mask Usage on Rates of Non-COVID Pneumonia

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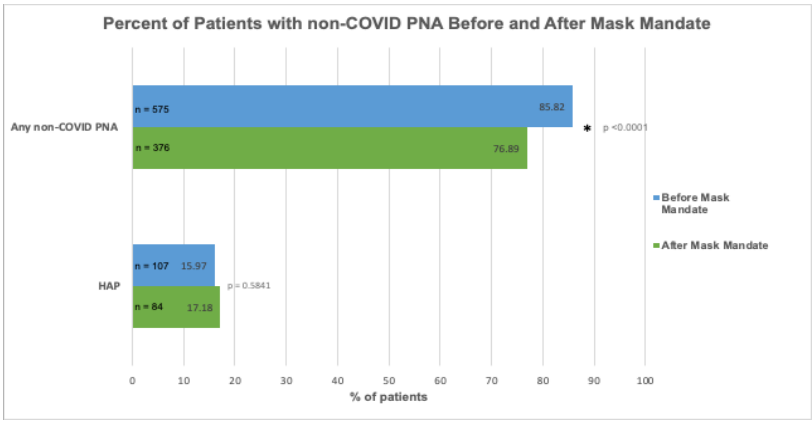
Introduction: The consensus in the scientific community is that face masks help slow the spread of COVID-19, and they may play a role in reducing the transmission of other airborne infectious diseases. Despite this, prior studies have shown that mask usage does not have a significant impact on the spread of other types of infections. This study focused on the impact of mask usage on the rates of non-COVID pneumonia hospitalization in the early months of the mask mandate. Community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP) rates were examined, both of which are associated with high morbidity and mortality rates, particularly in the elderly.

Methods: A retrospective cohort study was performed using patient data from Ascension Borgess Medical Center (BMC; Kalamazoo, MI) between March 15, 2020 and September 15, 2020, as well as from the same period in 2019, who were admitted with an ICD-10 code for any pneumonia. Demographic data along with medical history and hospital course were collected. A chi-square test was employed to determine if the frequency of HAP differed pre- and post-mask mandate. The frequency of non-COVID pneumonia of any etiology and Ventilator-Acquired Pneumonia (VAP) were also compared.

Results: 1159 patient records were included. Of these, 670 (57.81%) were from before the mask mandate and 487 (42.19%) were post-mandate. Before the mandate, 107 patients had HAP, 575 had all-cause pneumonia (CAP, VAP, and no discernible etiology), and 0 had VAP. After implementation, 84 patients had HAP, 376 had all-cause pneumonia, and two had VAP; 316 patients had COVID pneumonia. A significant difference was observed in all-cause pneumonia cases between pre-and post-mask mandate implementation ($\chi 2 = 13.3058$, $p < 0.0001$), but not in HAP cases ($\chi = 0.2996$, $p = 0.5841$).

Conclusion/Significance: Among hospitalized patients, the incidence of non-COVID pneumonia of any etiology was significantly lower during the mask mandate ($p < 0.0001$). For HAP, there was insufficient evidence to show a significant difference. These data suggest that mask usage helped slow the spread of CAP.



50. High Mortality in the Male Breast Cancer Community and the Need for a Change in Healthcare Policy

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Introduction: Male breast cancer (MBC) is a rare cancer with a predicted mortality of 18.92% in the United States in 2023[1]. Globally, this scenario is worse, which Breast Cancer Hub (BCH) has confirmed through global outreach programs.

Aims

1. To shed light on the role late detection plays in mortality.
2. To highlight epidemiological factors that contribute to MBC.
3. To promote early detection.

Methods: We sent a survey (BCH Survey) to the Male Breast Cancer Coalition (MBCC) in which members with MBC provided detailed information about their diagnosis(N=45). A separate data set (In Memoriam Dataset) was also provided by the MBCC with data from deceased MBC patients (N=77). In total, N= 122, a difficult number to obtain given the rarity of MBC.

Results/Discussion: Late detection of MBC may contribute to mortality. 85.30% of our survey takers had a grade 1 or 2 MBC, indicating that these cancers were slow growing. Additionally, 56% of patients who we lost to MBC were diagnosed at stage 4. Clearly, MBC follows a pattern of late detection, possibly contributing to mortality.

The lack of screening could be a culprit for late detection. 62.5% of survey takers reported that their cancer was identified through self-breast exam (although most had found it accidentally). Additionally, only 8.3% reported detection through a clinical breast exam (N=48). Genetics and BMI also showed some correlation with MBC.

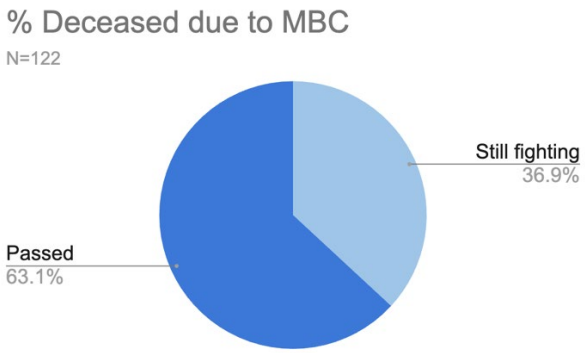

Figure 1. Pie chart of percent of patients lost to MBC.

IRB protocol # 20204167

Conclusion

Although MBC is a small subset of cancers, it still has a higher mortality. To prevent more loss of life, we believe that educating men and providers on early screening protocols is prudent.

References

1. Key Statistics for Breast Cancer in Men. Accessed March 13, 2023. https://www.cancer.org/cancer/breast-cancer-in-men/about/key-statistics.html

51. Safety and Efficacy of Upper Airway Stimulation for Obstructive Sleep Apnea in a Community Hospital

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Objectives: The vast majority of research on upper airway stimulation (UAS) for moderate-to-severe obstructive sleep apnea (OSA) comes from academic centers and clinical trials. This study evaluates UAS performed at a general otolaryngology practice within a community hospital.

Methods: The study design was a case series of consecutive patients. After IRB approval, all patients undergoing UAS surgery at Bronson Battle Creek Hospital in Battle Creek, MI from August 2016 to February 2021 were reviewed. Primary outcomes were the change in preoperative to postoperative apnea-hypopnea index (AHI), oxygen desaturation index (ODI), and Epworth Sleepiness Scale (ESS) scores. Secondary outcomes were technical failures, complications, and other adverse events.

Results: 91 patients underwent UAS with a mean age of 57.7 (standard deviation [SD]: 12.3), body mass index of 29.0 (SD: 3.1), and Charlson comorbidity index of 2.3 (SD: 2.2). There were no technical failures or reinterventions for device complications. Perioperative complications occurred in 7 (7.7%) patients, 2 (2.2%) of which experienced surgical site infections. 4 (4.4%) patients experienced perioperative pain. Postoperative polysomnograms after device activation were available for 24 patients. There was a significant improvement in median postoperative AHI (28.0 to 10.0; $p < 0.000024$) and ODI (20.7 to 5.0; $p=0.043$). Median ESS improved from 9.0 to 4.5 ($p=0.04$) after surgery.

Conclusions: When performed by an adequately trained general otolaryngologist, UAS is a safe and effective approach for patients with moderate-to-severe OSA presenting to community hospitals. More robust post-operative data would have been ideal to better assess the true nature of our results, however challenges from COVID restrictions and patients returning to their own sleep medicine physicians led to reduced patient follow-up. Nonetheless, investigation of long-term outcomes to assess the durability of UAS in this population is warranted.

IRB Number: WMed-2020-0673

52. Hot Patient? Stay Cool.

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Introduction: Prolonged fever or leukocytosis in patients treated for infection concerns clinicians because of a possible missed source of infection, a secondary infection, or inadequate antimicrobial therapy. We hypothesized that these patients suffer worse outcomes, including higher mortality and longer antimicrobial treatment.

Methods: From 2017 to 2022, data were prospectively collected on patients treated for infection in the SICUs of two university-affiliated hospitals. Demographics, microbiological data, severity of illness (APACHE-II score), and outcomes were recorded. Patients with white blood cell count (WBC) ≥15.0x109/L or a maximum temperature (TMAX) ≥38.5° C were divided into quartiles based on days until reduction of WBC to ≤15.0x109/L and days until normalization of temperature to ≤38°C for a full calendar day. Univariate analysis followed by logistic regression (LR) analyses were performed to predict factors associated with prolonged fever or leukocytosis, subsequent/secondary infections, and in-hospital mortality. Model performance was assessed using the Hosmer and Lemeshow test and ROC curve analysis.

Results: 697 patients were identified: 343 with WBC ≥15.0x109/L and 238 with TMAX ≥38.5° C. Mean time to normalizing WBC was 5.5±0.4 days with the highest quartile ≥7 days (prolonged leukocytosis-PL). The mean time to resolution of fever was 4.1±0.3 days with the highest quartile ≥4 days (prolonged fever-PF). By LR analysis, younger age, initial WBC, hospital days until diagnosis, and splenectomy were independently associated with PL; younger age and prior transfusion were associated with PF. Mortality in patients with leukocytosis was 21.9% and in patients with fever, 14.7%. By LR, only increasing age and APACHE-II score (but not PL or PF) were associated with increased mortality. Patients with PL received more days of antibiotics compared to patients without PL (18.5±3.0 vs. 9.5±0.5, $p < 0.0001$). Neither PL nor PF was associated with the development of a subsequent infection.

Conclusion: Neither prolonged fever nor leukocytosis was associated with worse outcomes, which may reflect inter-individual variations in the host inflammatory response instead of being markers of infection/inadequate treatment. When faced with a patient with prolonged fevers or leukocytosis, the best path is to treat these patients based on established evidence-based guidelines.

53. A Case of Nitrofurantoin Causing Liver Damage

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Introduction: Nitrofurantoin is a first line agent used for urinary tract infection prophylaxis and is one of the most common causes of drug induced liver injury, causing a hepatitis-like syndrome. The chronic form of hepatotoxicity can occur months to years after initiating the medication and is estimated to affect one in 1500 people. We present a case of hepatotoxicity caused by long-term nitrofurantoin prophylaxis.

Case Report: An 81-year-old woman presented with jaundice, diarrhea, and fatigue. Her past medical history was significant for chronic obstructive pulmonary disease, dementia, and recurrent urinary tract infections (UTI). The medication history included nitrofurantoin 50mg once daily, started over three and a half years prior for UTI prophylaxis, along with cranberry, lactobacillus, multivitamin, vitamin B12 and vitamin D. Initial laboratory values included aspartate aminotransferase (AST) 482 IU/L, alanine aminotransferase (ALT) 307 IU/L, alkaline phosphatase 405 IU/L, and total bilirubin 8 mg/dL. Initial workup was negative for viral hepatitis serologies, as well as EBV, CMV, and HSV. Imaging studies including ultrasound, MRCP, HIDA, and ERCP were conducted and none revealed a clear cause of these symptoms and lab abnormalities. Immune serologies did return positive for ANA, SMA, and RNP antibodies. Liver biopsy found portal tracts expanded by proliferation of bile ductules with associated neutrophilic infiltrate along with pericellular and early septal fibrosis. The pathologist interpretation gave a differential diagnosis of obstructive process, intrinsic process such as primary biliary cholangitis or primary sclerosing cholangitis, or a secondary cause such as drug induced liver injury.

Nitrofurantoin was discontinued shortly after admission. Throughout her hospitalization her liver markers steadily decreased and prior to discharge her labs demonstrated AST 186 IU/L, AST 144 IU/L and total bilirubin 3.4 mg/dL.

Conclusion: Liver injury from nitrofurantoin is a rare but serious adverse effect. It is believed that our patient experienced this adverse reaction with a Naranjo score of 4 (possible cause). Treatment consists of the discontinuation of the offending agent, and the liver markers are expected to decrease over time. Providers should be aware of this adverse effect.

54. Resident Perspectives and Practices Regarding Pediatric Weight Management

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Introduction:

The need to evaluate the perspectives and practices of residents in addressing pediatric weight management is imperative given the steadily increasing rates of obesity among children and adolescents. In Kalamazoo County, the prevalence of obesity among eleventh grade students is an astonishing 13.9%.[1] In order to address the high rates of obesity in Kalamazoo, providers must have the resources and training to effectively communicate with pediatric patients and their families. The aim of this study is to identify gaps in pediatric weight management education of WMed residents, to improve patient care and provider-patient conversations.

Methods: All pediatric, medicine-pediatric, and family medicine residents with pediatric patients were included in this study. Investigators created a survey addressing weight management practices, barriers to care, and resources available to patients for education and referrals. Surveys were administered to 72 residents via REDCap. Investigators analyzed the data to identify gaps in pediatric weight management education.

Results: The survey was completed by 13 residents. The results of this study show that the most common barrier in addressing weight management was time, reported by 69.2% of residents. Further, approximately 38.5% of residents reported both a lack of institutional training and a lack of available resources as barriers. Residents identified interest in receiving information on community-based programs centered around weight management to offer to their pediatric patients. Residents also expressed interest in offering overweight patient's resources for nutrition, access to healthy foods, and physical activity recommendations.

Conclusion/Clinical significance: Given the prominent barriers of time and lack of available resources, there is a need for an efficient intervention which combines both community resources and medical recommendations to effectively address pediatric weight management. Additionally, the reported lack of institutional training is concerning, and merits educational intervention at the resident training level. By addressing provider barriers in engaging in pediatric weight management conversations, resident training can help address the pediatric obesity rate in Kalamazoo.

References: Health starts where we live, learn, work, and play. Kalcounty.com. Published 2017. Accessed January 14, 2022. https://www.kalcounty.com/hcs/datahub/files/news/Childhood%20Obesity.pdf

IRB Reference number: WMed-2022-0930

55. Potential of Acetylcholine to Improve Rotator Cuff Patch Repair

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Introduction: Improper restoration of the tendon-to-bone interface (TBI) can lead to inflammation and secondary tears in patients recovering from rotator cuff repair surgery. Implantable scaffolds have aimed to improve the regenerative capacity of the TBI by introducing bioactive compounds and micro-architecture that is conducive to tendon adhesion [1]. Recent studies in murine models have shown that local supplementation of acetylcholine (ACh) to the TBI can significantly enhance the early stage of bone-tendon insertion healing by reducing inflammation [2]. However, the effect of ACh on osteoblast cells migration and differentiation remains largely unknown. This study aims to elucidate the effect of ACh on osteoblasts proliferation, migration, and bone formation.

Methods: Human-like osteoblasts (Saos-2) were cultured in Opti-MEM growth media (10% FBS, 1% P/S) until confluent. Cells were then transferred to 24-well plates, with each well containing a starting concentration of 3.104 osteoblasts. After an incubation period of 3 days, the media from each well was collected and replaced with ACh-containing media (with concentrations ranging from 10-3 M to 10-9 M). Osteoblast activity and differentiation was analyzed over the following 14 days using Alamar blue, ROS staining, gene expression for osteocalcin and Runx-2, and alkaline phosphatase activity. Osteoblast migration after Ach treatment was analyzed using the scratch test at 0, 4, 8, and 10 hours.

Results: Saos2 cells treated with Ach at concentrations ranging from 10-8 and 10-4 M resulted in an increase of cellular proliferation. At the highest dose of 10-3 M, Saos2 proliferation started to decrease after 5 days of culture, due to cytotoxicity of acetylcholine at this concentration. Ach had a positive impact on osteoblasts migration, as early as 4 hours post-treatment. The greatest overall effect was observed at concentrations of 10-5 M.

Conclusion/Clinical significance: Ach can be incorporated in scaffolds for rotator cuff repair applications. Ach will enhance cell migration, proliferation and differentiation which will enhance the repair of the tendon-to-bone interface.

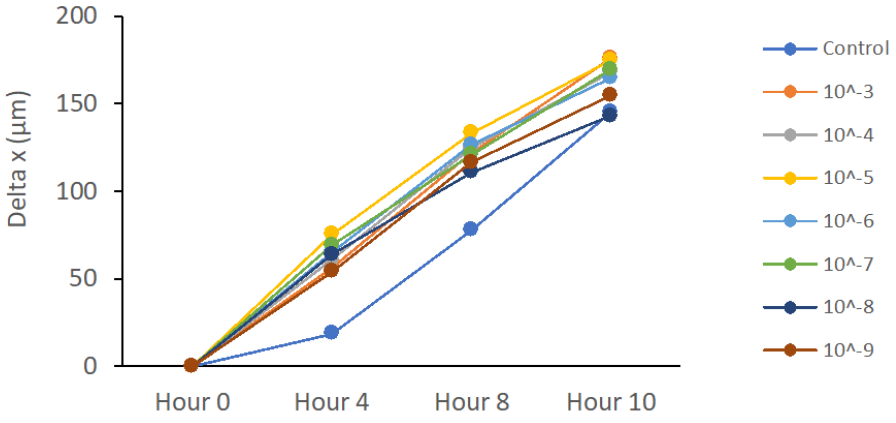

Figure: Saos2 migration after treatment with increasing concentrations of acetylcholine.

56. Phagocytic Response Patterns to Chemical Ablation of the Olfactory Epithelium in Adult Zebrafish

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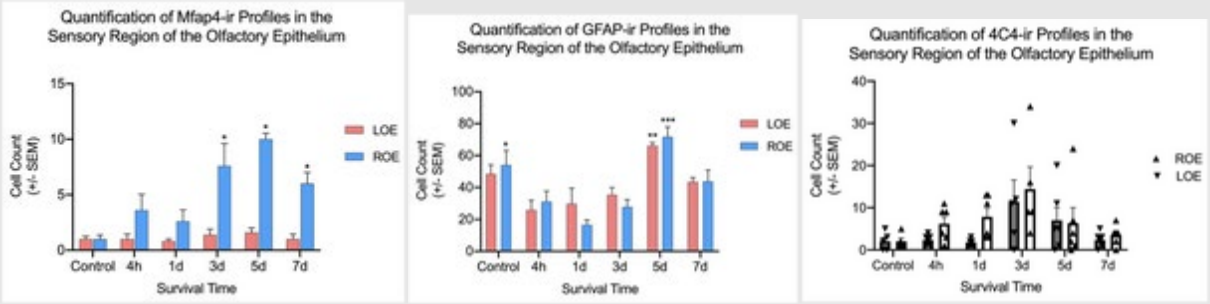
Introduction: Due to the rapid neurogenesis found throughout its body, the zebrafish is helpful for understanding neuroregeneration, a process which mammals do not effectively exhibit.[1,2,3] In the vertebrate olfactory system, three main cell types respond to olfactory injury: astroglia (astrocytes and olfactory ensheathing glia), peripheral macrophages, and central macrophages.[4] To elucidate the role(s) of each cell type in the neural response to peripheral nervous system damage, astroglia/olfactory ensheathing glia were labeled with anti-glial fibrillary acidic protein (anti-GFAP), peripheral macrophages with anti-microfibrillar-associated protein 4 (anti-Mfap4), and central macrophages with the zebrafish antibody 4C4.

Methods: The right nares of adult zebrafish were exposed to Triton X-100 to induce acute chemical ablation of the olfactory epithelium. After allowing the fish to recover for 4 hours, 1 day, 3 days, 5 days, and 7 days, the responses of peripheral macrophages, microglia, and astroglia/olfactory ensheathing glia were discretely quantified. A control group of untreated fish was established.

Results: Compared to untreated fish, there was a significant increase in the number of anti-Mfap-4-labelled cells in the right olfactory epithelia of treated fish at all recovery times. There were no statistically significant differences in the numbers of anti-GFAP-labelled or 4C4-labelled cells.

Conclusion/Clinical significance: Enhanced knowledge of the immune system's role in nervous system regeneration could potentially be applied to humans suffering from neurodegenerative conditions.

Figures:



Acknowledgments: The study was funded through Dr. Christine Byrd-Jacobs and a Western Michigan University graduate student research grant.

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57. New Onset of B Lymphoblastic Leukemia Manifesting as a Subdural Hematoma

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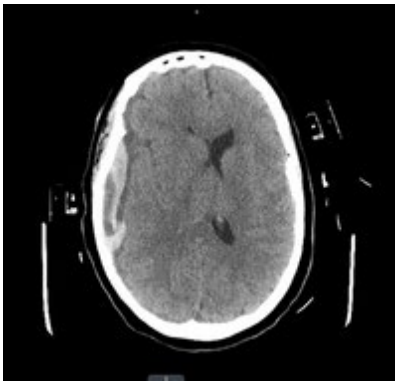
Introduction: Subdural hematomas (SDH) in the Emergency Department (ED) are often associated with traumatic events such as falls, assaults or motor vehicle collisions[1]. Chronic SDH can also occur but is more common in the elderly population or those with cerebral atrophy[2]. Coagulopathies including anti-thrombotic therapy are also risk factors for both traumatic and spontaneous SDH[3,4]. Presenting clinical features can vary significantly based on the degree of trauma or if bleeding is spontaneous versus chronic. This case presents a middle-aged female with increased bruising, falls and non-focal neurologic symptoms who presented with worsening altered mental status found to have a large SDH with mass effect.

Case Presentation: 45-year-old woman with past medical history of bipolar affective disorder, seizure disorder, hyperlipidemia and hypertension, presenting with altered mental status. In the last week, she developed confusion, altered speech as well as fever, nausea and vomiting. Prior to this, reported frequent falls, increased bruising and left sided weakness. Exam significant for patient being pale, somnolent but arousable. She is oriented to person and place; speech is hard to understand. Extremities are weaker on the left than right with ability to follow commands bilaterally. Significant labs included: WBC 48.3, Hgb 2.5 and Platelets of 12. CT head showed a large right convexity subdural hematoma with an 8 mm midline shift from right to left. Patient required multiple blood products prior to being able to undergo surgical evacuation of hematoma. Flow cytometry of blood confirmed B lymphoblastic leukemia/lymphoma.

Discussion: This case demonstrates the importance of maintaining a broad differential and adjusting work up and treatment in response to unexpected and unexplained findings. While the patient belongs to a population that generally would be low risk for SDH, the new and worsening nature of neurologic symptoms was teased out by the ED team, pushing them to take a broad approach that included imaging as well as labs, likely preventing any further delay in diagnosis of SDH. Likewise, the choice to obtain basic labs revealed grossly abnormal CBC findings, a critical clue in uncovering the hematologic malignancy which was ultimately the precipitating factor for SDH.

Figure:



58. Tuberous Sclerosis Complex Case Report

Leon Figueroa, MS, Marcel Castor, MD, Amanda O. Fisher-Hubbard, MD, Jared K. Brooks, MD
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Introduction: Tuberous sclerosis complex (TSC), also known tuberous sclerosis, is a rare autosomal dominant neurocutaneous syndrome that causes benign neoplastic masses to grow within the brain and several other areas of the body including the eyes, kidneys, lungs, heart, skin, and spinal cord. The life expectancy of these individuals is normal. We aim to report a case of sudden infant death where the individual was mid evaluation for tuberous sclerosis complex. Here, we present a case report of a 5-month-old infant postmortem examination findings and setting of death.

Case presentation: This case was investigated and certified by the Kalamazoo County Medical Examiner's Office. The content of this case and further information available in the electronic Case management system will be reviewed. Medical work-up at that time of arrival to the medical examiner's office included an MRI and several physician visits. Circumstances around the death of the decedent included an unsafe sleep environment of bed sharing an unsafe sleep surface. Neuropathological findings include an infant brain with subependymal nodules and multifocal cortical dysplasias. Cardiovascular pathology finding of rhabdomyoma of the heart.

Discussion: In the setting of sudden unexplained death of infants there are extrinsic factors to be considered such as unsafe sleep environment and intrinsic factors such as congenital/genetic abnormalities. For this case the differential must also include sudden unexplained death in epilepsy due to cortical dysplasias increasing the possibility of developing a seizure disorder.

Figure: Brain with subependymal nodule (1) and Cardiac rhabdomyoma (2) Acknowledgments: Stephen Cohle, MD.

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59. Factors Contributing to Low Usage of Intrapartum Long-Acting Reversible Contraceptives

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Objective: To estimate patients' knowledge of intra-partum long-acting reversible contraceptives (ipLARCs) and to evaluate factors that may lead to hesitancy of ipLARC use.

Methods: This was a cross-sectional study, using data collected at Western Michigan University Homer Stryker M.D. School of Medicine (WMed) primary care clinics between 2020-2022. The study included 38 physicians and 139 female patients. Patients self-reported if they were currently pregnant or non-pregnant. All participants completed a survey designed to elicit the following information: understanding of contraceptive options, frequency and quality of contraception education, barriers to contraception education, and hesitancy towards contraception use.

Results: Of the 139 female patients recruited in this study, there were 55 pregnant patients and 84 non-pregnant patients. Approximately 32.7% of pregnant patients and 30.7% of non-pregnant patients with previous pregnancies reported never receiving contraception counseling while pregnant. Most physicians (78.82%) reported providing patients with contraception counseling at least 2-3 times during pregnancy. Of the patients who reported barriers to contraception, the most frequently listed limitation was adverse effects. Among all patients, websites were the most frequently preferred format of contraception education. Physicians most commonly reported providing patients with high quality pamphlets.

Conclusion/Clinical Significance: There is a discrepancy in perception of contraception education between patients and physicians, which may contribute to low rates of ipLARC use. To increase patient familiarity with ipLARCs, physicians should provide contraception education in the patient's preferred format and tailor the content of counseling to the patient's concerns.

IRB exemption: WMed-2021-0838

60. Getting Under Your Skin: A Case of Dementia Complicating Morgellons and Severe Guttate Psoriasis Management

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Introduction: Dementia, psoriasis, and Morgellons Disease (MD) each carry high rates of neuropsychiatric comorbidity and stigma. MD, or "Ekbom syndrome," is a subtype of delusional disorder in which patients believe pathogens are embedded in the skin, leading to significant risk for self-harm to eradicate the infestation [1-2]. No known association between psoriasis and MD has been published. Although rare case reports of Ekbom syndrome and Lewy Body Dementia (DLB), Alzheimer's, multi-infarct dementia, and HIV dementia have been published, the relationship between MD and dementia is not well-characterized [3-9].

Case Presentation: A 74-year-old male with 3-year history of dementia presented for a court-ordered mental health evaluation after delusions of his wife's infidelity led him to hold a sword to her neck. At the emergency department, the patient had hallucinations of bugs crawling all over his skin but was otherwise calm. He was suspected to have mixed-etiology dementia, with histories of vascular disease and alcohol abuse contributing and was admitted. On reevaluation, the patient was noted to have actively bleeding upper extremity excoriations, attributed to picking "the little black bugs" that "hide in bumps and red spots," which began appearing a year ago. In addition, diffuse guttate psoriasis of the lumbosacral area and flexor and extensor surfaces of the legs was noted. Chart review revealed a history of psoriasis of at least 16 years. Figure 1 shows improved but still diffuse guttate psoriasis after one week of daily fluocinonide 0.05% topical application. He ceased to see bugs in his skin. During admission, the patient continued his home medications of sertraline 50mg, donepezil 10mg, and risperidone 0.5mg twice daily.

Discussion: Although both psoriasis and dementia are challenging, chronic diseases that require close management for symptom control, proper treatment of dermatological conditions is often overlooked in the setting of concurrent, complicated psychiatric diagnoses. Worsening psoriasis from lack of dermatological care may contribute to a cycle of increased delusions of parasites hiding in lesions, leading to worsened psoriasis from self-excoriation, and so forth. Physicians must address both dermatological and psychiatric conditions that synergize and lead to reductions in quality of life.

Figure 1:

61. Testosterone Stimulated Intestinal Cells to Release Larger Lipoproteins

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Introduction: Larger intestinal lipoproteins are more likely to be retained in the intestinal wall, allowing their fat to be hydrolyzed and taken up by the abdominal viscera. Since men generally accumulate more abdominal visceral fat than women [1], we hypothesize that testosterone stimulates the release of larger intestinal lipoproteins relative to estrogen and progesterone.

Methods: The effects of the physiological concentrations of sex hormones on intestinal lipoprotein secretion were examined ($n \geq 12$). Briefly, the differentiated Caco-2 cells were induced to produce intestinal lipoproteins by using the semipermeable membrane system that we have previously developed [2, 3]. The lipoproteins were isolated by using density gradient ultracentrifugation, and the amount of Apolipoprotein B (ApoB) and triglycerides (TG) were determined. Since each lipoprotein consists of only one ApoB, higher ratios of TG/ApoB suggest larger lipoproteins as shown by our previous studies [2, 3].

Results: While there was no dose-dependent effect of beta-estradiol ($p > 0.05$) and progesterone ($p > 0.05$), testosterone significantly ($p = 0.004$) increased the TG/ApoB ratio. When these hormones were combined to resemble the plasma, concentrations observed in men and the different phases of the ovarian cycle (follicular, ovulatory, and luteal), both the male ($p = 0.045$) and the luteal phase ($p = 0.043$) had significantly higher TG/ApoB ratios than the ovulatory phase. The ovulatory phase secreted significantly less amount of TG than the other groups, and the follicular phase secreted significantly less amount of TG than the male ($p = 0.0003$). ApoB was comparable among all these four groups ($p > 0.05$).

Conclusion/Clinical significance: In contrast to beta-estradiol and progesterone, testosterone significantly increased the size of intestinal lipoproteins. The ovulatory phase secreted the least amount of TG and produced significantly smaller intestinal lipoproteins than the male and the luteal phase. These studies support our hypothesis that through their testosterone effects, men produce larger intestinal lipoproteins. Larger lipoproteins tend to stay longer in the intestinal wall, allowing their fat to be taken up preferentially by the abdominal viscera. Our studies may partly explain why men are more likely to accumulate abdominal visceral fat, which is an independent predictor of mortality. [1]

62. Adult Still's Giant Cell Myocarditis

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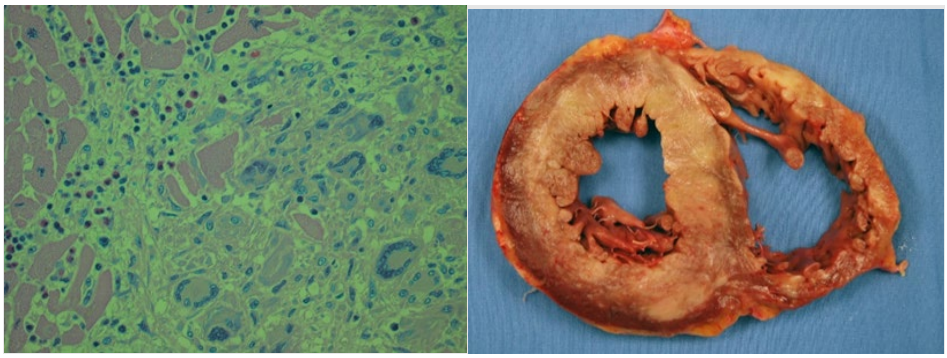
Introduction: Still's disease is a rare form of arthritis that affects children and is characterized by widespread joint inflammation as well as systemic symptoms including fever and rash. Adult Still's disease is a similar condition, but typically affects adults and tends to have a chronic course. Patients with Adult Still's disease commonly present with daily fever, arthritis and salmon-colored rash typically found on the trunk. Patients also typically present with lymphadenopathy, pharyngitis, and leukocytosis. There are very few cases in which Adult Still's disease presents with giant cell myocarditis, a rapidly progressive T lymphocyte mediated inflammation of cardiac muscle.

Case Presentation: Here we present the case of a 60-year-old female patient who was transferred to a hospital on ventilation and experiencing extreme hypotensive shock leading to her death. She had originally presented to an outlying emergency department with complaints of respiratory distress and hypotension. The patient had a significant history of Adult Still's disease, bullous pemphigoid, emphysema, hypertensive and coronary artery disease, as well as coronary artery bypass surgery and bilateral carotid endarterectomies. She took daily prednisone, as well as weekly methotrexate for her autoimmune diseases. A hospital autopsy was requested. At autopsy, gross examination of the enlarged heart revealed coronary artery atherosclerosis and quadruple bypass surgery but was most significant for the presence of a diffuse, tan-gray discoloration of a majority of the myocardium of the right and left ventricles. Subsequent microscopic examination revealed a severe giant cell myocarditis, consisting of giant cells, lymphocytes, macrophages, and eosinophils with widespread associated myofiber loss/fibrosis.



Discussion: The case is illustrative of a rare but impressive manifestation of severe giant cell myocarditis occurring in a patient with Adult Still's disease. Giant cell myocarditis can lead to fatal consequences and is present in the setting of many autoimmune conditions. It is important for any clinician to evaluate for this condition. By evaluating this patient's clinical presentation and histological findings, we can guide future prognosis and therapies.

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63. Carotid Cavernous Fistula following Flow Diverting Embolization of Right Internal Carotid Artery Aneurysm

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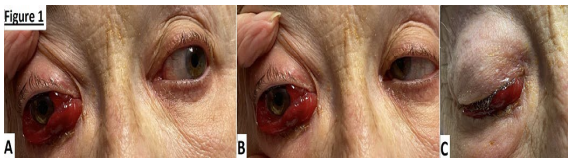
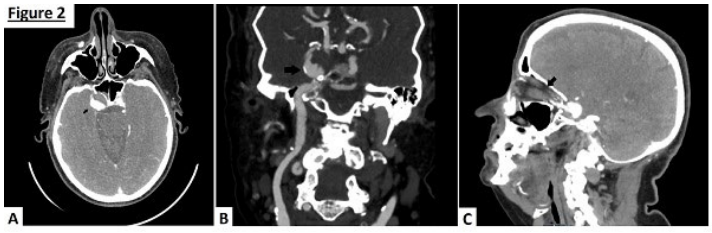
Introduction: Carotid cavernous fistula (CCF) is an abnormal connection between the cavernous segment of the internal carotid artery and the cavernous sinus [1]. The estimated incidence of CCF is around 0.2/100,000[2]. Etiology is most commonly traumatic with resultant shearing of the internal carotid artery (ICA) within the cavernous sinus. Rarely, it may occur spontaneously due to aneurysmal rupture of the ICA [3]. Clinical presentation varies in severity. We present a patient with delayed aneurysmal rupture of right ICA aneurysm despite flow diverting embolization with resulting CCF.

Case Report: An 86-year-old female presented to the emergency department with right eye pain and protrusion, headache, and hearing a "pulsatile rush" within her right ear. History was pertinent for an aneurysm of the cavernous segment of the right ICA status post flow diverting embolization. Physical exam findings included right eye proptosis with extensive chemosis and a 2mm nonreactive pupil (fig. 1). Ophthalmoplegia with cranial nerve III, IV, VI palsy was noted. Right eye intraocular pressure was 30 mmHg, visual acuity was 20/200. An ocular bruit was audible. CT angiography of the head and neck displayed rupture of the 2.1cm right ICA aneurysm with new associated CCF (fig. 2). After neurosurgical consultation, the patient underwent endovascular embolization of the fistula. However, she had residual visual deficits during an eight-week post-operative follow-up.

Discussion: CCF is a rare but serious ophthalmic complaint encountered in the emergency department which can be vision-threatening. Assessment for ocular bruit should be considered when examining patients with unilateral proptosis, especially in the setting of ophthalmoplegia [4]. If present, CT angiography should be obtained to rule out AV malformation [5]. Timely diagnosis and early neurosurgical consultation are key to prevent permanent ocular damage. Despite timely diagnosis and treatment, complications are not uncommon.





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64. Spinal Surgery Outcomes in Fibromyalgia: a Retrospective Cohort Comparison

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Background: Fibromyalgia is a chronic, widespread pain condition that affects about 2% of the adult population in the United States. National data suggests that people with fibromyalgia have worse outcomes after spinal surgery. Our study aims to evaluate if the local outcomes of spinal surgery in patients with fibromyalgia show similar concerning trends.

Methods: Our retrospective, cohort comparison study evaluates the length of stay, post-operative milligrams of morphine equivalents (MME), and post-operative anemia rates in fibromyalgia and non-fibromyalgia patients undergoing spinal surgery between 2018-2021 in our local hospital system. The cohorts were matched by age category, BMI, smoking status, gender, diabetes diagnosis, and surgery type.

Results: Of the 2147 individuals without fibromyalgia, 162 were selected by matching cohort variables. Those without fibromyalgia showed an increased average length of stay (100 hours versus 72 hours, p-value 0.004). Patients without fibromyalgia also showed an increased rate of post-operative anemia (p-value 0.016). The MME at 30 days post-surgery was greater in fibromyalgia patients (p-value 0.011); however, the difference in MME prior to surgery and 90 days post-surgery between groups was not significantly different (p-value 0.11).

Conclusion: This research suggests that spinal surgical outcomes may differ for fibromyalgia patients compared to those without this diagnosis. A notable difference we found is that fibromyalgia patients utilized more MME 30 days post-surgery. However, the MME were not different between groups after 90 days. Surprisingly, fibromyalgia patients were less likely to experience post-operative anemia and spent less time in the hospital. This research can help patients with fibromyalgia and their physicians better understand the risks and benefits of undergoing spinal surgery.

65. Coronavirus Disease-2019 (COVID-19) & Influenza Detected Among Deaths Occurring Outside the Healthcare Setting from 2021 to 2022

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Western Michigan University Homer Stryker M.D. School of Medicine, Department of Pathology and Office of the Medical Examiner, Kalamazoo, MI

Introduction: In the United States, most people with fatal COVID-19 infections are attended to within the clinical healthcare arena and are not reported to the Medical Examiner (ME). COVID-19 and other respiratory-infection-related deaths occurring outside the healthcare setting (OHS) might represent fulminant illness and are more likely for those with comorbidities. In cases where a suspected natural death is reported to the ME, jurisdiction may be released, and no postmortem exam occurs. In these cases, infectious disease testing is limited or absent. Enhanced surveillance for OHS respiratory deaths improves accuracy in reporting and death certification. Improved understanding of the clinical and epidemiologic characteristics of these deaths could inform prevention strategies.

Methods: The WMed Department of Pathology functions as the ME for 12 Michigan counties. In February 2021, additional postmortem laboratory testing for suspected OHS respiratory deaths was initiated as part of a multi-site study funded by the CDC and Council of State and Territorial Epidemiologists. Additional demographic and medical history data were also collected. All laboratory testing was completed at the Michigan Department of Health and Human Services Bureau of Laboratories (BOL). Nasopharyngeal (NP) swabs collected at the death scene were tested for SARS-CoV-2, Influenza A, and B. A subset was submitted for an expanded respiratory panel.

Results: Five WMed MPHME counties were included in the study from 2021 to 2022. In 2021 24.4% (n=269) of all decedents released directly to the funeral home (released jurisdiction) were sampled. In 2022 32.2% (n=392) of decedents released directly to the funeral home were sampled. SARS-CoV-2 was detected in 17.0% (n=46) and 11.9% (n=47) of study samples in 2021 and 2022, respectively. In cases where SARS-CoV-2 was detected 45.6% (n=21) and 36.1% (n=17) had COVID-19 infection identified as contributing to the cause of death in 2021 and 2022, respectively. Several Influenza A and B infections were also detected as well as many coinfections in various combinations of two or more viruses.

Clinical significance: This study provides insight into the true prevalence of COVID-19 and Influenza-related deaths in the community in a time where home testing, or no confirmatory testing is common.

69. Strangluted Recurrent Hiatal Hernia After Roux-En-Y Gastric Bypass

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Abstract: Roux-en-Y gastric bypass (RYGB) is a common surgical procedure for obesity management. Hiatal hernias occur in up to 40% of patients that undergo weight loss surgery. Here, we report a strangulated hiatal hernia with necrosis of the entire roux limb 3 months post successful RYGB.

A 67-year-old female presented to the ED with acute abdominal pain, SOB, and right chest pain. Three months prior, she underwent robotic RYGB with concurrent posterior crural repair for a known large hiatal hernia.

Upon presentation to ED, a CT of abdomen and thorax demonstrated a recurrent hiatal hernia with small bowel in the right chest.

Operation to repair the hernia began laparoscopically, however, was transitioned to a laparotomy, but both methods were unsuccessful in reducing the incarcerated bowel. Cardiothoracic surgery was consulted intraoperatively, and right-sided thoracotomy was performed. Necrotic-appearing small bowel was noted in the right chest. The diaphragm was opened sufficiently to facilitate reduction. However, once reduced, the entire roux limb was found to be non-viable and was resected.

The patient was left in discontinuity and a follow-up operation was performed two days later for reversal of her gastric bypass and feeding jejunostomy. Gastric pouch and remnant were found to be viable, as well as the remaining small bowel. An esophagogastroduodenoscopy (EGD) was performed to confirm the viability of the mucosa lining. We created a gastrogastric anastomosis with the gastric pouch and remnant. The gastrotomy was then closed and a repeat EGD was performed resulting in a negative leak test. The small healthy roux limb was brought to the abdominal wall as a feeding jejunostomy with use of a foley catheter as the jejunostomy tube.

Although hiatal hernias occur in 40% of patients undergoing weight loss surgery, those containing the Roux limb leading to obstruction are extremely rare, with only five cases reported. With such complications, necrosis of the Roux limb has not been previously reported to our knowledge. Strangulated hiatal hernia after Roux-en-Y can be a devastating complication following gastric bypass. We believe a multidisciplinary approach is important to the successful management of such a complication.

70. Racial Disparities in COVID-19 Treatment and Mortality in the ICU Setting

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Background: Since the onset, COVID-19 has disproportionately impact non-White ethnicities, due to a variety of cross-sectional factors such medical comorbidities, socioeconomic status, health literacy, and vaccine hesitancy (1). However, there is a lack of data about treatment differences by race and ethnicity. The objective of this study is to investigate the outcomes of patients admitted to the ICU with COVID-19. Our goal is to evaluate the association between race, critical care treatments, and mortality.

Study Design: This retrospective cohort study occurred at Bronson Methodist Hospital and included hospitalized patients with COVID-19 who were admitted to the ICU between January 1, 2020 and August 31, 2021. Patient demographic information as well as types of treatments were collected. The primary outcome was in-hospital mortality.

Results: Of the 424 patients who met the inclusion criteria of this study, the total mortality was 45.6%. Non-white patients were younger in age (54.8 vs 64.4, $p<.001$). We found that mortality was greater in white patients compared to non-white patients (Fig. 1). There was a slight predominance of non-white patients who were intubated compared to white patients (Fig. 2), although the difference was not statistically significant. In the total cohort, the mean ICU length of stay was 12.5 days, with no difference between White and non-White patients. Treatment modalities such as time on ventilator, Remdesivir usage, and steroid usage did not significantly differ between White and non-White patients.

Conclusions: In this study, we found that in patients with COVID-19 who were admitted to the ICU, non-White ethnicities had lower rates of mortality compared to White ethnicities. These findings indicate that once admitted to the ICU, patient mortality differs from conventional racial disparities in health outcomes. This suggests that interventions designed to reduce the disproportionate impact of COVID-19 on racial and ethnic minorities may require a broader focus on socioeconomic and structural determinants of health rather than in-hospital care.

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71. Potential Sex Differences in Mitral Cell Dendritic Morphology Following Injury and Recovery

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Introduction: Recovery after neuronal injury remains an enigmatic dilemma to the scientific community. The zebrafish olfactory system provides an excellent model to address neural regeneration due to its inherent plasticity. Mitral cells receive odorant information from the olfactory epithelium by synapsing with sensory neuron axons. Chronic damage to the olfactory epithelium causes a disruption of afferent input to the mitral cells. While many consequences of olfactory bulb deafferentation have been described, sexually dimorphic effects of sensory input loss on mitral cell dendritic arborizations remain unknown.

Methods: Chronic deafferentation was achieved through the repeated application of the detergent Triton-X 100 to the right olfactory organ every three days over a period of 8 weeks, after which fish were allowed to recover. Morphological measures of mitral cell dendrites were quantified based on number of tips, total length of dendritic branches, size of dendritic field, and distribution of fine processes. Comparisons were made with the internal control side and age-matched control fish.

Results: Combined data of males and females showed that 8 weeks of repeated damage affected mitral cell dendritic morphology, including significant reductions in number of tips, total length of dendritic branches, size of dendritic field, and distribution of fine processes. When zebrafish were allowed to recover for 3 or 8 weeks, these significant differences were alleviated as shown by a return of morphological structures to near internal control levels. Interestingly, preliminary results appear to show quicker recovery of branch length in males while the number of tips appeared to recover more quickly in females at the 8-week recovery time point.

Conclusions: This research furthers our understanding of potential differences between males and females in neuronal recovery. Understanding how injury and recovery is modulated between the sexes is essential to demystifying the processes underlying neural regeneration. Further elucidation of the differing recovery mechanisms between the sexes may lead to potential avenues for therapeutics in human populations.

72. Oxalate Nephropathy, A Late Complication of Roux-En-Y Gastric Bypass

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Abstract: Oxalate is an anion found in foods including spinach and rhubarb. Oxalate nephropathy (oxalosis) is a cause of renal injury secondary to oxalate deposition into the renal parenchyma, and usually presents with nephrolithiasis. Oxalosis occurs as a consequence of hyperoxaluria, a result of increased enteric oxalate absorption. One cause of increased oxalate absorption is gastric bypass surgery. This case involves oxalosis without nephrolithiasis found over 20 years after the original gastric bypass surgery.

The patient was a 73-year-old female with Stage 3 chronic kidney disease and history of Roux-en-Y bypass 22 years ago who presented to the hospital with altered mental status.

The patient was found to have acute-on-chronic kidney injury, presumed secondary to decreased oral intake. As renal function did not recover, additional investigations were pursued, ultimately resulting in renal biopsy. The patient was discharged after stabilization for outpatient nephrology follow-up, where dialysis was pursued. The biopsy results returned after discharge and showed oxalosis of the renal parenchyma.

Gastrointestinal tract disorders that promote fat malabsorption are known causes of enteric hyperoxaluria. Roux-en-Y gastric bypass is the most common bariatric surgery performed in the United States and, by design, results in decreased absorption of fats. Oxalate absorption is thus increased, as insoluble calcium oxalate is less likely to form.

For this patient, over two decades passed before oxalate nephropathy was noted. It is particularly interesting that this patient never developed nephrolithiasis.

Prevention of oxalate nephropathy and nephrolithiasis after bypass is an area lacking clear clinical recommendations. Increased water intake, renal diets, and low oxalate diets may have benefits. The use of oxalate carboxylase may aid in prevention of enteric hyperoxaluria but lacks clear evidence.

Oxalate nephropathy is an important and underrecognized complication of gastric bypass and other malabsorption syndromes. It should be considered in such patients presenting with acute and chronic kidney disease even in the absence of nephrolithiasis.

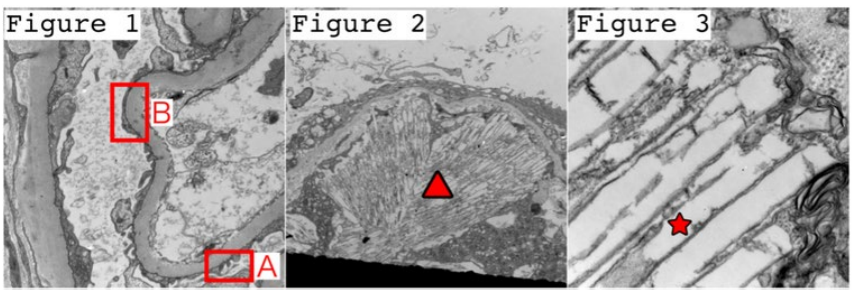

Figure 1) [A] Normal foot process structure vs [B] foot process effacement. Figure 2) The triangle indicates an area of calcium oxalate crystals in the parenchyma. Figure 3) The star indicates a magnified view of calcium oxalate crystals in the biopsy.

73. Circadian Rhythmicity of Autoantibodies in Type 1 Diabetes (T1D)

James Pearson[1], Craig Beam[2], Michelle Zhang[3]
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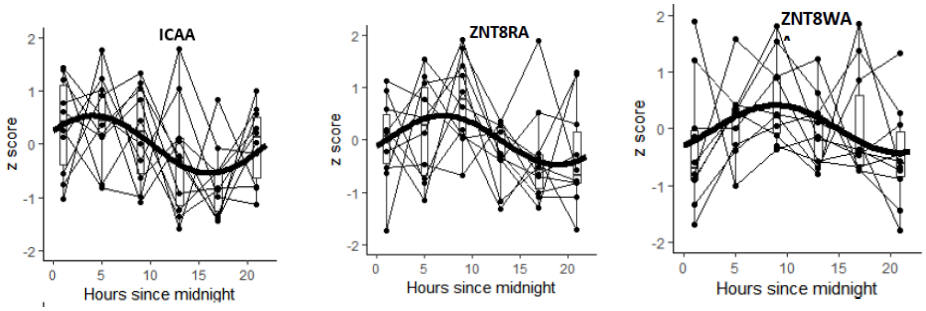
Objective: Type 1 Diabetes (T1D) has long been established as an autoimmune disease, however, immunomodulatory therapies, such as those focused on reducing the antibody response, have not been clinically successful in dampening disease progression. An emerging hypothesis focuses on the "chronotherapeutic" effect of immune therapies as a contributing factor to these challenges: previous vaccine research has found that the timing of vaccine administration can modulate its efficacy. In addition, our prior work established that the adaptive immune response in T1D has circadian variation, as was seen with oscillating peripheral B-cell levels. Thus, the circadian variation of the immune system and endocrine system (as seen in insulin secretion) both lend plausibility to the hypothesis that autoantibodies to proteins involved in insulin production by the pancreas may also show circadian variation.

The objective of this pilot study was to answer the question: "Do the autoantibodies related to type 1 diabetes (T1D) display significant circadian variation?"

Methods: Peripheral blood samples were obtained from 9 healthy controls (mean age: 32y, 40% female) and 10 subjects with T1D (mean age 28 y, 60% female). Each subject participated in an overnight stay in clinic with blood drawn every 4 hours beginning at 9 am and ending at 5 am the following morning. Plasma samples were used to measure the autoantibodies: IAA (to insulin), GADA (to glutamic acid decarboxylase), tyrosine phosphatase-related islet antigen 2 (IA2) and zinc transporter 8 (ZnT8; against both arginine (R) and tryptophan (W) amino acids) via radio-binding assays. Statistical analysis of circadian patterns was done using the COSINOR model.

Results: Of the five tested autoantibodies, IAA, ZnT8R and ZnT8W displayed statistically significant circadian patterns in the T1D subjects, as depicted in the figure. The plotted "z scores" represent the number of intra-subject standard deviations the titer was from the mean for the subject. The fitted patterns are shown as dark lines superimposed on the data.



Conclusions: This data confirms our main hypothesis that autoantibodies to the proteins involved in insulin production show circadian variation, raising the plausibility of a chronotherapeutic approach in T1D that may improve the efficacy of autoantibody-targeting vaccines.

74. Early Ddentification and Treatment of Peri-Partum Cardiomyopathy

Saima Khan, MD, MPH, Jessel Ramdass, MD, Mahsa Talebian, MD Family Medicine, Family Medicine Residency Program, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

Introduction: Cardiovascular disease (CVD) is the leading cause of pregnancy related mortality in the US, with cases increasing from 7.2 to 17.2 per 1000 between 1987 to 2015 (AHA 2021). PPCM is strongly associated with hypertensive disorders of pregnancy and has a higher incidence in racialized communities. Racialized women with hypertensive disease of pregnancy also have a higher likelihood of developing antepartum cardiac complications, with peripartum cardiomyopathy (PPCM) being an important cause of mortality. It remains a diagnosis of exclusion and can be challenging to identify due to non-specific clinical findings.

Case Presentation: A 25-year-old G6P2133 presented to the OB triage 1 month s/p vaginal delivery, with complaints of acute onset dyspnea and fatigue for 1 day. Pregnancy complications included postdates delivery (41w2d), postpartum uterine atony, endometritis, and new onset intrapartum pre-eclampsia without severe features. The patient had multiple BP readings in the severe pre-eclampsia range on admission. Lab work showed a Pr/Cr ratio of 3.47, mildly elevated Alkaline phosphatase, elevated hemoglobin/hematocrit, and thrombocytosis. The patient was found to have cardiomegaly with pulmonary edema on CTPE imaging, and a transthoracic echocardiogram was done which showed severely reduced LV systolic function (EF 20-25%). Other labs were WNL. Cardiology and MFM specialties were consulted, and treatment for non-ischemic cardiomyopathy along with IV Magnesium and HTN was initiated. The patient's symptoms improved, and she was subsequently discharged with close follow up. LV Systolic function returned to baseline over a period of 1 year.

Discussion: Early detection of PPCM can be key in preventing significant morbidity and mortality. Presentation can be nonspecific, leading to a delay in diagnosis. It is important to rule out other causes of cardiorespiratory distress and treat symptoms efficiently for improved outcomes. It can also be complicated by co-morbidities, especially in racialized patient populations with higher incidence of hypertensive disorders of pregnancy. Further research is needed to understand how co-existing conditions impact cardiovascular outcomes in at-risk populations.

75. Chondroprotective Effect of Strontium Through the Inhibition of ADAMTS-4 And ADAMTS-5 In Human Chondrocytes

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Introduction: Osteoarthritis (OA) is a degenerative disease of the joint and its prevalence increases with ageing [1]. Current OA pharmacological treatments, include non-steroidal anti-inflammatory drugs (NSAIDS), acetaminophen, tramadol and opioids, chondroitin sulfate, and glucosamine sulfate, which provide symptomatic relief with no effects on slowing down the disease progression. Aggrecan loss occurs in early-stage OA and proteinases such as ADAMTS-4 and ADAMTS-5 play a significant role in aggrecan cleavage and the structural damage of the cartilage [2]. Strontium is an orally administered drug for the treatment of severe post-menopausal osteoporosis and for prevention of high-risk fractures in the spine and hip. Recent studies have shown that oral administration of strontium effectively reduces articular cartilage degeneration in a rat model of OA [3]. However, it is unknown how strontium exerts its beneficial effects on human chondrocytes. In this study, we used 3D chondrocyte spheroids to test strontium chloride cytotoxicity, reactive oxygen species (ROS) production and cartilage degradation mediators' expression.

Methods: Chondrocyte spheroids were fabricated using 3D printed molds. Next, spheroids were cultured in increased concentrations of strontium chloride (0 to 100 mM). Spheroids were cultured in chondrocytes medium for up to 10-days. Cytotoxicity was tested using AlamarBlue and live/dead staining. Spheroids were stained with 2',7'dichlorodihydrofluorescein diacetate to visualize ROS production. Total RNA was extracted, and gene expression of ADAMTS-4 and ADAMTS-5 was performed using qRT-PCR.

Results: Strontium chloride enhanced the proliferation of chondrocyte spheroids at 25- and 50-mM concentrations after 3 days in culture. Strontium chloride reduced the production of ROS after 5 days in culture. qRT-PCR analysis showed a decrease in ADAMTS-4 and -5 expression as early as 3 days and this reduction was maintained at 10 days cultures.

Conclusion/Clinical Significance: Strontium administration represents a promising therapeutic to inhibit OA progression in early-stages by targeting ADAMTS-4 and ADAMTS-5.

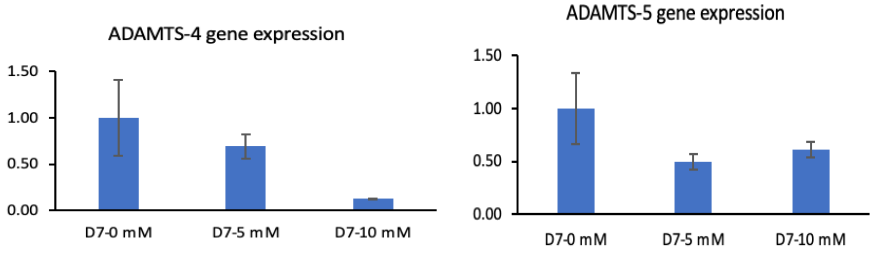

Figure**:** Strontium administration reduced the production of ADAMTS-4 and -5 in a dose-dependent manner**.**

References: [1] Richard F. Loeser. (2011) Curr Opin Rheumatol. 492-496. [2] Li T. et al. (2022) Biomolecules. 959. [3] Hu P. et al. (2020) Biol Trace Elem Res. 422-433.

77. Effects of Pirfenidone on Coculturing Fibroblast and Myoblast Model in Vitro

Nicholas Jacus[1], Brody Scholl[1], Kumail Naqvi[1], Juliana Overybey[1], Son Tran[1], Isabel Chiang[2], Haiying Pan[3], Yong Li, MD PhD[3]
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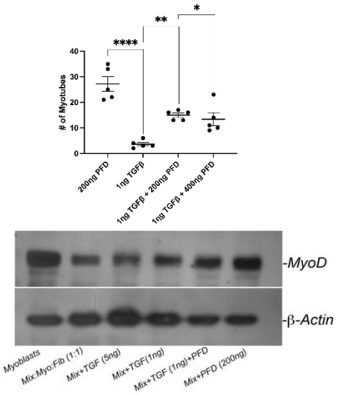
Introduction: Fibrotic scarring is characterized by inflammation, collagen overproduction, and excess cell proliferation at the site of injury. Our goal is to establish a co-culture system that includes fibroblasts and myoblasts to create a muscular fibrotic model in vitro using TGF-ß simulation. We also evaluated the effects of Pirfenidone (PFD), a drug approved for treating other tissue fibrosis on this coculture model.

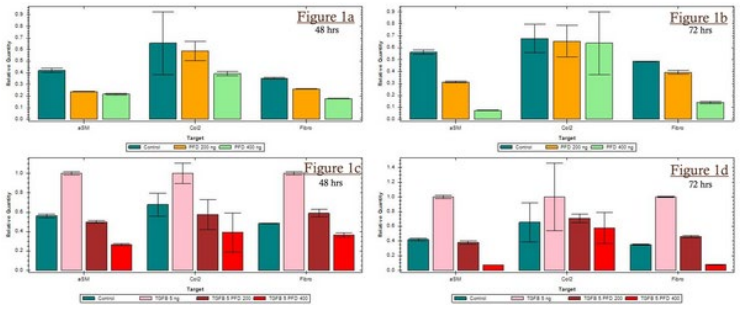
Methods: 1. Transcriptional changes evaluated by qPCR
2. Protein expression evaluated by Western blot
3. Myotube formation evaluated by DAPI immunofluorescent staining.

Results: In primary murine muscle cells, PFD limited expression of α-SMA and Fibronectin, with milder effects seen against Collagen 2 expression. Whereas, with TGF-ß alone, a significant increase was seen in α-SMA, Col2, and Fibro expression compared to control. Cells treated with TGF-ß and PFD exhibit return to baseline levels of α-SMA, Col2, and Fibro gene expression. Analysis by western blot shows decrease of MyoD in co-culture treated with TGF-ß, 1 ng or 5 ng. Myotube quantification has significantly decreased quantity in co-culture treated with TGF-ß alone compared to PFD alone.

Discussion: We successfully co-cultured fibroblasts and myoblasts to model muscular fibrosis in vitro. Decrease of α-SMA and Fibro in our model, suggests PFD to be a potent agent which could treat skeletal muscle fibrosis. A high dose of PFD did not significantly limit Col2 gene expression, indicating a separate mechanism of action to disrupt collagen formation or a higher PFD dose required. In addition, TGF-ß prevented myogenic differentiation through inhibited MyoD expression that can be rescued after PFD treatment, indicating plausible treatment utility. Moreover, significant increase of myotube formations when treated with PFD and TGF-ß vs. TGF-ß supports PFD's myogenic recovery properties. No significant difference of myotube formation amount with PFD dosing could indicate a limit on maximal effective utility. Our results support the proposed effect of PFD in suppressing fibrotic activity. Further research is needed to characterize the possible dose-dependent response.

Conclusion: An in vitro muscle fibrosis model was created and used to assess PFD's effects on muscle fibrosis. Our results suggest potential for improved skeletal muscle healing.





79. Medial Migration of a Cephalomedullary Nail Lag Screw After Open Reduction and Internal Fixation of a Right Intertrochanteric Fracture

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Introduction: Medial migration of the lag screw in a cephalomedullary nail is a rare complication following open reduction and internal fixation of an intertrochanteric femur fracture. The cause of hardware failure is multifactorial, but the root cause is usually due to fracture malalignment following reduction. This complication has been noted in the elderly population, likely due to the prevalence of hip fractures in this population. In this case presentation, we report on a 62-year-old female with a Body Mass Index of 63 kg/m2 who subsequently was treated with a hip hemiarthroplasty after hardware failure of her cephalomedullary nail.

Case Presentation: The patient is a 62-year-old female with extensive past medical history who presented to the orthopedic department with complaints of inability to bear weight after a ground-level fall. Plain radiographs demonstrated a right intertrochanteric femur fracture and the patient underwent open reduction and internal fixation with a cephalomedullary nail. Patient did well postoperatively and was discharged to inpatient rehabilitation. Approximately 4 months after initial presentation, the patient was admitted for right hip pain and was unable to bear weight without any associated trauma. Plain radiographs showed that the lag screw had migrated medially through the acetabulum. She was taken to the operating room for hardware removal and was converted to a right hemiarthroplasty.

Discussion: A majority of previously reported cases of similar complication attribute failure to issues with alignment or improper placement of a set screw. However, in this case, the reduction was confirmed intra- and postoperatively via radiographs. The set screw was confirmed to have been placed in the index procedure. Possible mechanism of complication more likely due to the patient's multiple co-morbidities and body habitus. The excess weight exerts a repeated diagonal stress on the implants when patient mobilize, leading to the loosening of the lag screw, and then medial migration. This effect was described by Werner-Tutschu and recreated in artificial models; they called it the "Z" effect.

Figure 1: Radiograph showing lag screw has migrated medially through the acetabulum. Figure 2: Radiograph showing the subsequent hemiarthroplasty repair.

Figure 1 Figure 2

80. Stroke in the Setting of OCP Use

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Western Michigan University Homer Stryker M.D. School of Medicine, Department of Community and Family Medicine, Kalamazoo, MI

Introduction: Oral contraceptive use has been shown to increase risk of stroke in women; most notably in the setting of additional risk factors such as cigarette smoking, hypertension, and history of migraines with aura. There is a dearth of data showing a clear association between OCP use in the setting of migraines with aura with increased incidence of stroke. Due to the potentially devastating effects of stroke; history of migraines with aura is stated to be an absolute contraindication for initiation of combined estrogen-progestin contraceptives by the American College of Obstetrics and Gynecology. This case report outlines the presentation, diagnosis, and treatment of a young female patient with a history of migraines with aura and recent initiation oral contraceptives who presents with clinical and radiologic findings suggestive of ischemic stroke.

Case Description: 33-year-old female with a history of migraines with aura presents to the emergency room with 3-day history of right upper and lower extremity weakness, numbness, and expressive aphasia. She also reported visual disturbances that started 2 days after initial symptom onset. CT brain showed a subacute infarct in the L frontal lobe with cerebral angiogram confirming thrombosis of distal M2 in the left hemisphere. She was managed medically with aspirin and her symptoms were noted to show improvement throughout hospitalization. She was discharged home and continued to work with outpatient neurorehabilitation.

Discussion: OCPs remain a widely used and commonly prescribed medication with growing number of indications for their use. This case highlights the importance demonstrates the need for further research into the interactions between OCPs and vascular risk factors. Furthermore, this case emphasizes the importance of conducting thorough review of medical histories and having an appropriate risk-benefit discussion with patients prior to stating any medications. Adequate identification of risk factors that may preclude the initiation of estrogen containing contraceptives as well as identifying the level of risk associated with various formulations and doses can serve to further guide risk-benefit discussions between clinicians and patients.

References: Practice Bulletin No. 110: Noncontraceptive Uses of Hormonal Contraceptives. Obstetrics & Gynecology 115(1): p 206-218, January 2010.

81. The Foot and Ankle in Ultramarathon Runners: Results of the Ultrarunners Longitudinal TRAcking Study

James Jastifer, MD[1], Martin Hoffman, MD[2]
[1]Department of Orthopaedic Surgery, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. [2]University of California Davis, Davis, CA

Introduction: The foot and ankle are critical for ultramarathon running, but injuries to this area are common. Understanding the preventative measures taken by ultramarathon runners may provide insights for injury prevention in other athletes. The aim of this study was to examine the injury rates and preventative care of the foot and ankle in ultramarathon runners.

Methods: The study used data from the Ultrarunners Longitudinal TRAcking (ULTRA) Study, the largest known prospective longitudinal study of ultramarathon runners. Participants reported general health status, running behavior and performance, as well as foot and ankle care, injuries, stretching frequency, and shoewear.

Results: 734 ultramarathon runners participated in the study. They exercised a median of 8 hours per week, including running a median of 25 miles per week. The mean number of foot and ankle injuries in the previous 12 months that limited running was 1.5 injuries per runner. Plantar fasciitis (24.1%), Achilles tendinitis (17.9%), stress fractures (8.6%), and other foot pain (7.2%) were the most common injuries. There were no significant correlations for sit and reach flexibility or stretching frequency with injury rate. The most common foot strike pattern was midfoot strike (51.2%), followed by heel strike (30.9%), and forefoot strike (9.2%). 63.7% of runners could not reach past their toes on a sit and reach flexibility test. 55.5% of runners reported performing daily or weekly Achilles or ankle stretching, with 44.5% reporting rarely or never performing stretching. 85.3% of runners agreed or strongly agreed with shoe comfort as a shoe selection method.

Conclusion/Clinical significance: The high incidence of foot and ankle injuries in ultramarathon runners does not appear to be influenced by stretching behavior or actual flexibility. Shoe comfort is a crucial factor in shoe selection. Clinicians can use these findings to guide shared decision-making with runners regarding routine care and injury prevention. This study challenges the belief that stretching is crucial for injury prevention in this population.

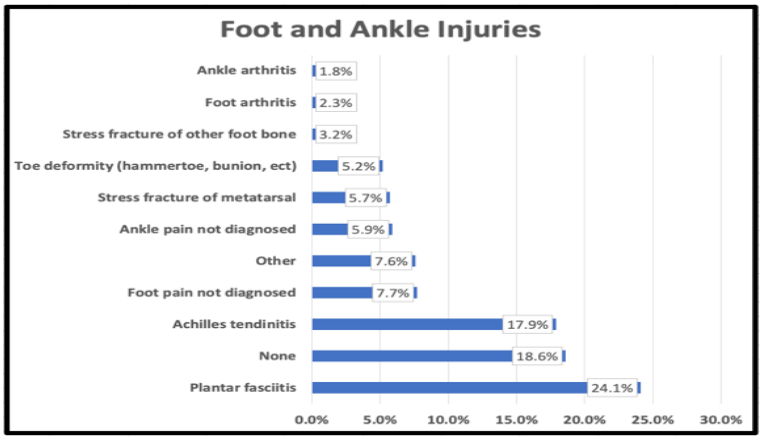

Figure 1: Foot and ankle injuries

84. Apoptosis Regulates in Vivo Tissue Regeneration and Neurogenesis

Pooja Acharya, Samantha Hack, MSc, PhD Candidate, Caitlin Nolff Undergraduate Researcher, Wendy Beane PhD Department of Biological Sciences, Western Michigan University, Kalamazoo, MI

Introduction: Cell death occurs during development and homeostasis, where removing unwanted or damaged cells is critical. Cell death is also, counterintuitively, required for regeneration in a process known as apoptosis-induced proliferation (AiP). Unregulated apoptosis is harmful during either process: failure to remove damaged cells can lead to tumorigenesis, while uncontrolled AiP promotes cancer re-emergence following therapy. Therefore, an outstanding question is what signals regulate apoptosis in these different contexts. Preliminary data suggests Caspase-3 regulates stem-cell mediated growth and neurogenesis in the highly regenerative planarian Schmidtea mediterranea. The executioner Caspase-3 can be activated through multiple apoptotic cascades including extrinsic (where outside stimuli target a cell for death) and intrinsic (where internal stimuli initiate cell death) apoptosis. To investigate the signaling associated with new growth, we inhibited both intrinsic and extrinsic apoptotic pathways pharmacologically. Our preliminary work shows Caspase-8 (extrinsic apoptosis) is required for de novo tissue regeneration and blastema formation while Caspase-9 (intrinsic apoptosis) is not. By assessing stem cell proliferation levels, we show inhibition of Caspase-8, but not Caspase-9, also prevents regenerative stem cell division. Our results suggest AiP signaling is potentially mediated by extrinsic apoptosis. Understanding the signaling associated with apoptosis mediated growth is an important step to manipulating cell death for targeted therapeutic outcomes for cancer and regenerative medicine.

Methods: We used pharmacological and genetic inhibition of caspases to target different apoptotic pathways to prevent cell death during regeneration in planarians. Effects on proliferation (phospho-Histone3) and blastema size (new growth) were measured. Effects on neurogenesis were assessed using pan-neural and photoreceptor neuron immunolabeling.

Results: General apoptosis and extrinsic pathway inhibitors blocked new growth during regeneration, where proliferation and blastema growth were inhibited. Caspase-3 inhibition specifically led to reduced brain:body size ratio and prevented visual neuron regrowth (studies with Caspase-8 are ongoing). Tissue growth and proliferation were not significantly different following inhibition of Casapase-9.

Conclusion/Clinical Significance: Our work has identified extrinsic apoptotic signaling as a mediator of adult tissue regeneration. These data provide a foundation for manipulating cell death to either enhance growth and neurogenesis (for regenerative medicine) or suppress it (for cancer therapies) in the clinic.

88. Investigation of Key Mediators of Cell Survival in Hypoxia and Chemically Induced Hypoxia

Joey Preziosi, BS[1], Melissa Schott, BS[1], Mallory Ruvina, BS[1], Jefferson DeKloe, BS[1], Genevieve Abd, PhD[2], Agata Parsons, DVM, MS[2], Yong Li, MD, PhD
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Introduction: Myoblast transplantation is an emerging technique for replacing diseased or injured skeletal muscles (1, 2). One problem, however, is that a large percentage of the transplanted cells die within the first 24 hours after transplantation (2). Here we show that hypoxic pre-conditioning of myoblasts leads to expression of the anti-apoptosis protein X-linked inhibitor of apoptosis (XIAP) and promotes cell survival in the setting of severe hypoxia or oxidative damage. Treatment with Cobalt Chloride and deferoxamine (DFX) can increase levels of HIF-1α, the major internal cell signal for hypoxia (3). Treatment with these hypoxia mimicking chemicals also increases XIAP expression, suggesting HIF-1α regulates the induction of XIAP in hypoxic conditions.

Methods: *Hypoxia*: C2C12 cells were cultured in either 5% oxygen (HYP) or 21% Oxygen (Control). After 24- and 48-hours, western blot was performed for XIAP. Cell survival in 1% oxygen was assessed using CytoSmart Cell counter.

Chemical Stimulation: Primary Myoblast cells were cultured in 100µM Cobalt Chloride or 100µM DFX. After 12-, 24- and 48-hours western blot were performed for XIAP. To determine optimal conditioning parameters with Colbalt Chloride to simulate hypoxia in the C2C12 cells, toxicity was evaluated using increasing concentrations of Colbalt Chloride. Cell survival was measured with MTT assay.

Results: Hypoxia Pre-conditioning increased cell survival to 1% oxygen Fig A. XIAP expression was robustly enhanced by both hypoxic conditioning Fig C, and by stimulation with both Cobalt Chloride and DFX Fig B.

Conclusion/Clinical significance: Increased expression of XIAP may be an adaptive way for cells to survive the stresses of transplantation. Stimulation of XIAP may allow clinicians to increase survival of donor cells after transplantation, through hypoxic pre-conditioning or chemical stimulation.

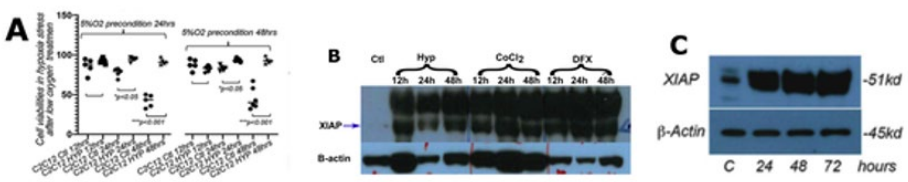

Figure**:** Cell survival rates of pre-conditioned cells in 1% oxygen compared to controls (A) XIAP expression increased after HYP, Cobalt Chloride and DFX (B) XIAP expression increased after hypoxic pre-conditioning (C).

Acknowledgements: Dr. Li's Grants and WMed Pilot Grants

References: 1.Skuk D, et al. Neuromuscular Disord. 2007. 2.Beauchamp JR, et al. J Cell Biology 1999. 3.Woo, Kyung Jin, et al. Biochemical and biophysical research communications 2006.

94. Now, That's a Great Question! Reflections on Five-Phase Design Process for a Research Survey of Street Medicine Organizations.

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Introduction: Street Medicine is a medical specialty providing direct care to people experiencing homelessness, a complex healthcare issue with multiple psychosocial facets, to further the goal of equitable healthcare. This is underscored by both the substantial health burden associated with homelessness and a long-standing sense in this population that the healthcare system stigmatizes, shames, and is generally unaccountable to homeless individuals. Informal reports show an explosion of interest in Street Medicine in the U.S., with Street Medicine programs operating in dozens of cities, often affiliated and integrated into the curriculum at medical schools, residencies, and allied healthcare training programs.

Despite this incredible growth in program number and complexity of the mission, there is a paucity of published data characterizing these programs: where they are; how they operate; what clinical services they provide; and what the educational opportunities they afford for medical and allied healthcare trainees. To address this concern, a research survey to capture key operational parameters of Street Medicine programs was created in five distinct phases: Initial Design, Refinement, Pretesting with Cognitive Interviews, Implementation, and Delivery.

Methods: The initial design phase began with a review of services (e.g., clinical, social) commonly rendered by Street Medicine programs and ancillary characteristics (e.g., funding, size) deemed important to a program's success. In the refinement and pretesting phases, the survey was continuously reworked based on discussions with biostatistical staff and insights from cognitive interviews with representatives of select Street Medicine programs. The implementation phase consisted of pre-review discussions with the IRB, implied consent documentation, and a data management plan, and locking changes to the survey. Lastly, the Delivery phase included developing a respondent communication protocol and blinding the researchers.

Discussion: The final design is an online survey with 95 fields split over 11 pages, with branching logic and mixed quantitative and qualitative questions. The design team unanimously endorsed pretesting with Cognitive Interviewing as an essential step in the survey design process. The survey received IRB approval and data will be collected and analyzed in Spring/Summer of 2023.

Acknowledgments: Research funding provided by Western Michigan University Homer Stryker MD School of Medicine.

96. Challenges to Timely Lovenox Prophylaxis in Trauma Patients

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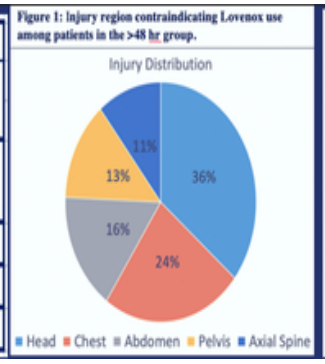
Introduction: Critically injured trauma patients are at high risk of venous thromboembolic events. These are increased in trauma patients for many reasons, one being immobilization1. Lovenox is utilized for chemoprophylaxis of venous thromboembolism in these patients. Trauma care guidelines recommend instituting Lovenox within 48 hours of admission to optimize prevention of thromboembolic events. Our study sought to identify how many trauma patients seen at a Level 1 Trauma Center met this goal. This would identify those needing additional surveillance and other methods of thromboembolic prevention.

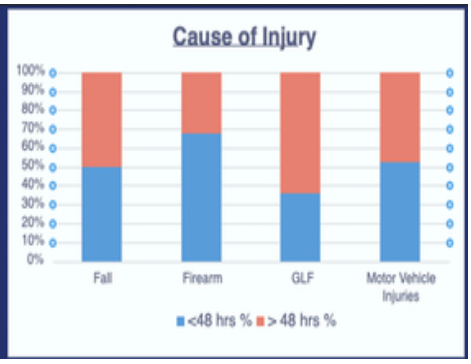
Methods: A retrospective review of Bronson Trauma Registry patients from January 1, 2022 to December 31, 2022 was performed. The assessed population included patients at least 18 years of age who suffered a traumatic injury and had a length of stay at least 24 hours. We identified the patients who did not receive chemoprophylaxis within 48 hours of admission and attempted to determine why this quality measure was not met.

Results: Data was collected from 529 patients. 326 received Lovenox within 48 hours and 113 were outside of the 48-hour window. 90 patients received no prophylaxis during their stay and were excluded from statistical analyses. Patients who received prophylaxis at greater than 48 hours had significantly increased length of stay ($p<0.001$) and a higher injury severity score (ISS) ($p<0.001$) than those who received within 48 hours (Table 1). The most frequent injury precluding Lovenox use within 48 hours of admission was head trauma, followed by chest and abdominal injuries (Figure 1).

Table 1: T-test for the difference of Age, ISS, and length of stay for group <48 vs >48.

Variable	Less than 48 hours		Greater than 48 hours		
	Average	Standard deviation	Average	Standard deviation	p-value
Age	50.53	21.28	54.75	21.36	0.08822
ISS	14.36	9.17	20.04	10.46	<0.001
Length of Stay	8.2	6.98	14.97	14.06	<0.001





Acknowledgments: Trauma registry data from Bronson Methodist Hospital: Amada Wyman, BSN, RN, MTQUIP Reviewer. Statistical analysis: Md Sakibur Hasan, MS, Department of Biomedical Informatics, Homer Stryker MD School of Medicine.

References: [1] Knudson M.M. et al. Thromboembolism after trauma: an analysis of 1602 episodes from the American College of Surgeons National Trauma Data Bank. Ann Surg. 2004 Sep;240(3):490-6; discussion 496-8.

97. Generalized Lymphadenopathy with Non-Specific Symptoms as Early Manifestation for Lupus Nephritis

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Introduction: Systemic lupus erythematosus (SLE) is an autoimmune disease affecting one or more organ systems. Symptoms can range from localized to systemic and may be life threatening. Most common features include arthritis, serositis, malar rash and Raynaud phenomenon. SLE is also associated with non-specific symptoms like weight loss, fever and fatigue. Early diagnosis is important so patients can start appropriate therapy and delay progression of disease. Definitive diagnosis can be difficult given the overlapping features of other autoimmune, infectious and hematologic diseases.

Case: A 42-year-old healthy male presented with concerns for flu-like symptoms for two months. He was experiencing fatigue, cyclical fevers and a 20lb unintentional weight loss. Initial work-up excluded infectious causes but revealed leukopenia, mild anemia of chronic disease and intact renal function. CT revealed diffuse lymphadenopathy both above and below the diaphragm, raising suspicion for lymphoma. Both ultrasound-guided lymph node biopsy and surgical excision of multiple lymph nodes revealed reactive lymphadenopathy. Within one month of presentation, the patient's symptoms worsened, and repeat laboratory evaluation revealed impaired renal function with glomerular filtration rate (GFR) less than 30. Autoimmune work-up was initiated. Antinuclear antibody (ANA) titers were positive at greater than 1:640, with multiple positive antibodies. Renal biopsy confirmed stage 4 lupus nephritis, and the patient was started on appropriate immunosuppressive therapy. From initial presentation to diagnosis the patient did not experience any arthralgia or cutaneous symptoms, and only developed a malar rash after diagnosis.

Discussion: The most current classification criteria for diagnosing SLE was developed in 2019 by the European League Against Rheumatism and the American College of Rheumatology (2019 EULAR/ACR). The criteria requires a positive ANA titer (≥1:80) and additional symptomatic criteria comprised of 24 items divided into 10 domains.[1] Lymphadenopathy is not one of the criteria and there are a limited number of case reports where generalized lymphadenopathy was linked to SLE. This case highlights the variable presentation of SLE and its symptomatic overlap with various illnesses. A high index of suspicion is required to make a timely diagnosis.

Reference: [1] Aringer M, et al. 2019 EULAR/ACR classification criteria for systemic lupus erythematosus. 2019Sep; 71:1400-1412

98. Levels of Reactive Oxygen Species Regulate the Degree of Tissue Regrowth at the Wound Site

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Introduction: When first discovered, biologically relevant reactive oxygen species (ROS) were thought just to be harmful byproducts of cellular metabolism, causing damage to lipids, DNA, and protein structures. We now know that ROS also play a significant role in development and regeneration, where ROS signaling drives cell migration, proliferation, and differentiation. However, precise regulation of intracellular ROS is vital. Extremely high ROS levels are known to induce apoptosis and cell death and are linked with cancer progression and other disease states. Conversely, lower ROS levels stimulate normal homeostatic function, growth, and regeneration. Using the planarian model system, which has a high rate of stem cell turnover and can replace all tissue types, we manipulated ROS levels in regenerating animals to investigate whether or not there are also concentration-dependent effects on blastema (new tissue) growth and eye formation.

Methods: We used the ROS inhibitor diphenyleneiodonium chloride at a range of 2-10 micromolar to limit ROS accumulation at the wound site after injury (DMSO vehicle controls). RNA interference to superoxide dismutase-2 was used to increase endogenous ROS levels. Accumulation was assessed by indicator dye assays: CM-H2DCFDA for general ROS, Peroxyorange 1 for hydrogen peroxide, and Orange 1 for superoxide. Analyses of anterior blastemas at different time points during regrowth were quantified to measure effects from modulating ROS.

Results: Our data suggest that loss of ROS accumulation blocks blastema formation, preventing functional regrowth, while low ROS concentrations lead to partial inhibition and stunted tissue growth. On the contrary, elevation of endogenous ROS levels promoted significant increases in the amount of tissue regrowth. Our current data implicate altering the amount of ROS at the wound site may also affect the timeline of eye formation (an area of current investigation).

Conclusion/Clinical Significance: Our work demonstrates that ROS are vital regulators of stem cell-mediated tissue growth, suggesting that they are not only necessary but may be sufficient to induce regeneration. These exciting data are critical to understanding ROS as a therapeutic target and indicate that elucidating the effects from ROS modulation will be critical in creating innovative approaches for cancer treatments and regenerative medicine.

99. Implementation of an Emergency Department Quality Improvement Program to Improve care in Opioid Use Disorder at four Southwest Michigan Hospitals

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Introduction: Opioid use disorder (OUD) causes significant, and still increasing, morbidity and mortality in the United States 1, 2. Opioid overdose remains one of the leading causes of death particularly among younger demographics3. There are three FDA approved medications available for treatment of OUD: methadone, buprenorphine, naltrexone3. Patients who receive medication for OUD (MOUD) experience decreased mortality, overdose rates and ED visits compared to those who do not4-7. Buprenorphine can safely be administered in the ED for patients in acute opioid withdrawal (from abstinence or naloxone reversal) or prescribed to patients not in withdrawal to start at home. Buprenorphine treatment plus referral for OUD treatment doubles the rate of engagement in treatment at 30 days compared to standard referral alone7.

Methods: In December 2022, the Bronson Health Foundation received a grant from the Michigan Opioid Partnership to develop an ED MOUD Program across Bronson Health System's four Emergency Departments. The goal of the program is to (1) identify ED patients with OUD during their ED visit, (2) begin MOUD during an ED encounter and (3) establish linkages with community prescribers for close follow up. Metrics include percentage of eligible patients with OUD offered treatment with buprenorphine, percentage of patients receiving a consult with medical social work/ peer recovery coach, and percentage of patients with OUD or on high doses of opioids discharged with a prescription for Narcan. Inclusion criteria are patients aged 18 and older cared for in a Bronson Emergency Department with an OUD related diagnostic code upon discharge from ED or admission to hospital.

Results: During January and February 2023, only 2% of patients with OUD were prescribed buprenorphine, social work was consulted in 51% patients with OUD, and Narcan was prescribed to 20% of patients with opioid related diagnoses.

	January	February	Totals
OUD Patients seen	25	24	49
Buprenorphine Prescriptions	0 (0%)	2 (4%)	2 (2%)
Social Work consult	13 (52%)	12 (50%)	25 (51%)
Narcan Prescription	3 (12%)	7 (29%)	10 (20%)

Table 1: Treatment data for OUD collected throughout the Bronson Health System EDs prior to intervention. Absolute number of patients in each cate is displayed with percentage of total OUD patients seen in parenthesis.

Discussion: A quality improvement initiative in March 2023 will offer ED providers education resources, ordersets with recommended buprenorphine dosing for both ED dosing and discharge prescriptions, and discharge referrals to community partners for follow-up buprenorphine treatment. These initiatives have the potential to expand appropriate ED care and follow-up to more patients with OUD systemwide.

101. CHIG Screenings as an Educational Tool in Pre-Clinical Curriculum

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Introduction: The Community Health Interest Group (CHIG) is a student organization at Western Michigan University Homer Stryker M.D. School of Medicine (WMed) that offers health screenings for unhoused people in Kalamazoo. Preclinical medical students take patient histories, vital signs, and offer over-the-counter medications under the supervision of a WMed physician. The objective of this study is to evaluate the educational value of CHIG screenings for pre-clinical medical students who have volunteered with the organization, and to identify any student apprehensions towards these screenings to make improvements in the future.

Methods: WMed medical students from the classes of 2025 and 2026 were emailed a 20-question survey. Descriptive statistics, including means and standard deviations, will be calculated using Microsoft Excel with a significance level of $p < 0.05$. If necessary, a Chi-Squared test will also be completed using Microsoft Excel.

Results: Survey data are still being collected, so preliminary results are included. Out of 70 student-volunteers, 26 completed the survey. When asked about their experience at CHIG screenings, 25 student-volunteers (96%) rated it as 4 or 5 out of 5 in terms of time-worthiness and 26 (100%) rated it as 4 or 5 out of 5 as an educational supplement to the pre-clinical curriculum and as an influence on their sense of purpose in medical school. Half of the respondents indicated it as an influence to pursue a career in primary care. When asked about their experience at CHIG screenings, 25 student-volunteers (96%) rated it as 4 or 5 out of 5 in terms of time-worthiness and 26 (100%) rated it as 4 or 5 out of 5 as an educational supplement to the pre-clinical curriculum and as an influence on their sense of purpose in medical school. However, 14 students (54%) indicated time commitment is a hindrance for some students to participate in more screenings, while 7 (27%) indicated no apprehensions to participating more.

Conclusion: These findings suggest that CHIG screenings offer a valuable learning experience for pre-clinical medical students and can positively impact their educational experience, communication skills, their sense of purpose in medical school, and their understanding of healthcare disparities.

102. Synthesis of a GO/DMSO-doped PEDOT Electroactive Nanocomposite for Electrical Stimulation Therapy

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Introduction: Electrical stimulation is being evaluated in regenerative medicine for its potential to promote stem cells adhesion, migration, and proliferation. Conductive polymers in tandem with electrical stimulation can act as a highly conductive substrate while remaining biocompatible. Poly(3,4-ethylenedioxythiophene) (PEDOT) is a conductive polymer with excellent biocompatibility and stability in aqueous environment [1]. To enhance the conductivity of PEDOT, bioactive dopants such as dimethyl sulfoxide (DMSO) and graphene oxide (GO) can be introduced during polymerization [2]. The solvent utilized during synthesis may also play a role in the properties of PEDOT. We hypothesize that the use of different solvents during the synthesis of PEDOT will affect the physicochemical and electrical properties of a GO/DMSO-doped PEDOT nanocomposite. The goal of this study is to synthesize a GO/DMSO-doped PEDOT and to assess its morphological, chemical, and electrical properties as well as its cytotoxicity on bone marrow mesenchymal stem cells (BMSCs).

Methods: Various PEDOT nanocomposites were synthesized by oxidative polymerization of 3,4-Etylenedioxythiophene (EDOT) in the presence of GO, DMSO, and ferric chloride ($FeCl_3$). $FeCl_3$ was dissolved in different solvents and added to EDOT (1:3 ratio) under stirring overnight at 70 °C. The solvents studied were H_2O, ethanol, methanol, 50/50 H_2O/ethanol, 50/50 H_2O/methanol, and 50/50 ethanol/methanol. The resultant dark solutions were washed with methanol/H_2O, then dried in vacuum oven. Nanoparticles were characterized by a combination of spectroscopic and microscopy techniques (SEM, TEM, EDS and XPS). Electrical properties were measured by four-point resistance measurements. Cytotoxicity and cellular proliferation were assessed by MTT assay on BMSCs.

Results: Different solvents used in polymerization resulted in various morphologies and different electrical and chemical properties. BMSCs cultured in direct contact with GO/DMSO-doped PEDOT did not show a cytotoxic effect for 24 hours.

Conclusion/Clinical Significance: This suggests that the GO/DMSO-doped PEDOT nanocomposite could potentially be used as an electroconductive substrate in future electrical stimulation therapies to enhance bone, muscle, or skin regeneration.

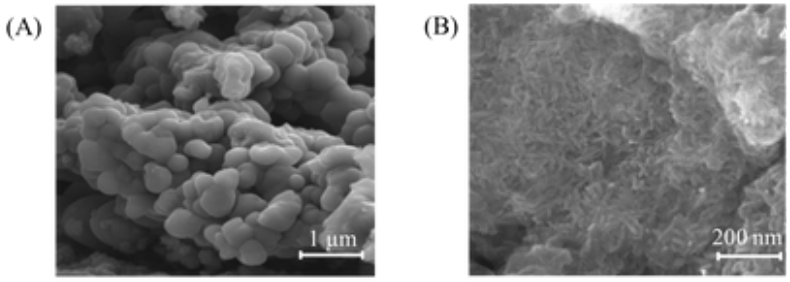

Figure: SEM images of synthesized GO/DMSO-doped PEDOT using (A) ethanol and (B) 50/50 H_2O/ethanol.

References: [1] Niu X. et al. (2015) JBMR Part A; [2] Ouyang J. et al. (2004) Polymer.

103. Ankle and Foot Arthroplasty and Prosthesis: A Review on the Current and Upcoming State of Designs and Manufacturing

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Introduction: The foot and ankle form a complex system composed of 26 bones and 33 joints, and serve vital purposes in weight bearing, balance, and flexibility to variable terrain. There is wide variety in ailments affecting the foot and ankle, ranging from osteoarthritis, to trauma, to amputations, making treatment options difficult to identify. This review of literature highlights various devices and technologies that are used for foot and ankle prosthesis and orthosis.

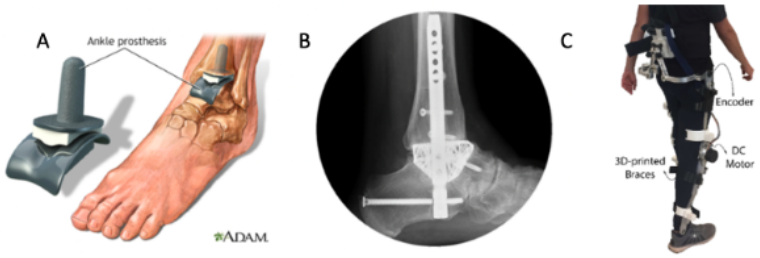
Methods: We searched PubMed, Scopus, and Web of Science for research papers on ankle/foot prosthesis, ankle replacement, additive manufacturing of ankle/foot prosthesis, and related topics from 2018–2023. We analyzed the data using the qualitative content analysis method.

Results: For patients with degenerated ankle, Total Ankle Arthroplasty (TAA) has become the popular treatment option, as it allows for preservation of mobility in the joint. TAA showed high failure rates as the implants did not conform to the anatomy of the patient. To address these challenges, additive manufacturing (AM) was used to create customized implants to patient anatomy, as well as porous implant cages that provide structural support and allow for bony ingrowth (Fig. A).

In cases of avascular necrosis of the talus, a Total Talus Replacement (TTR) has been developed as an alternative to TAA or AA, where AM has been employed to develop porous, patient-specific replica of the talus bone out of alloys including titanium, cobalt-chromium, aluminum-ceramics, and more (Fig. B). These implants have shown success in preserving the stability and mobility of the joint, and in achieving fast recovery.

Ankle prosthesis and orthosis have been indicated for use with lower limb extremity amputations or locomotor disability, leading to the development of powered exoskeletons. AM strategies are being employed to develop customized, lightweight exoskeletons with multifunctional actuators that integrate motor, brake and clutch functions (Fig. C). Devices have demonstrated significant improvements in gait rehabilitation, gait assistance, and augment strength for patients.

Figure (A) Representative image of Total Ankle Replacement implant (B) Radiograph of implanted AM custom, porous talus replacement and (C) Labeled image of powered exoskeleton including custom 3-D printed components



Conclusion/Clinical significance: These data will give a deep insight to medical students, orthopedic surgeons, and biomedical engineers on the current state of foot and ankle implants, manufacturing methods and the upcoming developments in the biomedical space.

104. Implementation of Electronic Self-Scheduling of Colonoscopy

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Purpose/Background: Colorectal cancer (CRC) is the second leading cause of cancer-related deaths in the United States and worldwide. Colonoscopy remains the gold-standard screening test. Due to the increasing backlog of colonoscopies related to COVID-19 and recently updated guidelines decreasing the age of CRC screening, we implemented an electronic colonoscopy self-scheduling system to address these needs. The primary endpoint was the utilization of the new system. Secondary outcomes were cost-effectiveness and patient satisfaction.

Methods/Interventions: This single institutional retrospective observational analyzed the data of all patients referred to our institution for screening colonoscopy. Group A included those patients who underwent the process of scheduling and completing their colonoscopy in the 6-months prior to implementation of the electronic system (1/2021 – 6/2021). Group B were individuals who underwent the process in the 6-months after implementation (10/2021 – 3/2022). Data from both groups were compared, the cost savings of the new system was evaluated, and the patients in group B were surveyed about their experience with this new system.

Results/Outcomes: Out of the 9,395 patients included in this study, 4,365 patients were in group A. Seventy percent (n = 3,079) of those were scheduled for colonoscopy, all by staff. Of those scheduled, 1,715 (56%) underwent colonoscopy within six months. In group B, there were 5,030 patients, seventy-six percent (n = 3,844) of whom were scheduled for colonoscopy. 2,326 (60.5%) were scheduled by staff and 1,518 (39.5%) electronically. Colonoscopy was completed in 1242 (53%) of staff-scheduled patients and 768 (51%) of electronically scheduled patients (p=0.225). There was a significant decrease in the proportion of patients scheduled by staff before and after implementation of the new system (100% vs. 60.5%, p<0.001).

The survey of patients in group B demonstrated that 64.7% preferred electronic self-scheduling, and 76.4% plan to do so in the future. Positive comments centered on efficacy and convenience. Negative comments centered on colon preparation instructions.

Conclusions/Discussion: Implementing electronic self-scheduling colonoscopy system is an innovative approach that is convenient, efficient, and has high patient satisfaction. The transition from staff scheduling to electronic should be considered for patients requiring routine screening or surveillance colonoscopies.

IRB number: WMed-2022-0899

105. Data Visualization Software: Do you get what you pay for?

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Introduction: There are multiple programs that can be employed for data visualization, segmentation, processing and analysis of computed tomography (CT) scans. These programs range from freeware, like 3D Slicer, to paid subscriptions like Amira/Azizo. This research tests the reproducibility of calculating subcutaneous and visceral adipose tissue from CT scans using these two different platforms. The objective is to identify if freeware is a viable alternative to paid resources for adipose volume measures.

Methods: Subcutaneous and visceral adipose tissue were calculated from the superior aspect of the first thoracic vertebra to the inferior of the fifth lumbar in ten female decedents. CT scans were obtained from the New Mexico Decedent Image Database, an online database of full-body CT scans with known data. Since this research involves decedent data the WMed IRB determined this was not human subjects' research. Volumes were obtained using a different protocol for each platform and compared in cm^3. The volumes were not normally distributed therefore a Wilcoxon signed-rank test was performed in SAS v9.4 for each type of adipose tissue.

Results: For subcutaneous adipose volumes, the p-value for the signed-rank test was p=0.06. For visceral adipose volumes the p-value was 0.16. Since both p-values were greater than 0.05 the null hypothesis, that there is no difference between the values, cannot be rejected. Body mass index values for the ten females in this analysis ranged from 19 to 43. The average volume of the visceral adipose tissue in 3D Slicer was 15,211.72 cm^3 and 14,056.59 cm^3 in Amira/Avizo. The average volume for subcutaneous adipose tissue was 4,682.48 cm^3 in 3D Slicer, and 4,412.62 cm^3 in Amira/Avizo.

Conclusion/Clinical significance: The values of adipose tissue were within the ranges seen in other studies using different programs when compared by Body Mass Index values. Therefore, the values for both visceral and subcutaneous adipose volumes are within the ranges expected. Since both programs produce values not significantly different from one another, either program can be used to determine these values. The freeware program provides comparable data and has a less involved protocol; therefore, it is a good alternate.

106. The Plan-Do-Study-Act (PDSA): An Iterative Approach to Optimize Residence Performance in ABSITE

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Introduction: American Board of Surgery In-Training Examination (ABSITE) preparation requires an effective study approach. In 2014, the ABS announced the alignment of ABSITE to the SCORE® Curriculum. We hypothesized that implementing a Plan-Do-Study-Act (PDSA) approach would help residents improve their performance on ABSITE.

Method: Over 20 years in a single institution, resident ABSITE performance was evaluated over three timeframes: Time A (2003-2013), no specific curriculum; Time B (2014-2019), an annual comprehensive pre-ABSITE SCORE®-based multiple-choice exam was administered; and Time C (2020-2022), like Time B with the addition of the PDSA approach for those with less than 60% correct. A study plan was then initiated, determining topics of focus (Plan), implementing the SCORE curriculum (Do), assessing the results/scores (Study), and identifying appropriate next steps (Act). Correlational analysis was performed between ABSITE scores and pre-ABSITE exam scores in the three timeframes. The primary outcome was to evaluate changes in the proportions of ABSITE scores <30%ile.

Results: A total of 274 ABSITE scores of 94 residents (34 females and 60 males) were analyzed. We found stronger correlation between the correct percentage on ABSITE and pre-ABSITE SCORE®-based scores in Time C ($r = 0.732$, $p < 0.0001$) compared to Time B (0.62, $p < 0.0001$). The ratio of ABSITE scores lower than 30%ile dropped from 14.0% to 3.3% ($p = 0.029$).

Conclusion: Implementing the Plan-Do-Study-Act (PDSA) approach using the SCORE® curriculum significantly enhances residents' performance on the ABSITE exam. Surgery residents are encouraged to use this approach and to utilize the contents outlined by the ABS in their study plan.

References: General Surgery Content Outline for the ABS In-Training Examination. The American Board of Surgery. (2021) https://www.absurgery.org/xfer/GS-ITE.pdf [Accessed March 13, 2023]

107. Caretaker and Pediatrician Knowledge on Current Nutrition Guidelines and Perceptions of Healthy Eating Counseling in Outpatient Clinics: A Cross-Sectional Survey

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Introduction: Many factors influence diet in pediatric populations, but parent nutritional beliefs are the main predictor of a child's nutritional quality and knowledge.[1] Existing research shows high quality parent-provider communication is associated with higher satisfaction and recommendation adherence.[2,3] Nutritional counseling varies widely among pediatricians. No current studies specifically compare pediatrician and caretaker nutritional knowledge. This study aims to assess the nutritional knowledge difference between caretakers and pediatricians, studying the success of nutritional counseling by pediatricians.

Methods: This is a cross-sectional survey study. The subjects were pediatricians and primary caretakers of patients 18 years old and younger at two outpatient community pediatric clinics over a 3-month period. Pediatricians were provided an electronic survey, and caretakers were provided a paper or electronic survey at their well child visits. Surveys included 19 general nutrition knowledge questions, 4 nutrition recommendations questions, and 3 demographics questions.

Results: 12 pediatricians and 84 caretakers completed the survey. Preliminary results showed that pediatricians score significantly higher in nutritional knowledge than caretakers (p=0.00548). A range of correlations between questions were found. 58% of providers talk about nutrition every visit; 55% of caretakers report the same. Of note, 6.5% of caretakers report never receiving nutrition counseling. 74% of caretakers take nutrition advice from providers; 26% from over 10 other sources. 33% of providers feel their recommendations are understood; 84% of caretakers feel they understand these recommendations.

Conclusion: This investigation comparing nutritional knowledge between pediatricians and caretakers in the local community demonstrates a significant knowledge gap. This difference is insightful as the majority of caretakers reported they fully understood provider recommendations, suggesting the need for improved provider-caretaker communication, including an emphasis on consistent discussion during well-child visits.

References:

[1] Eliason J. et al. (2020). Children's consumption patterns and their parent's perception of a healthy diet. Nutrients, 12(8), 2322.

[2] Nicely S. et al. (2019). Parents' perceptions of 5210 nutrition messaging and child weight status, Journal of Nutrition Education and Behavior, 51(5), 629-635.

[3] Pelto G. et al. (2004). Nutrition counseling training changes physician behavior and improves caregiver knowledge acquisition, Journal of Nutrition, 134(2), 357-362.

108. Marijuana Use and Breastfeeding: Provider Practices in a Newly Legalized State

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Introduction: The prevalence of marijuana use and its potency has increased significantly over the past decade in the context of a changing legal landscape. This raises concerns for increased maternal marijuana use during the postnatal period. Lack of specific guidelines and strong evidence addressing marijuana use during lactation may lead to discrepancies in recommendations from providers. Little is known about providers' attitudes toward marijuana use or how these changes are impacting providers' practices and recommendations. The aim of this study is to understand provider attitudes and current practices related to breastfeeding and marijuana use, as well as identify additional need for provider education and support surrounding this issue.

Methods: An online survey was administered via email consisting of 13 questions assessing providers' current practices, attitudes, and comfort levels, surrounding marijuana use and breastfeeding. Two of these questions were adapted from a previous study surveying lactation specialists. The survey was administered to clinical faculty and residents in a variety of specialties.

Results: Out of the respondents who care for breastfeeding patients, 84% reported they are likely or very likely to have a conversation with their patient about marijuana use in pregnancy. When asked about comfort level in talking about marijuana and breastfeeding with patients, 69% reported they are comfortable or very comfortable having these conversations, though 19% of respondents reported having very little knowledge about this topic. 96% of the respondents have no formal continuing education on the impact of marijuana use while breastfeeding and 96% are interested to learn more about marijuana use and breastfeeding.

Conclusions: Though respondents overall are comfortable having conversations about marijuana and breastfeeding with patients, not all respondents are knowledgeable about this topic. There were inconsistencies among respondents in how to specifically advise breastfeeding patients who are using marijuana, which may be due to limited literature and inadequate clinical guidelines for this population. This creates difficulty in having a conversation with mothers regarding marijuana use in lactation. There is a high level of interest for continuing education on this topic.

IRB#: WMed-2022-0954

109. Emergency Medical Services Encounters at Yellowstone and Grand Teton National Parks, 2015-2020

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Introduction: Yellowstone National Park (YNP) and Grand Teton National Park (GTNP) are visited annually by approximately 4 million and 3.5 million people, respectively. A retrospective chart review of all prehospital patients evaluated by the National Park Service's Emergency Medical Services (EMS) providers within YNP and GTNP has not previously been conducted. This study aimed to describe, compare, and contrast EMS encounters at YNP and GTNP.

Methods: A retrospective chart review of YNP and GTNP EMS calls documented in emsCharts from 01/01/2015 - 12/31/2020 was performed. Authors abstracted data including patient demographics, provider licensure level, chief complaint, location type, and disposition. Descriptive statistics were computed.

Results: During the study period, 5153 patient encounters were documented for YNP and 1397 for GTNP. Most encounters occurred during the summer (5/1-10/31): 88.8% YNP and 91.4% GTNP. Forty-six percent of YNP patients were female compared with 49% in GTNP. Patient age distributions were similar, with 41-64 years comprising the greatest volume: 32% in YNP and 33% in GTNP. Four of the top five dispatch chief complaints were the same in each park (YNP / GTNP): fall (6.9% / 13.5%), difficulty breathing (9.8% / 6.7%), traumatic injury (10.4% / 13.1%), and traffic accident (11.1% / 8.2%). Animal bites comprised 0.4% of calls at each park. In YNP, 1.4% of encounters were in wilderness areas versus 3.7% in GTNP. Air ambulance utilization was 5.2% in YNP and 1.9% in GTNP. The "no transport" rate was 36% in YNP and 32.7% in GTNP. Fourteen different healthcare facility destinations were documented for YNP prehospital patients compared with 3 for GTNP.

Conclusion: Prehospital patient encounters were significantly greater in YNP. The summer months accounted for the majority of EMS activations, with traumatic mechanisms encompassing the greatest proportion of calls throughout the year. Aeromedical transport is utilized more frequently by YNP. GTNP has proportionally more encounters in wilderness areas. The no-transport rate is greater in YNP. This research may help guide YNP and GTNP EMS leadership with regard to staffing, training and preparedness.

111. Community-Level Intervention to Drive Interest in STEM: An Active Learning Somatosensation Lesson Developed by Medical Students for Rural Middle Schoolers

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Background: Early exposure to engaging science education can have a significant impact on student interest and success in pursuing careers in STEM. However, rural communities often lack resources and opportunities for effective, hands-on science education leading to decreased interest in science careers. Attitudes towards science are often fixed by the time students enter high school which makes middle school an optimal period to motivate students. This project implemented a community-level intervention in which medical school students designed and taught a lesson on somatosensation for 8th grade students in a rural middle school.

Methods: The 1-hour lesson plan was designed by medical students and delivered to 8th grade students (IRB Protocol: WMed-2019-0538). Four classrooms averaging 20 students each were taught throughout the school day. The neuroscience lesson focused on identifying the different forms of somatosensation, understanding the mechanics of somatosensory receptors, and recognizing the primary somatosensory cortex and its position in the brain. The students performed two activities to reinforce these concepts. A matched pre- and post-test design was used to assess the effectiveness of the lesson.

Results: Students' knowledge of somatosensation improved following the lesson. Paired t-test analysis of pre-test and post-test scores indicated a statistically significant increase following the event (p-value < 0.0001; 95% CI [25.42-40.26]). Average improvement in test scores was 32.84%.

Conclusion: This active learning neuroscience lesson plan designed by medical students is an effective teaching method for eighth grade students. Building upon this model, designing and sharing additional data-driven lesson plans could serve as an opportunity to enrich STEM education in rural communities across the country. This community-level intervention could potentially drive interest in medicine in rural communities.

112. Timely Pain Management in Pediatric Patients with Suspect Long Bone Fractures

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Background: Adequate pain control is integral in the management of long bone fractures. Numerous reports have highlight inadequate pain management in pediatric populations (Davis et al., Dong et al., Noble et al.). Despite efforts from the several pediatric agencies these inadequacies remain (Schuman et al., Heilman et al.).

Project Aims: Quality improvement project aimed to determine/reduce time from ED arrival to order/administration of analgesic and determine/improve pre/post pain scores for pediatric patients with confirmed/suspected long bone fractures.

Methods: Retrospective chart review of patients 2-years of age or greater presenting to the Bronson Emergency Departments with confirmed long bone fracture from January 2020 through December 2021. Implement a nurse triage protocol that allows administration of analgesics (Tylenol, ibuprofen, or fentanyl) based on reported pain score to pediatric patients 2-years of age or greater presenting with suspected long bone fracture (obvious deformity, significant swelling, significant tenderness/crepitus on palpation).

Results: 625 patients were included in this project (355 patients prior to institution of protocol, 270 following). Time to order was 96.71 min vs 101.85 min in pre- and post-institution groups, respectively. Time to medication given was 125.43 min vs 125.27 min. In pre-institution group, mean pain scores (1-10) pre and post medication given were 6.71 and 5.16. In post-institution group, mean pain scores pre and post medications were 6.81 and 6.05.

Conclusion: While this project failed to demonstrate significant difference in time to medication administration or improvement in pain scores, analgesia in pediatric long bone fractures remains an area to further study and improve in. This study was limited by a variety of factors including significant variance in wait times during the COVID-19 pandemic, nursing and staff reluctance of administering intranasal fentanyl in triage if unable to room patient immediately, and overall awareness of protocol by some new staff and travelers (RNs, etc.). Repeating or performing a different study with more defined and agreed upon protocols would be needed to improve utilization and potential efficacy.

114. Road Design as Public Health: Case Study of an Arterial Roadway in Kalamazoo County

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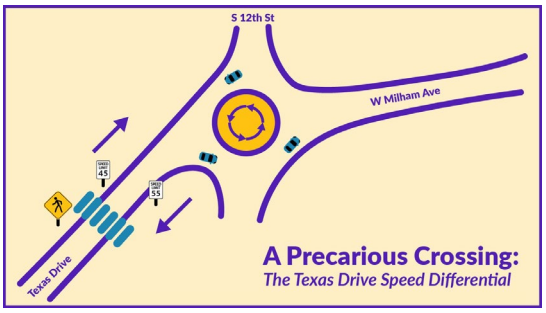
Introduction: The number of pedestrian deaths on U.S. roadways is at a 40-year high, with a recent steady climb since 2009[1,2]. Nearly 7500 pedestrians died in accidents in 2021, with 55 pedestrian-involved accidents and 3 deaths in Kalamazoo County alone[2,3]. Potential contributing factors include the increasing popularity of larger, heavier automobiles[2], roadway design which promotes high traffic volume at the expense of pedestrian safety, and an increase in walking behavior during the COVID-19 pandemic, particularly among low-income communities[4].

Case Description: Texas Drive is a major arterial roadway in Kalamazoo County that ends at a traffic circle. Several hundred feet South-West of the traffic circle is a busy pedestrian crosswalk accessing a nature preserve. Between the traffic circle and crosswalk are two speed limit signs directly parallel to one-another, facing opposite directions. The speed limit for vehicles approaching the crosswalk from the traffic circle reads “55” mph and is not visible to pedestrians while the speed limit approaching the traffic circle is “45” mph. Thus, auto traffic driving at the speed limit will approach the pedestrian crosswalk 10 mph faster in one direction, unbeknownst to those pedestrians.



Discussion: The relationship between pedestrian fatality rate and vehicle speed in an accident follows an exponential curve[5,6]. Why then is traffic permitted to flow at 45 mph (~50% fatality) in one direction but at 55 mph (~90% fatality) from the other? Studies have shown a decrease in pedestrian mortality when efforts to reduce vehicle speed have been enacted[7,8]. Texas Drive is an emblematic example of the preference given to auto traffic at the expense of pedestrian safety in modern road design, and of the larger shift from roadways as pedestrian-friendly mixed-use public spaces to high-speed connections designed for automotive efficiency that provide no apparent protection for pedestrians.

Future Directions: An observational study recording traffic speeds near the crosswalk may further characterize the increased risk that pedestrians face, which will be used to commission a formal traffic study and eventual change in speed limit. This investigation points to the need for increased public scrutiny of public safety measures as an area of further study.

116. Blood Clots as Biologically Active Scaffolds for Chondrogenesis and Osteogenesis

David Richter[1], Kayla Keckler[1], Victor Hung[1], Logan Morrey[1], Genevieve Abd[1], Kristi Bailey[2], Mitchell Kenter[1], Adil Akkouch, PhD[1], Yong Li, MD[1]
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Introduction: Blood clots (BCs) contain numerous biologically active factors that aid the natural healing process of cartilage and bone. Additionally, a growing body of research suggests that mesenchymal stem cells (MSCs) may promote bone and cartilage healing [1]. Therefore, this study investigated the ability of BCs loaded with MSCs to grow cartilage and bone in vitro. We hypothesized that: 1) BCs loaded with MSCs would exhibit superior growth relative to controls, and 2) samples inoculated with chondrogenic or osteogenic media would exhibit changes characteristic of such tissues.

Methods: Blood was collected from C57BL/6J mice by cardiac puncture and allowed to clot without additives (control) or in the presence of MSCs or chondrogenic cells (5x106 cells/mL; experimental groups). After forming stable BCs, samples were inoculated with either control, chondrogenic, or osteogenic media. Normoxic and hypoxic replicates were cultured at 37°C; media was changed every two days, and used media was stored for analysis. After 8 weeks, BCs were prepared for histology (H&E, Masson's Trichrome, Alcian Blue) and molecular analysis (ELISA, qPCR).

Results: BCs loaded with MSCs or chondrogenic cells, and cultured in chondrogenic or osteogenic media, showed increased cartilage or bone formation, respectively. Grossly, Mason's Trichrome and Alcian Blue revealed changes in BC composition that were indicative of ongoing chondrogenesis and osteogenesis. Continuing experiments are examining trends in VEGF and TGFβ concentration, in addition to the expression of genes associated with bone and cartilage anabolism.

Conclusion/Clinical significance: Autologous BCs loaded with MSCs or chondrogenic cells resulted in formation of tissue-like structures within four weeks of culture. Additionally, we noted increased release of tissue-specific factors in the media of such samples. Therefore, autologous BCs loaded with MSCs or chondrogenic cells may provide an effective vehicle to accelerate local healing following bone and cartilage injury.

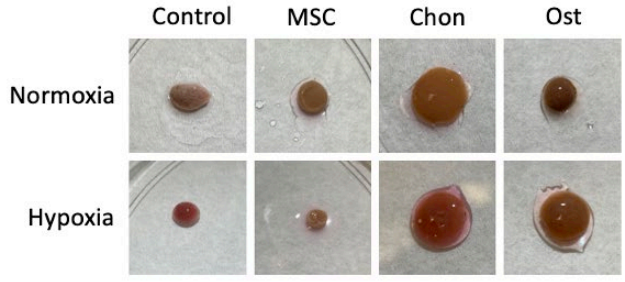

Fig 1. Gross morphology of BCs after 8 weeks culture. Width of each box is 2 cm.

Acknowledgments: This project was funded by the WMed Pilot Research Project Support Program.

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117. Data Visualization Software as a Process Improvement in Student Lead Screenings

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Introduction: Ministry with Community and Gospel Mission are local shelters providing basic needs to the unhoused of Kalamazoo County. The Community Health Interest Group (CHIG) provides healthcare screening services to these shelters, but continuity of care and following patients over time has been challenging. To address this, a data visualization technologic infrastructure was developed to improve the quality of care.

Methods: Initially, data privacy and protection were secured through hosting of raw data on a Virtual Data Warehouse (VDW) with access strictly limited to the leaders of CHIG. To ensure consistency of existing data inflow, the data collection tools were reviewed for feasibility of visualization, and data points were filtered for importation without alteration. Furthermore, all selected data points were chosen for explicit usage of trending purposes with the goal of maximizing impact for clients served. An algorithm was written to match data points to predetermined graphical and chart visualizations in Microsoft PowerBI. Beta testing was conducted to ensure data from different sources could update the tool without failure, and a hosting site for the visualization tool, Microsoft SharePoint, was selected for private, protected storage. With the architecture completed, multiple design iterations of the visualization tool were created with ease-of-use prioritized.

Results: The visualization tool was designed with two separate halves split into two separate tabs. The first tab focused on patient demographic and vital information, and the second tab displayed historical medical information. The final iteration of the tool included data filtering slicers, three charts, five tables, and twelve master variables. The tool was deployed after a training session to be utilized both alongside the data entry forms and for initial lookup for each patient at sign in.

Conclusion: By being able to understand a member's health history in a low-cost, custom-designed manner, health screenings were transformed into health pseudo-clinics, increasing the impact generated. The tool's development is an important step toward providing better continuity of care and following patients over time in shelters, ultimately improving the quality of care provided.

119. Does Resident's Postgraduate Year Impact the 30-Day Outcome After Esophagomyotomy?

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Background: Heller myotomy is the most common and currently the gold standard procedure for achalasia of the esophagus. It is a commonly performed procedure during general surgical residency. Further training during fellowship increases proficiency in performing this procedure. We hypothesize that the 30-day outcome would be better when senior residents/fellows participate in performing this procedure with attending surgeons.

Methods: Using the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) registry, we identified patients who underwent laparoscopic and open esophagomyotomy (Heller myotomy) between 2005 and 2017 with both attending and surgical residents/fellows and divided the study population into three groups: A) junior residents (PGY1-3); B) senior residents (PGY4-5); and C) advanced/fellow surgical trainees (>PGY6). Fisher exact tests, Pearson's X2 tests, and parametric/non-parametric tests were used to compare patient demographics, comorbidities, and 30-day complications. ANOVA tests were used to compare operative time and length of hospital stay between the 3 groups, with statistical significance defined as $P < .05$.

Results: A total of 1,298 esophagomyotomies were performed by group A (n = 249, 19.2%), group B (n = 662, 51.0%), and group C (387, 29.8%). Laparoscopic esophagomyotomy was performed in 983 (75.7%) while an open approach was performed in 315 (24.3%). A higher proportion of open surgery was performed by junior residents (28.9%) while advanced trainees participated in higher proportions of laparoscopic procedures (78.8%). Patient demographics and comorbidities were similar among the three groups. Overall, there were no differences between the three groups in 30-day postoperative outcomes. Reoperation and readmission rates were very low amongst all groups. Overall morbidity was slightly higher in senior residents groups compared to advanced/fellows and juniors (4.4% vs. 1.3% vs 2%, p = 0.011). Operative time and LOS were similar between the juniors, seniors, and advanced groups.

Conclusions: Postgraduate year of training of residents participating in Heller myotomy is not associated with differences in the 30-day postoperative outcome when working with faculty. This study demonstrates the safety of resident participation in one of the most meticulous procedures of the esophagus.

120. Andersen-Tawil Syndrome: A Rare Phenotype of Hypokalemic Periodic Paralysis

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Introduction: Andersen-Tawil Syndrome is a genetic disorder characterized by a triad of episodic flaccid muscle weakness, ventricular arrhythmias and prolonged QT interval, and presence of variable anatomical anomalies.

Case Presentation: A 31-year-old male presented to the emergency department with near-complete paralysis involving his entire body that started the morning of presentation. He reported having approximately 20 similar, though less severe, episodes previously however no diagnosis was ever offered. Patient denies any other symptoms. Denied fevers, chills, atypical physical exertion, numbness, focal weakness, dysarthria, dysphagia, or acute vision changes. The EMS report did mention non-specific changes in the patient's heart rhythm en route to the hospital. There was profound global weakness on exam. No cranial nerve abnormalities or focal neurological deficits. Normal sensation throughout all dermatomes. Patellar reflexes 1+ and symmetric. No insect bites or rashes. Interestingly, multiple anatomical anomalies noted on visual inspection including clinodactyly and hypertelorism. Immediately following initial assessment, supplemental potassium was administered intravenously prior to obtaining any results from workup. Laboratory analysis remarkable for hypokalemia (1.6 mmol/L), low TSH (0.01 iU/mL), elevated free T4 (3.5 ng/dL), hypophosphatemia (2.0 mg/dL). CK normal at 69 U/L. EKG showed a prolonged QTc of 522ms. These findings together with clinodactyly and hypertelorism in the setting of periodic paralysis likely secondary to hypokalemia raised suspicion for Andersen-Tawil syndrome. After 3 hours of potassium infusion, the patient experienced gradual improvement in his global weakness. Endocrinology consultant initiated methimazole for hyperthyroidism. After the patient was hospitalized for continued intravenous treatment overnight, he had returned to baseline and was ambulatory at time of discharge home the following day.

Discussion: Recognition of this phenotype is crucial as there is a positive correlation between patient age and frequency of life-threatening arrhythmic events resulting in a suggested association between delayed detection and increased morbidity.

Acknowledgements: None

References: Natural history and risk stratification in andersen-tawil syndrome type 1. Journal of the American College of Cardiology. 2020;75(15):1772-1784.

121. Acute Cholecystitis with Intrahepatic Perforation

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Introduction: Perforated cholecystitis is a rare complication of acute cholecystitis that requires prompt management [1]. Intrahepatic perforation synchronous with acute cholecystitis is especially uncommon and raises many questions about optimal timing of surgical intervention vs conservative management [2]. We present a case of perforated cholecystitis with large hepatic abscess.

Case Presentation: A 44-year-old Spanish speaking man with a history of non-medicated diabetes presented with 1 week of persistent right upper quadrant abdominal pain. He was found to have acute cholecystitis contiguous with a large, 9x10cm intrahepatic abscess. He successfully underwent IR drainage of his hepatic abscess followed by laparoscopic cholecystectomy.

Discussion: Perforated cholecystitis with intrahepatic (or type II) perforation is an uncommon presentation of acute cholecystitis and its optimal management is not well-defined. There are many questions about optimal timing of surgery, specifically whether to perform upfront cholecystectomy at the time of abscess drainage vs placement of cholecystostomy tube and interval cholecystectomy [3].

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122. HSV Lymphadenitis in an Immunocompromised Patient with Chronic Lymphocytic Leukemia: A Case Report

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Introduction: The treatment of Chronic Lymphocytic Leukemia (CLL) has improved with new cytotoxic agents, resulting in higher response rates. However, patients remain vulnerable to major infections due to immunosuppressive therapy and immune dysregulation from the malignancy, including dormant viral infections. Here, we present a case of HSV lymphadenitis mimicking Richter's transformation (RT) in a CLL patient.

Case Presentation: A 62-year-old male with a history of treated Rai Stage I CLL presented with a mildly painful, firm, and tender right inguinal mass, leukocytosis with lymphocytic predominance, mild normocytic anemia, and elevated lactate dehydrogenase. Our patient quickly developed fevers, fatigue, pain, and weight loss. PET/CT showed bulky and mildly hypermetabolic right inguinal lymphadenopathy, raising suspicion for RT. Core needle biopsy revealed CD5+ B-cell lymphoma and positive immunostains for HSV-1 and HSV-2. The patient's presentation was determined to be a CLL recurrence with an HSV infection. The patient was treated with Acyclovir for 21 days, followed by prophylactic Valaciclovir. The patient's inguinal mass subsequently shrank with concomitant improvement of his B symptoms. He was then deemed stable to proceed with CLL treatment with daily Venetoclax and monthly rituximab infusions.

Discussion: Richter's Transformation is a type of progressive CLL that worsens the patient's prognosis and often requires rapid alterations to patient care. Although most patients with progressive CLL present asymptomatically, certain individuals may exhibit classic symptomatology that includes lymphadenopathy, elevated serum lactate dehydrogenase, fever, night sweats, and weight loss. HSV lymphadenitis closely resembles these lymphomatous processes. CLL patients are particularly susceptible to severe viral infections not only due to the immunosuppressive effects of CLL therapies, but the disease itself also poses significant immune defects. CLL B cells have elevated levels of HSV entry mediator and CLL T-cell population subsets show Th2/Th1 imbalances along with increased presence of regulatory T cells. While these changes favor immunity against extracellular parasites, CLL patients are left more vulnerable to viral infections. This case highlights the importance of considering atypical presentations of dormant viral infections in the setting of CLL recurrence, which can be treated with antiviral therapy, especially in progressive cases with poorer prognosis.

123. Acute Cholecystitis Secondary to Gallbladder Volvulus

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Introduction: Gallbladder volvulus is an incredibly rare cause of acute cholecystitis, with only a few cases described in the literature. The etiology is unknown, as the gallbladder, usually attached to the cystic plate, cannot freely rotate within the peritoneum [1]. It has previously been hypothesized that an abnormally long mesentery or abnormal vascular pedicle leads to volvulus, with diagnosis often made at the time of surgery [1].

Case Presentation: A 93-year-old female with history of CAD, T2DM, HTN, HLD who presented with a four-day history of abdominal pain and was found to have acute cholecystitis with gallbladder volvulus on CT scan. She subsequently underwent laparoscopic cholecystectomy and intraoperatively was found to have gangrenous cholecystitis with volvulus of the mid-body of the gallbladder. Following cholecystectomy, the patient was maintained on antibiotics and was ultimately discharged home.

Discussion: Gallbladder volvulus occurs when the gallbladder rotates on its axis, causing subsequent interruption of blood supply and bile flow, presenting as acute cholecystitis [2]. In elderly patients, it is hypothesized that the lack of visceral fat and cystic artery tortuosity leads to an increased incidence [1]. The decision to operate on acute cholecystitis in the elderly patient can be difficult due to the comorbidities associated with general anesthesia and major abdominal surgery [3]. In the case of volvulus, delayed intervention can lead to perforation, septic shock, and death [1, 2]. We present a case of gallbladder volvulus in an elderly patient diagnosed on imaging and successfully managed with laparoscopic cholecystectomy.

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124. Treatment of Patients with Diabetic Foot Ulcers in Kalamazoo by Multidisciplinary Teams: Patterns Between Referral and Patient Outcomes During COVID-19

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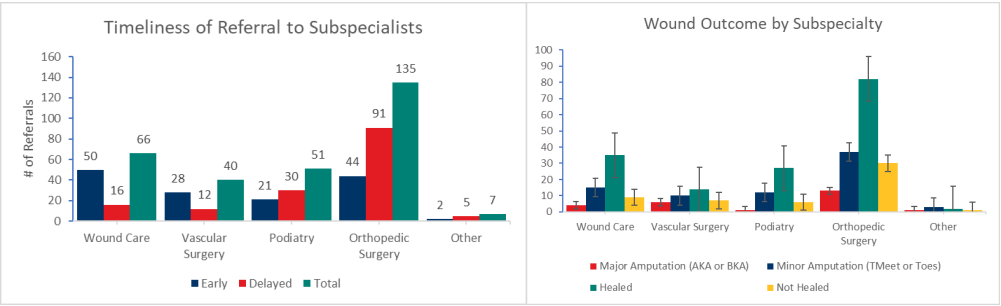
Project Background: One of the most debilitating sequelae of diabetes is the risk of limb amputation secondary to ulcers. However, these events may be preventable with early intervention. Our hypotheses are a) Delayed referral results in an increased major amputation rate and b) wounds diagnosed during the COVID-19 pandemic have a higher amputation rate.

Methods: This study was a retrospective cohort record review. Inclusion criteria: patients with type 2 diabetes mellitus, age greater than 30 years, lower extremity wound diagnosis seen at an outpatient facility. Patients were seen between June 1, 2018 - December 31, 2021. These dates served as a point-of-entry and patients were followed until resolution, expiration, amputation, or lost to follow-up. Subjects were identified through the WMed EHR. An early referral was defined as <4 weeks. Referral providers evaluated were Wound Care, Vascular surgery, podiatry, orthopedic surgery, and other. All procedures were carried out according to the protocol approved by the WMU Homer Stryker MD School of Medicine IRB (IRB 2022-0889).

Results: Overall, 187 patients met the inclusion criteria. The referral time for 135 patients was reviewed, 91 patients had early referrals and 44 had late referrals suggesting there is a significant difference in referral times (p<0.001). For patients in the wound care group, delayed referrals resulted in significantly more major amputations than those in the early referral group (p = 0.04). Between groups, there was a significantly higher proportion of early referrals to wound care (n = 50, < 0.001) and orthopedic surgery (n = 44, < 0.001). The other provider types had an adjusted p-value >0.01. Our results also displayed a significant increase in the proportions of amputations during the COVID-19 pandemic (pre = 74, post = 102, p = 0.03).



Conclusions: We conclude that there is variation in referrals for diabetic ulcer patients. Patients with delayed referral to wound care had significantly higher rates of major amputations. There were significantly higher rates of early referral to the wound care and orthopedic surgery groups indicating a referral pattern in Kalamazoo. There was a higher proportion of amputations during COVID-19 which may be due to detection lapses during COVID-19 restrictions.

125. The Effect of PEDOT Concentrations on MEW PEDOT Scaffold Mechanical Properties

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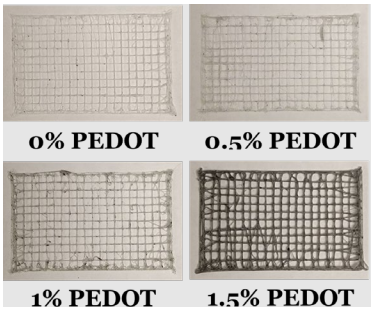
Introduction: Bone-related injuries continue to be a growing concern within the healthcare community. To resolve this problem, we propose fabricating melt-electrowritten scaffolds using an electroconductive polymer made via a mixture of polycaprolactone (PCL) and GO/DMSO-doped PEDOT, to promote bone regeneration. In order to support proper bone growth, the PEDOT scaffolds must be able to maintain structure and mimic the mechanical properties of its surrounding native tissue. Having demonstrated the biocompatibility and noncytotoxicity of these MEW scaffolds, we now aim to evaluate the printability and mechanical properties of PCL-[GO/DMSO-doped PEDOT] scaffolds to determine if these scaffolds are viable substrates for recapitulating the bone environment.

Methods: PEDOT nanoparticles were synthesized by oxidative polymerization of the 3, 4-ethylenedioxythiophene monomer (EDOT) in the presence of GO, DMSO, and ferric chloride. PCL was mixed with PEDOT and melted in a microwave to create mixtures of 0%, 0.5%, 1%, and 1.5% PEDOT. Composites were loaded into the Axo-A3 3D bioprinter (Axolotl Bio) and melt-electrowriting was conducted using an electrical field of 5 kV. Scaffolds with the various concentrations of PEDOT underwent mechanical testing in order to evaluate their mechanical properties.

Results: Scaffolds using the PCL-[GO/DMSO-doped PEDOT] electroconductive polymer were successfully printed using melt electrowriting (Figure 1). The printing process did not demonstrate any major issues or errors, and all scaffolds were found to print completely and appeared structurally sound.

Future Work/Clinical Significance: Since the scaffolds have demonstrated successful printability, they will undergo mechanical analysis to evaluate their mechanical properties. Ultimately, we hope to implant promising scaffolds within bone defects in vivo and use electrical simulation to conceivably promote bone regeneration.



126. An Acquired Factor V Inhibitor Successfully Treated with Rituximab: A Case Report

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Introduction: It is uncommon to acquire inhibitors toward factor V (FV), with an incidence of 0.023 to 0.09 per million people each year. The clinical presentation of an acquired FV inhibitor varies widely, from asymptomatic abnormalities in laboratory values to critical life-threatening hemorrhage. We report the case of a patient with an acquired FV inhibitor who showed a complete response to rituximab and glucocorticoids.

Case Presentation: A 58-year-old male with history of chronic obstructive pulmonary disease and a severe COVID-19 infection resulting in tracheostomy and gastrostomy tube dependence presented to the hospital due to behavioral and psychiatric issues. The patient later developed oozing at the peripheral IV and tracheostomy sites and was found to have markedly abnormal coagulation findings. He had an elevated aPTT greater than 200.0 s, an elevated PT of 58.0 s, an elevated INR of 6.78, hemoglobin of 11.6 g/dL, and elevated fibrinogen. A 1:1 mixing study did not correct the aPTT and PT indicating the presence of a circulating inhibitor. Specific factor assays showed a FV level of <1% and FV inhibitor activity level of 184.3 Bethesda units/mL. The patient was given blood products, glucocorticoids, and intravenous immunoglobulin with partial improvement. The patient's coagulopathy only significantly started correcting with rituximab.

Discussion: Our patient did not present with catastrophic bleeding and had a few episodes of epistaxis and oozing. Infections and/or medications were high in the differential as causes associated with the development of FV inhibitors. Also, COVID-19 has also been reported as a potential factor in the development of factor inhibitors including two cases of FV inhibitor acquisition following COVID-19 infection. No definitive treatment has been established for an acquired FV inhibitor and treatment is typically unnecessary for asymptomatic patients. Other options, such as the bypassing agent recombinant activated factor VII (rFVIIa), cyclophosphamide, and plasmapheresis, were reserved for severe bleeding but ultimately not required. We added the immunosuppressive anti-CD20 monoclonal antibody rituximab. After four weeks of treatment with rituximab and glucocorticoids, there was a significant improvement in his coagulopathy, and he was discharged with a prednisone taper.

127. Myomatous Erythrocytosis Syndrome: A Case of Uterine Fibroid Associated with Erythrocytosis

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Introduction: Myomatous Erythrocytosis Syndrome (MES) is a rare syndrome of uterine fibroids associated with significant erythrocytosis. The diagnosis of MES is typically done retrospectively as it requires surgical removal of the myoma to restore normal hematologic values.

Case Presentation: A 55-year-old post-menopausal woman presented with fatigue, easily bleeding gums, occasional shortness of breath, and sleep disturbances found to have marked erythrocytosis on routine bloodwork. Her RBC count was 6.76 million/mm^3, hemoglobin 19.5 g/dL, and hematocrit 63%. Previous hemoglobin six months prior was 15.0 and hematocrit of 46.6%. EPO levels were mildly elevated at 20.1 iU/ml. Most notably, molecular studies were negative for JAK2 V617F, JAK2 exon 12–15 mutations, along with other primary and secondary causes of erythrocytosis including athletic performance enhancing agents, renal causes, and pulmonary causes. CT of the abdomen and pelvis revealed a large mass occupying nearly all of the dorsal myometrium, indicative of a very large fibroid. Patient underwent radical hysterectomy with bilateral salpingo-oophorectomy, after which her hematologic parameters returned to normal within a few weeks, confirming a diagnosis of MES.

Discussion: MES is one of several EPO secreting tumor-associated polycythemia syndromes that can lead to unnecessary phlebotomy. There are only 40 cases of MES reported over the past six decades. Interestingly, MES is not linked to JAK2 mutations. Recent studies suggest that MES is caused by high production of EPO in myomatous tissues due to intramyomatous arteriovenous shunting causing local hypoxia. Diagnosis of MES can only be done retrospectively by the return of EPO levels to baseline after resection of the fibroid. Therefore, clinical vigilance and exclusion of other causes of erythrocytosis are crucial prior to surgical intervention. After removal of the fibroid, patients tend to not need any further treatment.

128. Elbow Gout Resulting in Triceps Tendon Rupture: A Case Report

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Background: Gout is a common form of inflammatory arthropathy caused by the deposition of uric acid crystals in tissue. Gouty infiltration of tendon tissue can lead to tendinopathy and rupture. However, gout-induced tendon rupture of upper extremities is extremely rare, with only six cases reported in existing literature, none of which were located in the triceps tendon.

Case Presentation: A 53-year-old male with a history of gout presented with pain, weakness, and decreased range of motion primarily in his left elbow one month after impact in a car collision. MRI was obtained which showed a rupture of the triceps tendon. The patient was taken to the operating room for primary repair of his left triceps tendon. Notably, the patient presented 9 months later with right elbow pain and was diagnosed with a right triceps tendon repair. Similarly, there was significant gouty infiltration present in his right olecranon bursa and surrounding the tendon. He did well after repair of both of his triceps' tendons.

Conclusions: We report the first case of gout-induced tendinopathy and rupture of the triceps tendon, diagnosed through intraoperative observations. For patients diagnosed with triceps tendon rupture and with a history of gout, the possibility of gout-induced tendinopathy and subsequent rupture should be considered. Patients should be counseled about these increased risks of tendon rupture in clinic.

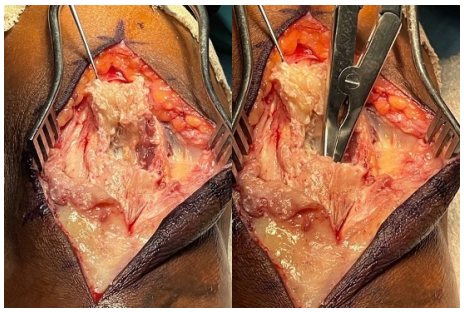

Figure: Gross anatomy images of gout crystals surrounding triceps tendon

132. Robotic Spleen-Sparing Distal Pancreatectomy in a Pediatric Patient with a Solid Pseudopapillary Tumor

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Purpose: We present a video showing the use of robotic technology to perform a spleen-sparing distal pancreatectomy of a rare tumor in a pediatric patient. The video also highlights the technique of suturing for retraction, decreasing the need for extra trocars.

Case Presentation: An 11-year-old female was found to have an incidental distal pancreatic mass on CT as part of her evaluation following a motor vehicle accident. MRCP confirmed the findings and showed no local invasion into surrounding structures. She only had complaints of vague intermittent abdominal pain and was otherwise asymptomatic. Her abdominal exam was soft, and nontender. The patient underwent a robotic spleen-sparing distal pancreatectomy. Dissection was performed using the vessel sealing device as well as hook electrocautery. The pancreas was divided using an endostapler with a blue load. The staple line was oversewn with silk suture in a continuous fashion, then covered with fibrin glue and an omental patch. A drain was placed.

Results: Operative duration was 5.25 hours. Estimated blood loss was 10 ml. The patient had an uneventful postoperative course and was discharged home on postoperative day 5 after drain removal. Pathology revealed a solid pseudopapillary tumor (Frantz tumor) that was 3.6 cm x 3.2 cm x 2.5 cm in size, well encapsulated, with a 0.8 mm margin. There was no lymphovascular or perineural invasion. Current management guidelines recommend surgical resection as the mainstay of treatment with no clear role for chemotherapy. Regular follow up with annual or semi-annual imaging studies is recommended. 5-year survival rate has been found to be 97% even if metastases are present at the time of diagnosis.

Conclusion: This video demonstrates the use of robotic technology for curative resection of a rare distal pancreatic tumor in a pediatric patient.

133. A Rare Case of Acute Concomitant Aortic and Pulmonary Dissection

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Introduction: Pulmonary artery (PA) dissection is a rare and fatal condition often with rapid progression to death [1]. There are limited case reports of acute aortic dissection with concomitant pulmonary artery dissection [2]. Rapid progression to cardiac tamponade and cardiogenic shock is often lethal with most patients diagnosed on post-mortem examination.

Case Presentation: We report a rate case of a 74-year-old male with known coronary artery disease and tobacco abuse who was initially admitted with a non-ST segment myocardial infarction. He underwent cardiac catheterization and urgent 5-vessel coronary artery bypass grafting. His post-operative course was uncomplicated, and he was discharged at home in stable condition on post-operative day 5. He presented to an outside emergency room on post-operative day 6 with complaints of shortness of breath and initial CT scan of the chest showed small pleural effusions but was otherwise unremarkable. He was transferred back to the operative hospital for further care and monitoring. At the time of admission to the operative hospital the patient strained to have a bowel movement at which time he became diaphoretic and lightheaded. He then complained of new arm numbness and was found to have no pulses in the left upper extremity. An urgent CT angiogram was performed which showed a new Stanford Type A aortic dissection with concomitant main pulmonary artery dissection. The family elected to pursue comfort measures and the patient ultimately expired one hour following his CT angiogram.

Discussion: Pulmonary artery with simultaneous aortic dissection is extremely rare with few cases reported in the literature. Given the high lethality, timely diagnosis and rapid surgical intervention are prudent to reduce mortality [2]. We suspected that the dissection occurred secondary to straining while having a bowel movement.

References:

Hsu, HH., Tzao, C., Tsai, CS. et al. Acute concomitant pulmonary artery and aortic dissection with rupture. Int J Cardiovasc Imaging 23, 411–414 (2007). https://doi.org/10.1007/s10554-006-9160-1

Hostiuc S, Dermengiu C, et al. Sudden Death Due to Dissection of the Thoracic Aorta Associated with Dissection and Rupture of the Pulmonary Artery: Report of Two Cases. https://www.clinicalkey.com/#!/content/playContent/1-s2.0-S0379073813005550?returnurl=https:%2F%2Flinkinghub.elsevier.com%2Fretrieve%2Fpii%2FS0379073813005550%3Fshowall%3Dtrue&referrer=

134. Periodic Spontaneous Hypothermia Syndrome (PSHS): Looking Beyond Shapiro Syndrome

Ruqiya Shama Tareen, MD, Vidur Solanki, MD, Salman Abdul Majeed, MD
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Background: PSHS is an extremely rare condition, only around 70 cases has been reported since initially it was identified in 1969 as Shapiro syndrome, which is characterized by a triad of episodic hypothermia, hyperhidrosis, and agenesis of corpus callosum. The underlying mechanism is not fully understood however some form of hypothalamic dysfunction especially in posterior nucleus area, neurotransmitter disequilibrium especially of Dopaminergic system, inflammatory process, autoimmune disorders like multiple sclerosis and epilepsy has been associated. Recently it has been postulated that PSHS is a variant of Shapiro syndrome. Episodic hypothermia seen in severe COVID cases there is renowned interest in this area.

Case Report: Patient is a 62-year-old single female, on disability and lives in an AFC for last 20 years. She was brought to the ED by police after she was found wandering in Walmart late at night. She has recurrent episodes of hypothermia, type 2 diabetes, CKD stage III, schizoaffective disorder-bipolar type, mild intellectual disability. At the time of presentation her core body temp was 90.3 ^{o}F (32.4 ^{o}C). Current home medications include Atorvastatin, Klonopin 0.5mg, ferrous sulfate, multivitamin and vitamin C. She has been treated at Community Mental Health for schizoaffective disorder but not on antipsychotics since hospitalization with PSHS in December 2022. There is no history of substance abuse. This is the patient's 4th presentation with hypothermia to this hospital since Feb 2021.

Lab work & Imaging: - CMP: Creatinine 1.3, Albumin 3.1, ALP 188, AST 151, ALT 143.CBC: WMC 2.1, Hgb 9.4, HCT 29.3, Platelets 44. U/A: LE ++ve, Nitrite and Bacteria +ve. UDS: negative. CT scan of the brain was negative. MRI f 3/15/2022: prominent hyperintense signal abnormality involving the bilateral globi pallidi, new compared to 3/27/2018. Repeat MRI pending. The patient is on antibiotics for UTI and started on Cyproheptadine 4 mg TID a first line treatment in PSHS.

Conclusion: PSHS is a very rare disease which is still very ill defined thus making it difficult to identify and treat it properly. By this presentation we hope that we can enhance the understanding of PSHS to help treat patients with PSHS in a better way.

137. Quality of Life and Treatment Outcomes after Peritonsillar Abscess Treatment Following a New Emergency Department Protocol

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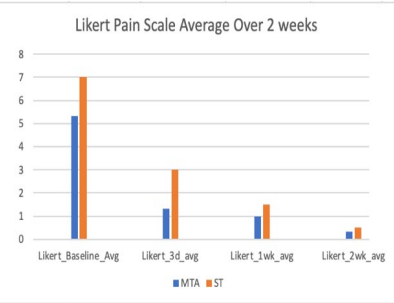
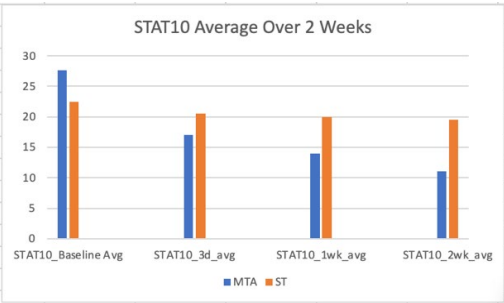
Introduction: Peritonsillar abscess (PTA) is an infection of the oropharynx and is a pus-filled pocket that forms behind the tonsils. This is the most common deep neck space infection affecting more than 30 per 1,000 individuals every year [1,2]. Left untreated, PTA may spread and cause complications including airway compromise, aspiration, and extension into deep neck spaces [3]. Traditionally, PTA is managed with surgical therapy (ST) via incision and drainage (I&D) or needle aspiration (NA), followed by medical therapy, including antibiotics with or without steroids. This treatment is effective with PTA recurrence rates of ≤ 10% for ST [4]. ST has the potential to induce anxiety, increased pain, more prescription opioid requirements, and more days off from work compared to treatment with medical therapy alone (MTA) [5]. MTA is being adopted as standard of care for PTA as no significant difference in treatment failure has been found [6,7,8]. Previously, a treatment algorithm for PTA in the ED was devolped8. We will measure quality of life (QOL) via patient-reported outcome surveys. The primary objective is to demonstrate that patient QOL is improved under this treatment protocol.

Methods: Bronson Methodist ED records are checked daily for PTA patients. Patients meeting inclusion criteria are consented and administered a baseline survey, including: (1) the Sore Throat Assessment Tool 10 [STAT-10], (2) A Likert pain scale of 0 to 10, and (3) an assessment of pain medication used in the last 24 hours. Surveys are readministered at 3-, 7-, and 14-days post-treatment.

Results: Preliminary results comparing ST versus MTA are limited by number of complete survey responses (n=5). There may be a trend supporting MTA over ST regarding QOL over 2 weeks.

Conclusion/Clinical significance: Though recent data demonstrates the efficacy of MTA compared to ST, there is a paucity of literature exploring QOL in patients suffering from PTA. It is imperative that we are considering anxiety, pain, opioid requirements, and time-off from work, and the like when treating patients.





Acknowledgements: We would like to acknowledge Aaron Zeblosky, MD and Jack Dewey, MD for their work on the inception of this project.

WMed-2021-0815

138. No Difference in Bleeding Complications in Patients on Concomitant Nonsteroidal Anti-Inflammatory Drugs and Oral Anticoagulant Therapy after Total Hip Arthroplasty

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INTRODUCTION: To minimize the risk of blood loss, it has been recommended that patients taking oral anticoagulants (OAC) avoid non-steroidal anti-inflammatory drugs (NSAID) following orthopaedic procedures. However, there is a paucity of literature that observes whether concomitant NSAID usage is associated with hematologic complications in these patients. Therefore, the purpose of this study was to compare the incidence of hematologic complications in those taking both OACs and NSAIDs following total hip arthroplasty (THA) when compared to those only taking OACs.

METHODS: A retrospective cohort analysis of patients undergoing elective primary THA was conducted using a large national claims database. Patients were stratified into two cohorts: those with postoperative prescription claims (within 30 days) for OACs alone and those with claims for NSAIDs and OACs. Patients with malignancy or THA indicated for fracture were excluded. The cohorts were matched in a 1:1 ratio for age, gender, and Charlson Comorbidity Index. Bivariate analysis was performed comparing 7, 14, and 30-day hematologic complications following THA. Subsequently, a multivariable logistic regression was performed, while controlling chronic NSAID use, history of prior venous thromboembolism, history of a bleeding disorder, history of liver disease, and history of a gastrointestinal bleed.

RESULTS: Following matched analysis, patients with NSAIDs and OACs within 7 days of undergoing THA had no significant difference in the incidence of posthemorrhagic anemia ($p = 0.127$), bleeding complications ($p = 1.00$), and blood transfusions ($p = 0.609$) when compared to patients with OACs alone. Similarly, no difference was observed at 14 and 30-day time points. Patients with NSAIDs and OACs within 30 days of undergoing THA had significantly lower odds of deep vein thrombosis (odds ratio; 95% CI; p-value [0.71; 0.64 - 0.79; <0.001]) and pulmonary embolism (0.63; 0.55 - 0.73; <0.001) when compared to patients with prescription claims for OACs alone.

CONCLUSION: This study found no difference in bleeding risk and decreased risk for VTE with concomitant NSAID and OAC therapy after THA in a national database, suggesting it may be reasonable for select patients to receive NSAIDs as part of multimodal pain management and VTE prophylaxis in the postoperative period following THA.

140. Concomitant Distal Claviculectomy is Associated with Higher Reoperation Rates to the Distal Clavicle Following Rotator Cuff Repair

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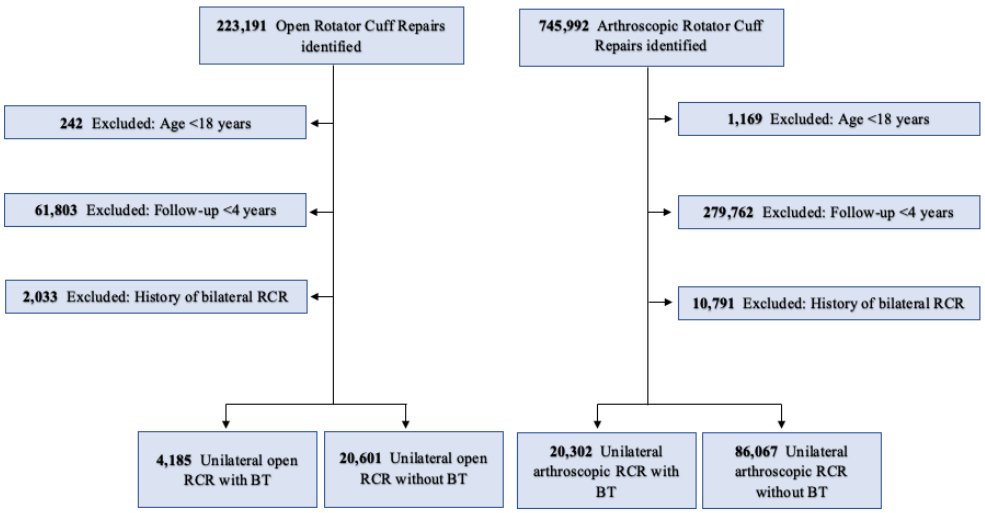
BACKGROUND: Current literature has shown differing views on the efficacy of concomitant distal claviculectomy (DC) during rotator cuff repair (RCR) in preventing reoperation. Therefore, the purpose of the study was to investigate the reoperation rate between RCR with DC and RCR performed without DC.

METHODS: A retrospective cohort analysis was performed utilizing a national claims database. Patients undergoing open or arthroscopic primary rotator cuff repair with or without concomitant DC were identified using Current Procedural Terminology (CPT) and International Classification of Diseases (ICD) 10 codes. The primary outcome was 4-year shoulder reoperation rates. To account for the laterality of the index procedure and reoperation, laterality-specific ICD-10 codes were paired with the CPT codes for each operation. Univariate analysis was performed using Chi-Squared or Student T-tests. Multivariable analysis was conducted using a logistic regression.

RESULTS: A total of 131,232 patients undergoing RCR were included in our analysis. Of those, 39,941 underwent concomitant DC while 91,291 did not. After controlling for patient comorbidities and demographics, patients who underwent RCR with DC were associated with significantly higher odds of requiring a subsequent DC procedure (OR: 1.49; 95% CI: 1.35 – 1.64; p = <0.001) but significantly lower odds of any reoperation (OR: 0.87; 95% CI: 0.83 – 0.91; p = <0.001) in the ipsilateral shoulder within 4 years of index procedure compared to those who underwent RCR without DC.

CONCLUSION: Although associated with a lower rate of overall reoperations within 2 and 4 years of RCR, those who underwent RCR with DC were 85% more likely at 2 years and 49% more likely at 4 years to undergo reoperation of the distal clavicle when compared to those without concomitant DC.



141. The Deficiency of the Early B cell Protein λ5 Leads to Accelerated Bone Aging

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Introduction: Progenitor B cells express λ5 and μ heavy chain (μHC), both key components of the preB cell receptor (preBCR) whose expression regulates early B cell development. Progenitor B cell numbers and λ5 expression decline with age, paralleling the decline in bone mass that marks skeletal aging. Both progenitor B cells and bone cells share are housed in same bone marrow microenvironment niche. This suggests their possible crosstalk.

Methods: Young, one-month old λ5 deficient ($\lambda5^{-/-}$) mice, μHC deficient ($J_H^{-/-}$) mice and double deficient ($J_H^{-/-}\lambda5^{-/-}$) mice, had normal bone mass. However, whereas adult, six-months old $J_H^{-/-}$ mice had normal bone mass, bone mass in single $\lambda5^{-/-}$ and in double mutant $J_H^{-/-}\lambda5^{-/-}$ mice had declined below the level expressed by aged, 22-months old WT mice, suggesting accelerated bone aging.

Results: Irradiated double mutant $J_H^{-/-}\lambda5^{-/-}$ mice reconstituted with WT bone marrow showed recovery of trabecular bone, whereas transfer of $J_H^{-/-}\lambda5^{-/-}$ marrow into irradiated WT mice led to trabecular bone loss. Screening for additional cellular sources of λ5 led to identification of a subset of mesenchymal λ5 protein expressing stromal cells (MSCs). The numbers of λ5-expressing MSCs also decreased with age. Studies are underway to assess the role of known λ5 ligands (e.g., heparan sulfate, galectins and cadherins) in bone homeostasis.

Conclusion: We have shown that λ5 is expressed by both progenitor B cells and MSCs and influences bone mass during aging. λ5 may be a novel therapeutic target for age related decrease in bone mass.

142. Medical Student Community Garden: Growing Healthy Habits with the Kalamazoo Community

Tiffany Hangse, BA, Jennifer Vosters, BS, Noelle Fukuda, BS, Samantha Mazurek, BS, Erik Larson, PhD
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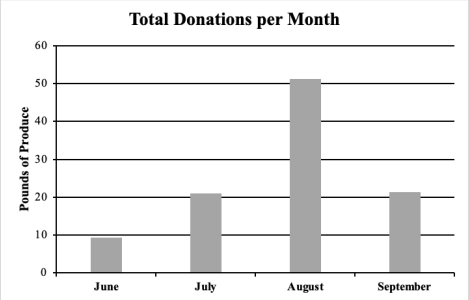
Introduction: In Kalamazoo, Michigan, 1 in 10 children are considered food insecure [1]. Children living in these communities, often composed of people of color, have increased risk of co-morbidities such as type 2 diabetes and obesity [2]. Therefore, increasing access to nutritious foods and adequate nutritional education must be addressed. The Garden Interest Group (GIG) was formed by first-year medical students in 2021, with the intent to contribute to resolving these issues.

Methods: An all-school survey for an on-campus garden was sent. Receiving positive feedback, GIG then collaborated with the Dean, Facilities, Departments of Wellness and Student Affairs, and Office of Development and Alumni affairs for funding.

Supplies/Equipment: Four 8' x 4' galvanized steel planting beds and soil were purchased. Plants, including zucchinis, tomatoes, and lettuce, were donated by local greenhouses [Fig].

Medical school community involvement: The WMed community was invited to the initial planting day. Afterwards, a weekly watering volunteer schedule was sent.

Results: Over a four-month period, approximately 110 pounds of produce were donated [Fig], with the vast majority going to Kalamazoo Gospel Ministries (KGM) and Loaves and Fishes, two local food banks. Additional produce went towards the WMed community through basket donations and an end-of-the-year Spaghetti Night Dinner made from garden produce.



Produce	Total Amount Harvested
Lettuce	6 bags
Kale	2 bags
Broccoli	8
Banana Peppers	70
Bell peppers	14
Cayenne peppers	65
Habaneros	22
Zucchinis	27
Cucumbers	53
Chives	3 bunches
Basil	0.5 bags
Gooseneck squash	1
Cherry tomatoes	43

Conclusions: GIG's first year donations exceeded expectations and importantly, helped raise awareness about food insecurity and nutrition through community engagement both within WMed and Kalamazoo. GIG plans to continue these efforts through a small-scale outreach to a local elementary school [Fig]. By initiating hands-on lessons on gardening and nutrition, the aim is to evaluate whether medical student led interventions can have a positive impact on the health behaviors of children. Thus, GIG hopes to contribute to long-term wellness and food security within the community.

References: [1] Renée Johnson, Renee. "Defining Low-Income, Low-Access Food Areas (Food Deserts) - Congress Renée Johnson." Congressional Research Service, 1 June 2021, https://crsreports.congress.gov/product/pdf/IF/IF11841. [2] Kelli, Heval M., et al. "Association between Living in Food Deserts and Cardiovascular Risk." Circulation, vol. 10, no. 9, 1 Sept. 2017, https://doi.org/10.1161/circoutcomes.116.003532.

143. Cystic Fibrosis Lung Transplant Transition Regional Dissemination Network, Current and Future Quality Improvement Initiatives at the WMed Cystic Fibrosis Program

Jessica Ziccarillo, Medical student, Carolina Herrera, RRT, Debra Wells-Schmidt, RN, Sally Bonnema, RD, Nichole Vess, RN, Teresa Bailey, PharmD, BCPS, BCACP, FCCP, Julie Hovey, MA, Nia Jacob, LphT, Mariam Ischander, MBChB
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Introduction: In February of 2022, the Western Michigan University Homer Stryker M.D. School of Medicine Cystic Fibrosis (CF) Program identified the need for quality improvement (QI) in the lung transplant referral process. The National Cystic Fibrosis Foundation initiated the CF Lung Transplant Transition (LTT) Regional Dissemination Network (RDN) as a part of a nationwide effort to support new CF referring programs, adapt best practices, create high performing CF LTT processes and systems, connect CF Referring and Lung Transplant Programs, and improve care for cystic fibrosis patients with advanced lung disease. The WMed CF Program joined Wave 7 of the RDN and was paired with the Spectrum Health lung transplant team. Over the last year, the WMed CF Program has been working to improve CF lung transplant transition processes and systems by focusing on effective communication and both patient and team education. One of the goals of WMed CF Program was to improve CF team knowledge about CF lung transplant by 30%.

Methods: Shortly after the launch of the CF LTT RDN, bimonthly meetings were held between the WMed CF Program team and the RDN QI team coach to discuss how to best use QI tools to meet its goals. Additionally, monthly regional meetings with the other Michigan teams were conducted to allow teams to "share generously and steal shamelessly" in an effort to improve care for all. Team CF lung transplant knowledge was assessed with a baseline survey, then tested again after a literature review and a lecture from Spectrum Health.

Results: On the baseline staff knowledge survey, initial results were 52%. Following literature review, this increased to 70%, and following lecture, 84%. This result falls just short of the 30% improvement goal (Figure 1).

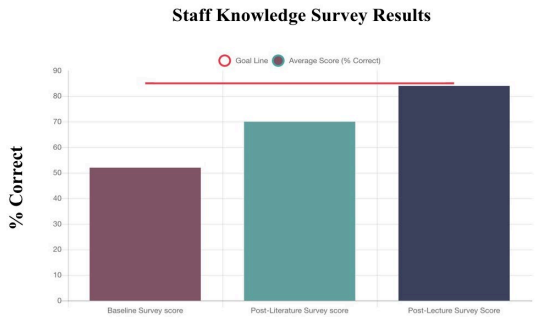

Figure 1: Staff knowledge survey results, falling just shy of goal.

Conclusion: With the guidance of the CF LTT RDN, the WMed CF Program has already made great strides towards quality improvement. Additionally, future initiatives on patient education are already being planned with the goal of creating a comprehensive, standardized patient education presentation & packet to add into the clinic workflow by the end of 2023.

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*If no program code was given for a submission, then this will show the submission serial number

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