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Research Day

WMU Homer Stryker M.D. School of Medicine

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4-2022

## Research Day 2022 Program

Western Michigan University Homer Stryker M.D. School of Medicine  
*Western Michigan University Homer Stryker M.D. School of Medicine*

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A vertical banner with a light blue background and a blurred image of a microscope. The text '2022 RESEARCH DAY' is written vertically in large, white, sans-serif capital letters.

2022  
RESEARCH DAY

40<sup>th</sup> Annual Kalamazoo  
Community Medical &  
Health Sciences

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CELEBRATING  
RESEARCH

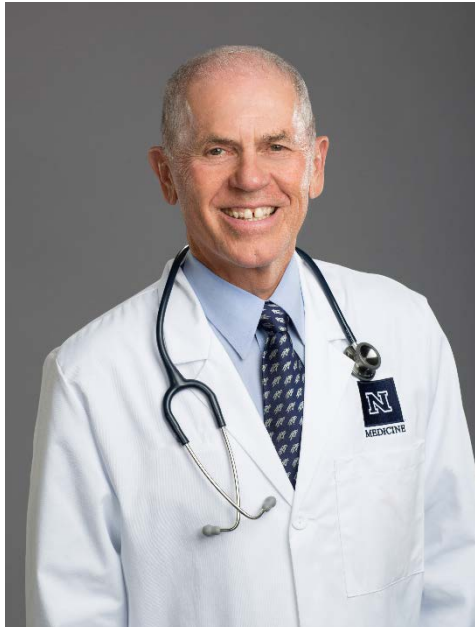
TRANSFORMING  
HEALTH

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WMU Homer Stryker M.D.  
School of Medicine  
W.E. Upjohn M.D. Campus



## KEYNOTE SPEAKER



### **Thomas L. Schwenk, MD**

Former Dean of the School of Medicine and Vice  
President of Health Sciences,  
University of Nevada, Reno

Former Chair, Department of Family Medicine,  
University of Michigan Health System

Thomas L. Schwenk, MD, recently retired as Dean of the School of Medicine and Vice President of Health Sciences at the University of Nevada, Reno, having served in those positions since July 2011. Dr. Schwenk was previously on the faculty of the University of Michigan Health System, where he was a member of the faculty for 27 years and served as Chair of the Department of Family Medicine from 1986-2011.

Dr. Schwenk earned his B.S. degree in chemical engineering and M.D. from the University of Michigan. Following residency training in family medicine at the University of Utah, he practiced in rural Utah and served on the faculty of the University of Utah for several years, where he also completed a research fellowship. He is board-certified in Family Medicine and Sports Medicine.

He has served on the Board of Directors of the American Board of Family Medicine (2000-2005, vice president 2004-2005), and was elected to the National Academy of Medicine in 2002. He also served for four years on the Administrative Board of the Council of Deans of the Association of American Medical Colleges. Dr. Schwenk's research has focused on the care of patients with depression and mental illness in primary care, with a recent emphasis on mental health and wellness in medical students, residents, and physicians. He has co-authored over 160 publications and has consulted to over 50 medical schools and teaching hospitals in various capacities.

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The complete program including abstracts is available on the WMed website:

<https://med.wmich.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.

Credit amount subject to change.

### **IPCE Credit**

This activity was planned by and for the healthcare team, and learners will receive 1.5 Interprofessional Continuing Education (IPCE) credits for learning and change.

### **Physicians**

Western Michigan University Homer Stryker M.D. School of Medicine designates this live activity for a maximum of 1.5 *AMA PRA Category 1 Credits*<sup>™</sup>. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

## **DISCLOSURES**

Please see the handout offered at the registration table for a listing of disclosure statements from today's presenters.

Dear Colleagues,

On behalf of the Organizing Committee Members, I am very pleased to welcome you to the 40<sup>th</sup> Annual Kalamazoo Community Medical and Health Sciences Research Day.

The commitment and participation of Western Michigan University Homer Stryker M.D. School of Medicine (WMed), its faculty, and the Kalamazoo scientific community in “Research Day” continues on this day marking a 40<sup>th</sup> anniversary milestone. Overall, 91 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 (WMU) for their research collaboration with our medical 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 of time to endeavor to bring you an exceptional learning and networking opportunity. Members of this year’s committee were:

Adil Akkouch	Yvonne Jackson	Harrison Seltzer
Andrew Alfred	Krishna Jain	Mahesh Shrestha
Laura Bauler	Liz Lorbeer	John Spitsbergen
Karen Bovid	Consuelo Obaid	James Springstead
Sandra Cochrane	Juliana Overbey	Julie Torrence
Mireya Diaz Insua	Maureen Owens	Ramona Wallace
Jack Dewey	Christine Pink	Daphne York
Nichol Holodick	Courtney Puffer	

We hope this year’s Research Day will inspire you to pursue your own research and to, as well, support the basic, medical, and healthcare research of our southwestern Michigan community colleagues.



Adil Akkouch, PhD  
Chair 2022 Research Day

## ACKNOWLEDGMENTS

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

### WMed Office of the Dean

Julie Torrence

Chelo Obaid

Kate Butler

### WMed Departments Chairs

<b>Name</b>	<b>Department</b>
Tom George, MD; Tristan Wilson, MD	Anesthesiology
Philip Kroth, MD	Biomedical Informatics
David Riddle, PhD	Biomedical Sciences
David Overton, MD	Emergency Medicine
Lisa Graves, MD	Family and Community Medicine
Thomas Rothstein, MD, PhD	Investigative Medicine
Michael Busha, MD, MBA	Medical Education
Tyler Gibb, PhD, JD; Michael Redinger, MD, MA	Medical Ethics Humanities and Law
Elizabeth Lorbeer, EdM	Medical Library
Santhosh Koshy, MD, MBA	Medicine
Marijo Snyder, MD	Obstetrics and Gynecology
Keith Kenter, MD	Orthopedic Surgery
Joyce deJong, DO	Pathology
Dilip Patel, MD, MBA	Pediatric and Adolescent Medicine
Rajiv Tandon, MD	Psychiatry
Brandon Tommina, MD	Radiology
Robert Sawyer, MD	Surgery

### Abstracts Reviewers for Research Day 2022

Adil Akkouch	Lisa Graves	Christine Pink
Andrew Alfred	Jeffrey Greene	Harrison Seltzer
Laura Bauler	Nichol Holodick	Mahesh Shrestha
Katherine Beenen	Mireya Diaz Insua	John Spitsbergen
Karen Bovid	Miriam Ischander	Timothy Trichler
Sandra Cochrane	Krishna Jain	Erica VanderKooy
Jayce DeLeon	Liz Lorbeer	Timothy VanderKooy
Jack Dewey	Joshua Mastenbrook	Peter Vollbrecht
Maureen Ford	Thomas Melgar	Ramona Wallace
Theotonijs Gomes	Tracy Mersfelder	

### Moderators for Research Day 2022

Prentiss Jones	Jessica McCoy	Christopher Uggen
Santhosh K.G. Koshy	David Overton	

## **Presentations Judges for Research Day 2022**

Adil Akkouch  
Benjamin Avner  
Steven M. Crooks  
Jayce Deleon  
Lisa Graves  
Ann Harris  
Gregory Vanden Heuvel

Nichol Holodick  
Mireya Diaz Insua  
Keith Kenter  
Benjamin Koestler  
Catherine Kothari  
Richard Lammers  
Elizabeth Lorbeer

Yong Li  
Silvia Linares  
Jessica J McCoy  
Christine Pink  
Paula M. Termuhlen  
Holly Turula  
Ramona Wallace

## **WMed Technology & Media Services**

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## **WMed Facilities Services**

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Danny Boulter



# W.E. UPJOHN M.D. CAMPUS FLOOR PLANS

## First Floor



- Entrance
- TBL Hall 1
- Lobby
- Classroom 111
- Auditorium

## Second Floor



- TBL Hall 2
- Classroom 211

## PROGRAM

### Wednesday, April 13

4:30 – 5:00pm	<b>Check-in</b> <b>Refreshments available</b>	1 <sup>st</sup> Floor Lobby
5:00 – 7:00pm	<b>1<sup>st</sup> poster session</b>	1 <sup>st</sup> & 2 <sup>nd</sup> Floor Lobby

### Thursday, April 14

7:30am – 8:00am	<b>Check-in</b> <b>Refreshments available</b>	1 <sup>st</sup> Floor Lobby
8:00am – 8:30am	<b>Welcome Address</b> Paula M. Termuhlen, MD, FACS Gregory Vanden Heuvel, PhD Adil Akkouch, PhD	Auditorium
	<b>Keynote Speaker Introduction</b> Medical student representatives	
8:20am – 9:20am	<b>Keynote Address</b> Thomas L. Schwenk, MD	Auditorium
9:20am – 9:30am	<b>Break</b>	
9:30am – 11:00am	<b>Oral Presentations</b> Session 1: Immunology and infectious diseases Session 2: Disparities and barriers in promoting health Session 3: Care quality improvement Session 4: Musculoskeletal research and regeneration Session 5: Bedside to benchside research	Auditorium TBL 1 Classroom 111 TBL 2 Classroom 211
11:00am – 12:00pm	<b>Poster Presentations</b> <b>Workshops</b>	1 <sup>st</sup> & 2 <sup>nd</sup> Floor Lobby
12:00pm – 12:30pm	<b>Student Research Awards and Farewell</b>	Auditorium

## ORAL PRESENTATIONS

SESSION #1	IMMUNOLOGY AND INFECTIOUS DISEASES	AUDITORIUM
	<b>Moderator:</b> Santhosh K.G. Koshy, MD, MBA	
9:30-10:00 am	<b>Faculty Oral Presentation:</b> Nichol Holodick, PhD	
10:00-10:12 am	<b>Ruchi Ojha PhD Candidate</b> , Benjamin J Koestler PhD Characterizing the role of Shigella flexneri diguanylate cyclases in pathogenesis Abstract no 33	
10:12-10:24 am	<b>Michael Gutknecht PhD</b> , Nichol Holodick PhD, Tom Rothstein MD, PhD Immunoglobulin M is Packaged into B Cell-Derived Extracellular Vesicles and can be Transferred to Secondary Cells Abstract no 53	
10:24-10:36 am	<b>Sarah Webster PhD</b> , Duncan Vos MS, Thomas Rothstein MD, PhD, Nichol Holodick PhD Influence of age, sex, and environment on the diversity of the murine gut microbiome and expression of pro-inflammatory cytokines Abstract no 49	
10:36-10:48 am	<b>Emma Swayze MS</b> , Hayley Barker BS, Brett Jagger MD, PhD The Association between Methamphetamine Abuse and Sexually Transmitted Infections (STI) in Kalamazoo, Michigan between 2017 and 2021 Abstract no 11	
10:48-11:00 am	<b>Tam Doan BS</b> , Maya Giaquinta BA, BS, Andrew Alfred BS, Sydney Les BS, Wilo Issack MS, Mariam Ischander MBChB Asthma Education Project at Western Michigan University: A Quality Improvement Initiative to Improve Asthma Control in Children in Southwest Michigan Abstract no 86	

**SESSION #2      DISPARITIES AND BARRIERS IN PROMOTING HEALTH      TBL #1**  
**Moderator:** Jessica McCoy, MD

- 9:30-10:00 am    **Faculty Oral Presentation:** Lisa Graves, MD
- 10:00-10:12 am    **Catherine Kothari PhD**, Katherine Corbit MPH, Joi Presberry MPH, Terra Bautista BA, Brenda O'Rourke RN, Deb Lenz MPA, Nia Evans MPH, Marcel Coleman BS  
Race, Multiraciality, Income, and Infant Mortality: Markers of Racial Equity  
Abstract no 57
- 10:12-10:24 am    **Angie Tsuei MD**, Emma Swayze MS, Rachel Tomassi BS, Silvia Linares MD  
Racial disparity in post-operative pain management following laparoscopic salpingectomies  
Abstract no 45
- 10:24-10:36 am    Shaan Manawar MD, **Lindsey Young BS**, Karen Bovid MD  
No-Shows in a Pediatric Orthopaedic Clinic: Is SCFE a Risk Factor?  
Abstract no 75
- 10:36-10:48 am    **Shelby DeWaard BS**, Zachary Dewyer BS, Nelson Hauber MD, Corbin Donham MD, Adam Wuensch MD Joshua Recknagel MD, Elizabeth Hoffiman MD, Rachael Gallup BS, Maureen Ford MD  
Quality Improvement (QI) Intervention seeking to increase COVID-19 vaccination rates among unvaccinated patients aged 20-64 years in the Emergency Department  
Abstract no 72
- 10:48-11:00 am    **Tiffany Hangse BA**, Noelle Fukuda BS, Rubie Villela BS, Jennifer Vosters BS, Prentiss Jones Jr. PhD  
Para-Fluorofentanyl: The New Speedball?  
Abstract no 23

<b>SESSION #3</b>	<b>CARE QUALITY IMPROVEMENT</b>	<b>CLASSROOM 111</b>
	<b>Moderator:</b> David Overton, MD	
9:30-10:00 am	<b>Faculty Oral Presentation:</b> Ramona Wallace, DO	
10:00-10:12 am	<b>Emily Bon DO</b> , Claire Clifton DO, Joseph Billian MS, Philip Pazderka MD, David Overton MD, Kathryn Redinger MD, Joshua Mastenbrook MD Emergency Medicine Residents in the prehospital setting: Does this augment training? Abstract No 3	
10:12-10:24 am	Elizabeth Corpuz BA, <b>Brittany Sullivan BS</b> , Emily Beck BS, Emily Carroll BA, Joi Presberry MPH, Debra Lenz MS, Brenda O'Rourke RN, BSN, Terra Bautista BA, Catherine L Kothari PhD Preventing Sleep-related Deaths Using Fetal Infant Mortality Reviews Abstract No 71	
10:24-10:36 am	<b>Henry Higby MD</b> , John Hoyle MD, Glenn Ekblad DO, MSN, MPH, Alyssa Woodwyk MS, Richard Brandt MS, Bill Fales MD, Kevin Putman MS EMS Pediatric Transport Impressions in the State of Michigan Abstract No 18	
10:36-10:48 am	<b>Dakota De Cecco BS</b> , Abigail Grande MPH, Amanda Fisher-Hubbard MD Revisiting Trends in the Certification of Choking-related Deaths Abstract No 94	
10:48-11:00 am	<b>Joi Presberry MPH</b> , Catherine Kothari PhD, Grace Lubwama DPPD, Terra Bautista BS, Brenda O'Rourke RN, Deb Lenz MPA Care Coordination Registry Identifies System Gaps and Strengths Abstract No 97	

**SESSION #4      MUSCULOSKELETAL RESEARCH AND REGENERATION      TBL #2**

**Moderator:** Christopher Uggen, MD

- 9:30-10:00 am      **Faculty Oral Presentation:** Yong Li, MD, PhD
- 10:00-10:12 am      **Jalen Martin BA, Karen Bovid MD**  
Bilateral slipped capital femoral epiphysis in a non-obese Amish girl with multiple affected family members  
Abstract No 41
- 10:12-10:24 am      **Zeena Qiryaqoz BS, Adil Akkouch PhD**  
Biocompatibility Analysis of 3D Bioprinted Construct for Enhanced Bone Regeneration  
Abstract No 44
- 10:24-10:36 am      **Jordan Boivin MD, Chris Traynor MD, Kevin Stehlik BS, James Jastifer MD**  
Radiographic measurements of the foot and ankle following a tibiotalar arthrodesis  
Abstract No 31
- 10:36-10:48 am      Daniel Byrne, **Jacob Poliskey PhD**  
Build It Yourself! Modeling Vessels on Biplane Angiography using Visible Light  
Abstract No 50
- 10:48-11:00 am      **Shelby Chaney MS, Zeena Qiryaqoz BS, Adil Akkouch PhD**  
Strontium Decreases Mitochondrial Reactive Oxygen Species Production in Chondrocyte Spheroids  
Abstract No 63

**SESSION #5      BEDSIDE TO BENCHSIDE RESEARCH      CLASSROOM 211**

**Moderator:** Prentiss Jones, PhD

- 9:30-10:00 am    **Faculty Oral Presentation:** Benjamin J Koestler, PhD
- 10:00-10:12 am    **Rachael Tolsma BS**, Lisa Miller MD, FACS  
Medical Student Perceptions of Assessments of Critical Thinking Process in the  
General Surgery Clerkship  
Abstract No 34
- 10:12-10:24 am    **Greg Vanden Heuvel PhD**, Kemin Su PhD  
The Cux1 and Polycystin1 proteins are regulated by the Notch signaling pathway in  
the developing kidney  
Abstract No 109
- 10:24-10:36 am    **Lilly Ruell BS**, Hong Phan BS, James Springstead PhD, Adil Akkouch PhD  
The Effect of Low-Density Lipoprotein Particles on Osteoblast Differentiation  
Abstract No 70
- 10:36-10:48 am    **Samantha Hack PhD Candidate**, Wendy Beane PhD  
Different Cell Death Pathways Regulate Stem Cells During Homeostasis vs  
Regeneration  
Abstract No 32
- 10:48-11:00 am    **Lubaina Ehsan MD**, Janine Fung MD, Mackenna Senti, Nina Mathew MD, Nital  
Murthi MD, Berrin Ergun-Longmire MD  
Insulin-responsive Severe Hypertriglyceridemia in New-Onset Type 1 Diabetes  
Mellitus  
Abstract No 8

**ORAL  
PRESENTATION  
ABSTRACTS**



### ***3: Emergency Medicine Residents in the prehospital setting: Does this augment training?***

Emily Bon DO<sup>1</sup>, Claire Clifton DO<sup>1</sup>, Joseph Billian MS<sup>2</sup>, Philip Pazderka MD<sup>1</sup>, David Overton MD<sup>1</sup>, Kathryn Redinger MD<sup>1</sup>, Joshua Mastenbrook MD<sup>1</sup>

<sup>1</sup>Emergency Medicine, <sup>2</sup>Department of Biomedical Sciences, Division of Epidemiology and Biostatistics, Western Michigan Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Emergency medicine (EM) residency curricula are designed to prepare future physicians for independent practice. Although the Accreditation Council for Graduate Medical Education requires that EM residents have prehospital experiences, very few programs augment this experience with a dedicated resident response vehicle. There are minimal data demonstrating the utility of such an approach.

**Purpose:** Our three-year EM residency program staffs a dedicated response vehicle with a PGY-2 or PGY-3 resident 24/7/365 to respond to high-acuity EMS calls. Additionally, from 0800 to 2300, the on-duty resident fields all of the prehospital radio/phone consults for the agencies operating within our county. Each resident averages one 24-hour shift per 4-week EM block. The purpose of this study is to describe the prehospital educational experiences and curricular contributions that this program provides.

**Methods:** We conducted a retrospective longitudinal study of all EMS calls which had EM resident involvement while staffing the response vehicle over a 42-month period. Data were abstracted from a locally developed google-survey-based charting system used by the residents specifically for the response vehicle program. Basic statistics were computed to quantify the number and type of prehospital encounters per resident.

**Results:** Ninety-four unique resident users were identified in the charting system. The mean number of encounters per resident was 31.3 (SD = 22), with a range of 1 to 99 encounters per resident documented. Over the study period, our residents managed 824 out-of-hospital cardiac arrests, 25 of which were pediatric, 681 refusals, 314 death pronouncements, 121 critical trauma patients, and answered 1267 complex phone/radio EMS consults.

**Conclusions:** This study quantified the prehospital experiences attained by senior EM residents in a program with a resident response vehicle. Our longitudinal EMS curriculum gives residents significant exposure to prehospital patient care strategies and challenges along with the opportunity to develop confidence and autonomy in managing critically ill patients. The most common scene encounter documented was “cardiac arrest.” This study was limited in that the data were obtained from a database created from the charting system which relied solely on our residents to ensure full documentation of all encounters in which they participated.

## ***8: Insulin-responsive Severe Hypertriglyceridemia in New-Onset Type 1 Diabetes Mellitus***

Lubaina Ehsan MD, Janine Fung MD, Mackenna Senti, Nina Mathew MD, Nital Murthi MD, Berrin Ergun-Longmire MD

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

**Introduction:** Severe hypertriglyceridemia is a rare complication of Type 1 Diabetes (T1D), especially among the pediatric population. We present a case of a 16-year-old previously healthy male who presented to the outpatient clinic for a sports physical examination.

**Case Report:** At the clinic, he had elevated blood glucose of 443 mg/dL and severely elevated triglyceride of 2228 mg/dL (<150 mg/dL). He also reported polydipsia, polyuria with nocturia, and unintentional 70-pound weight loss in the last 5-6 months. He was admitted for new-onset diabetes. His vital signs were normal, and his physical exam was unremarkable except for skin thickening over his neck. His repeat labs showed glucose of 387 mg/dL and fasting triglyceride of 3125 mg/dL. His labs were also remarkable for elevated beta-hydroxybutyrate of 3.8 mmol/L (0.02-0.27 mmol/L), increased anion gap of 14 mmol/L, normal bicarbonate of 26 mmol/L (23-32 mmol/L), and low c-peptide of 1.1 ng/mL (1.4-4.4 ng/mL). His urinalysis showed moderate ketones and his HbA1c was 16.4% (4.4-5.6 %). He was not in diabetic ketoacidosis. He was started on a basal-bolus insulin regimen. The patient's history, age, and presence of low c-peptide were suggestive of T1D. After only a month of outpatient intermittent basal-bolus insulin regimen, his triglycerides decreased from 3125 mg/dL to 130 mg/dL. Although rare, severe hypertriglyceridemia may co-exist with new-onset T1D in a pediatric patient.

**Discussion:** In adult literature, hypertriglyceridemia is reported due to insulin deficiency and resolution after starting treatment with insulin which is similar to our pediatric case. Some patients may also require medical therapy for persistent hypertriglyceridemia to prevent and treat triglyceride-induced pancreatitis, however, literature among the pediatric population is limited.

## ***11: The Association between Methamphetamine Abuse and Sexually Transmitted Infections (STI) in Kalamazoo, Michigan between 2017 and 2021***

Emma Swayze MS<sup>1,2</sup>, Hayley Barker BS<sup>1</sup>, Brett Jagger MD, PhD<sup>1</sup>

<sup>1</sup>Medical student. Department of Medicine, Western Michigan Homer Stryker M.D. School of Medicine, Kalamazoo, MI. <sup>2</sup>Boston University, Boston, MA

**Introduction:** There has been a striking increase in the incidence of Gonorrhea and Chlamydia in Kalamazoo County as well as a rise in the use of methamphetamine. We hypothesize there is a relationship between methamphetamine abuse and acquisition of Chlamydia, Gonorrhea, and HIV in Kalamazoo.

**Methods:** We conducted an IRB approved (WMED690) case control study to evaluate whether there is a relationship between methamphetamine abuse and the odds of having a sexually transmitted infection (STI). We estimated the prevalence of methamphetamine abuse and incident diagnosis of Gonorrhea, Chlamydia, and HIV, in patients 15 and older, with one or more encounter at a WMed Health clinic between 2017 and 2021. Patients were stratified into groups of those who had a history of or current methamphetamine abuse and those that did not. Continuous baseline characteristics were reported as median (interquartile range [IQR]) and categorical variables reported as frequency (%). To evaluate the association between methamphetamine use and each STI, a multivariate logistic regression was used adjusting for factors including ethnicity, race, marijuana use, and vaping. Significance was assessed at an alpha of 0.05. All tests were two-sided. SAS v9.4 was utilized for analysis.

**Results:** Between the years of 2017 and 2021, we identified 869/26,499 patients that engaged in methamphetamine abuse; a prevalence of 3.28% (95% CI: 3.06%, 3.49%). We found 748/26,499 of patients were infected with Chlamydia, Gonorrhea, or both; a prevalence of 2.82% (95% CI: 2.62%, 3.02%). While 56% (487/869) of patients that had abused amphetamines reported having Medicaid HMO as an insurance provider, only 25.5% (6,547/25,630) of patients that did not abuse amphetamines reported Medicaid HMO as an insurance provider (p<0.01). Patients that had abused methamphetamine had a 1.78 increased adjusted odds ratio (AOR) of having Gonorrhea (95% CI 1.16, 2.72). Patients that had abused methamphetamine had significantly increased odds of having HIV (AOR 2.39, 95% CI 1.76, 3.26).

**Conclusion/Clinical significance:** Our findings can inform targeted STI education and screening in the Kalamazoo patient population. Public health initiatives to reduce STIs in persons using methamphetamine are warranted in Kalamazoo.

## ***18: EMS Pediatric Transport Impressions in the State of Michigan***

Henry Higby MD<sup>1</sup>, John Hoyle MD<sup>1,2</sup>, Glenn Ekblad DO, MSN, MPH<sup>1</sup>, Alyssa Woodwyk MS<sup>3</sup>, Richard Brandt MS<sup>4</sup>, Bill Fales MD<sup>1</sup>, Kevin Putman MS<sup>1</sup>

<sup>1</sup>Department of Emergency Medicine, <sup>2</sup>Department of Pediatrics and Adolescent Medicine, <sup>3</sup>Department of Biomedical Sciences, Division of Epidemiology and Biostatistics, <sup>4</sup> Department of Medical Education, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Michigan has a pediatric population totaling 2.1 million<sup>1</sup>. Emergency Medical Services (EMS) personnel have infrequent encounters with pediatric patients. Data describing the types of encounters can aid in training and preparation.

**Objective:** To describe the most common impressions/chief complaints for EMS pediatric transports in Michigan.

**Methods:** As part of a pre-existing quality improvement study, we collected data on 16 EMS agencies from the Michigan Emergency Medical Services Information System (MI-EMSIS). We conducted a retrospective analysis for patients < 13 years old between 6/1/2016 and 5/31/2017. EMS run impressions were sorted and counted. There is a lack of common/unified verbiage across Electronic Medical Record (EMR) platforms, therefore we grouped “Stab/Gunshot wound,” “Hemorrhage/Laceration,” and “Traffic/Transportation Accident” under the title “Traumatic Injury;” and we combined “Not Applicable” and “Not Available,” as well as “Unknown” and “Unknown Problem/Man Down.”

**Results:** 752 pediatric runs by 16 Michigan EMS agencies were identified, sorted, and grouped. Eight EMS agencies (53.3%) had less than 10 pediatric runs documented; 1 EMS agency (6.7%) had no documented pediatric runs. Among the most common impressions/complaints identified were “Breathing Problem” (28.7%), “Seizure/Convulsions” (21.4%), “Traumatic Injury” (13.0%), “Allergic Reaction” (6.1%), “Transfer/Interfacility/Palliative Care” (4.1%), “Cardiac Arrest” (3.3%), “Unconscious/Fainting” (3.1%), and “Burns” (1.1%). 10.8% of Pediatric EMS runs were given an impression of “Not Available,” “Not Applicable,” “Unknown,” or “Unknown Problem/Man Down.” An additional 5.9% of pediatric patients were given the impression “Sick Person.”

**Conclusions:** Our findings demonstrate the infrequency of pediatric encounters for EMS personnel in Michigan. More than half of our EMS agencies reported < 10 pediatric encounters. This emphasizes a need for regular and frequent training of EMS personnel to provide high quality medical care for a small, but vulnerable, patient population. Greater than 15% of impressions were “unknown,” “not available,” or “sick person.” Our results also highlight the need for improvement and standardization of EMS EMR system impressions which would provide more clarity and allow for ease of interagency communication and research.

[1] Population by Age. Accessed July 27, 2021.  
<https://vitalstats.michigan.gov/osr/Population/npPopAGe.asp>

**IRB #:** 201608-03-FC

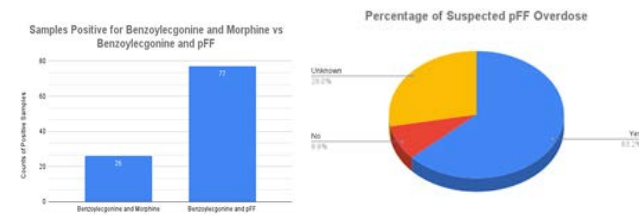
### 23: Para-Fluorofentanyl: The New Speedball?

Tiffany Hangse BA, Noelle Fukuda BS, Rubie Villela BS, Jennifer Vosters BS, Prentiss Jones Jr PhD  
Department of Pathology, Western Michigan University Homer Stryker M.D. School of Medicine,  
Kalamazoo, MI

**Introduction:** In 2019, over 70,000 Americans died from drug overdose. Between 2020 and 2021, this number topped 100,000. Approximately 75% of deaths involved opioids. Michigan accounts for about 3.2% of opioid-related deaths, placing Michigan in the Centers for Disease Control and Prevention’s highest range category. para-Fluorofentanyl (pFF), an analog of fentanyl never intended for human use, has been identified at Western Michigan University Homer Stryker M.D. School of Medicine (WMed) since October 2020. Fentanyl, reported to be 80-100 times stronger than morphine, is commonly substituted for heroin. According to the U.S. Drug Enforcement Administration, pFF is stronger than fentanyl. Given this analog's greater toxicity raises the question: what benefits of its use outweigh its risks? An answer may lie in speedballing. Speedballing refers to simultaneous use of a stimulant and depressant. Classically, speedballing involves cocaine (stimulant) and heroin (depressant), creating a “push-pull” reaction in the brain that generates an intenser high. Data from the National Institute on Drug Abuse demonstrates a sharp uptick of overdose deaths from the combination of cocaine and opioids, roughly a 268% increase from 2014 to 2020. Opioids were not individually identified; however, it is possible pFF was included.

**Methods:** Retrospective analysis of WMed opioid surveillance results for 193 decedents from 17 counties in southwest Michigan and 2 counties in northern Indiana. An assessment of possible association between pFF and cocaine (as benzoylecgonine, metabolite of cocaine) was compared against any association between benzoylecgonine and heroin (as morphine, metabolite of heroin).

**Results:** Preliminary results indicate benzoylecgonine was almost 3 times more likely to be associated with pFF (77 encounters) than benzoylecgonine with morphine (26 encounters).



**Conclusion/Clinical significance:** To our knowledge, these findings are the first mention of possible speedball combination. The presence of these compounds do not alone prove concomitant use; further studies (e.g., pharmacokinetic of cocaine in the presence of pFF, antemortem assessments) are needed. Recognizing this drug combination calls attention to a potential threat to Michigan public health and safety.

**Acknowledgments:** Thanks to the Michigan Department of Health and Human Services for funding the opioid surveillance program at Wmed.

**IRB #:** WMed-2022-0872

### ***31: Radiographic measurements of the foot and ankle following a tibiotalar arthrodesis***

Jordan Boivin MD<sup>1</sup>, Chris Traynor MD<sup>1</sup>, Kevin Stehlik BS<sup>2</sup>, James Jastifer MD<sup>1</sup>

<sup>1</sup>Department of Orthopedic Surgery, <sup>2</sup>Medical student, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Tibiotalar arthrodesis is a common treatment for tibiotalar osteoarthritis due to consistent pain relief, a low reoperation rate, and the ability to correct significant deformities.[1] When fusing the ankle, it is recommended to place it in neutral dorsiflexion/plantarflexion to avoid back-knee thrust and vaulting gait pattern.[1] For patients with concomitant tibiotalar arthritis and flat foot, tibiotalar arthrodesis has the potential to affect talar position and the alignment of the longitudinal arch of the foot. The purpose of this study is to assess the relationship between ankle position in the sagittal plane and the longitudinal arch of the foot before and after ankle arthrodesis.

**Methods:** We retrospectively reviewed a single-surgeon series of patients who had undergone tibiotalar arthrodesis. 73 were identified and after exclusion, 29 met inclusion criteria. Pre-operative and post-operative radiographic measurements were obtained by an orthopedic resident. The measurements included lateral tibiotalar angle (LTTA), lateral talometatarsal angle (LTMA), lateral talocalcaneal angle (LTCA), cuneiform height (CH), and calcaneal pitch (CP). Additional data collected included demographics, fusion construct type, and visual analog scale (VAS) measurements.

**Results:** On radiographic examination, the LTTA was increased from  $67.8^{\circ} \pm 7.5^{\circ}$  pre-operatively to  $74.7^{\circ} \pm 6.2^{\circ}$  post-operatively ( $p = 0.001$ ), LTMA increased from  $-2.2^{\circ} \pm 10.3^{\circ}$  to  $3.9^{\circ} \pm 9.8^{\circ}$  ( $p < 0.001$ ), LTCA increased from  $44.0^{\circ} \pm 10.7^{\circ}$  to  $44.9^{\circ} \pm 6.7^{\circ}$  ( $p = 0.541$ ), CH increased from  $21.6 \text{ mm} \pm 7.9 \text{ mm}$  to  $26.5 \text{ mm} \pm 8.2 \text{ mm}$  ( $p < 0.001$ ), and CP increased from  $22.7^{\circ} \pm 8.6^{\circ}$  to  $24.2^{\circ} \pm 6.4^{\circ}$  ( $p = 0.188$ ). VAS decreased from  $5.7 \pm 2.9$  to  $1.6 \pm 2.6$  ( $P < 0.001$ ).

**Conclusions:** Correcting the talar alignment in the sagittal plane improved the radiographic parameters associated with flatfoot, contributing to the restoration of the longitudinal arch. It is unclear whether this has a clinical correlation to improvement in pain associated with flat foot. With correction of the longitudinal arch, ankle arthrodesis could be a viable treatment option for those with ankle arthritis and concomitant flatfoot deformities.

**IRB #:** Wmed-2021-0790

**References:** [1] Coughlin M, Saltzman C, Anderson R. Mann's Surgery of the Foot and Ankle. 9th ed. Philadelphia, PA: Elsevier Saunders; 2014.

## ***32: Different Cell Death Pathways Regulate Stem Cells During Homeostasis vs Regeneration***

Samantha Hack PhD Candidate, Wendy Beane PhD

Department of Biological Sciences, Western Michigan University, Kalamazoo, MI

**Introduction:** Cell death is crucial during development and homeostasis, where the removal of unwanted or damaged cells is critical. Cell death is also, counterintuitively, required to stimulate new tissue growth during 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 cell death in these different contexts. Our preliminary data suggests that different signaling pathways regulate apoptosis during homeostatic cell turnover versus stem cell-mediated regeneration. Using the planarian model, which has a high rate of normal cell turnover and the robust ability to replace all tissue types, we found that inhibition of intrinsic apoptosis (where the cell targets itself for death) regulates homeostasis while inhibition of extrinsic apoptosis (where outside stimuli target a cell for death) regulates regenerative growth. These data suggest the mechanism that induces cell death directs the proliferative response of surrounding cells. Understanding these signaling programs is an important first step to manipulating cell death for targeted therapeutic outcomes for cancer and regenerative medicine.

**Methods:** We used pharmacological inhibition of caspases (executioners of cell death) to target either the intrinsic or extrinsic apoptotic pathway to prevent cell death during homeostasis and regeneration in the planarian *Schmidtea mediterranea*. Effects on proliferation (phospho-Histone3) and blastema size (new growth) were measured.

**Results:** Our results show that both general apoptosis and extrinsic pathway inhibitors block new growth during regeneration, while intrinsic pathway inhibitors have no effect on proliferation levels or blastema size. Conversely, intrinsic pathway inhibitors block proliferation during homeostatic cell turnover. These preliminary data suggest that extrinsic apoptosis may be a regeneration-specific modulator of stem cell-mediated growth, whereas the intrinsic pathway regulates homeostatic proliferation.

**Conclusion/Clinical Significance:** Our work has identified differential signaling that modulates apoptosis associated proliferation during cell turnover and adult tissue regeneration. These data provide a solid foundation for future studies aimed at manipulating cell death, to either enhance growth (for regenerative medicine) or suppress it (for cancer therapies) in the clinic, without disrupting homeostatic processes.

### 33: Characterizing the role of *Shigella flexneri* diguanylate cyclases in pathogenesis

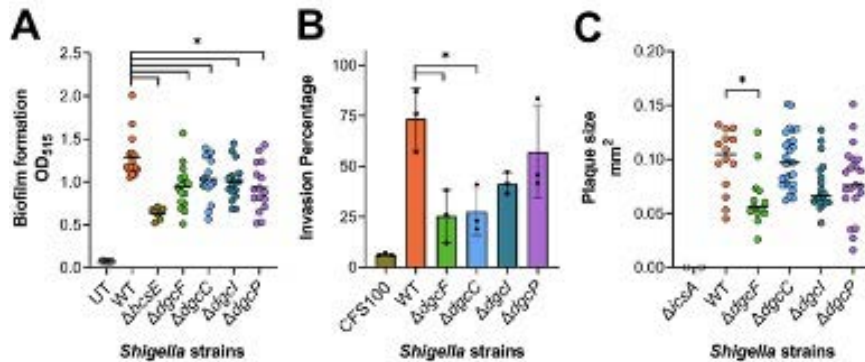
Ruchi Ojha PhD Candidate, Benjamin J Koestler PhD

Department of Biological Sciences, Western Michigan University, Kalamazoo, MI

**Introduction:** *Shigella flexneri* is a gram-negative human pathogen that causes bacillary dysentery. This bacterium targets the colonic epithelium, resulting in bloody diarrhea. Approximately 1.1 million *Shigella* cases are reported worldwide every year. There is no vaccine for the prevention or treatment of *Shigella* infection, and antibiotic resistance is on the rise for *Shigella*, making it a high priority target for antibacterial therapy development. It is important for gastrointestinal bacteria like *Shigella* to be able to rapidly adapt to changing environments; other bacteria do this using cyclic diguanosine monophosphate (c-di-GMP) signalling. C-di-GMP is made by enzymes called diguanylate cyclases (DGCs). Bacteria typically have many DGCs encoded in their genome. C-di-GMP is involved in regulating many processes, such as biofilm formation; a biofilm is aggregates of bacteria encased in sticky substance called extracellular matrix that stick to various biotic and abiotic surfaces to form a matrix that can tolerate stressful conditions such as acid stress or high doses of antibiotics in a host.

**Methods:** *Shigella* encodes 4 DGCs (dgcC, dgcF, dgcI, dgcP), and it is unknown if they regulate *Shigella* virulence. I generated individual mutants of each of *S. flexneri*'s 4 DGCs and hypothesized that deleting DGC will reduce biofilm formation and increase virulence. Biofilm results were quantified using crystal violet staining and analyzed by measuring OD<sub>515</sub>. Virulence assays including invasion and plaque were setup by infecting in vitro tissue culture cells. Results were analyzed after Wright Giemsa staining under light microscope.

**Results:** My results show that DGC deletion strains significantly reduce *Shigella* biofilm formation,  $\Delta$ dgcC and  $\Delta$ dgcF show significant reduction in invasion frequency and the  $\Delta$ dgcF strain shows a reduction in cell to cell spread (Figure 1).



**Conclusion:** *S. flexneri* has developed efficient mechanism through which it can easily survive, invade and replicate within the host cell. There is still a knowledge gap on the scope of c-di-GMP signalling in *S. flexneri* pathogenesis. From these data, I conclude that deletion of certain *Shigella* DGCs detrimentally impacts virulence phenotypes.



### ***34: Medical Student Perceptions of Assessments of Critical Thinking Process in the General Surgery Clerkship***

Rachael Tolsma BS<sup>1</sup>, Lisa Miller MD, FACS<sup>2</sup>

<sup>1</sup>Medical Student, <sup>2</sup>Department of General Surgery, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Components factoring into medical student general surgery clerkship grades vary by institution, but may include preceptor evaluations, Observed Standardized Clinical Encounters (OSCEs), oral examinations, clinical documentation, and written examinations. While evaluators attempt to remain unbiased when evaluating medical student performance, subjectivity and implicit bias remain an issue. Our institution recently implemented a case-based structured oral examination to provide the general surgery clerkship director objective insight into students' clinical reasoning skills and knowledge base. Our hypothesis is that medical students believe this exam is a fair assessment of clinical knowledge and that it increases students' awareness of their own clinical reasoning skills.

**Methods:** Upon completion of their general surgery clerkship, third year medical students in the class of 2023 at our institution were sent a survey evaluating their perceptions of the assessments used for grading their performance. Each of the components were graded on fairness and level of insight into clinical reasoning based on a five-point Likert scale, ranking (1) strongly agree, (2) agree, (3) neutral, (4) disagree, and (5) strongly disagree.

**Results:** The oral examination was the most highly regarded assessment tool, with 79% (CI 62-95%) agreeing or strongly agreeing that it was both a fair assessment and gave them insight into their clinical reasoning skills. Alternatively, only 48% (CI 28-67%) of students agreed or strongly agreed that preceptor evaluations were an accurate assessment of their clinical knowledge and reasoning.

**Conclusion/Clinical Significance:** Medical students favor a case-based oral examination over other assessment tools. While multiple assessment tools are used to gather maximum information about student performance, this oral examination can provide clerkship directors with more objective data to assess medical students more fairly and help them improve their clinical reasoning skills.

**Acknowledgements:** Melissa Sherfield (WMed Database Specialist), Daphne York (WMed Research Navigator), Cuyler Huffman (WMed Department of Epidemiology and Biostatistics)

***43: Bilateral slipped capital femoral epiphysis in a non-obese Amish girl with multiple affected family members***

Jalen Martin BA, Karen Bovid MD

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

**Purpose:** Slipped capital femoral epiphysis (SCFE) is the most common hip pathology of adolescence. Most cases of SCFE present in obese children, particularly boys. Prior reports of SCFE in the Amish note affected patients had lower BMI, increased incidence of bilaterality, and increased positive family history compared to non-Amish white children with SCFE. Lack of usual risk factors places Amish children at risk of missed or late diagnosis of SCFE unless a high index of suspicion is maintained.

**Methods:** We present the case of an 11-year-old Amish girl who developed bilateral SCFE despite a normal BMI and endocrine evaluation. Patient has an extensive maternal family history of SCFE and early onset hip pathologies.

**Results:** An 11-year-old Amish female presented with a 3-week history of right hip pain. BMI 19.7 (76th percentile). Radiographs confirmed right SCFE and normal left hip. Labs showed no endocrine abnormalities and normal vitamin D level. Screw fixation of right SCFE was performed. One year later she developed a left SCFE, also treated with in-situ fixation. Two years following her initial surgery physes are closed, she asymptomatic, and back to full activities. Her 15-year-old sister had bilateral SCFE and her mother underwent hip replacement at 36 years related to hip problems in adolescence. Three of her mother's cousins had early hip arthroplasty and several of their children were diagnosed with SCFE. Genetic consultation including panel for Stickler Syndrome was negative. Further evaluation with whole exome sequencing is planned.

**Conclusion:** This case highlights the importance maintaining high index of suspicion of SCFE in non-obese patients, especially those of Amish heritage. Consideration of prophylactic pinning may be warranted in the setting of positive family history. A combination of genetic and environmental factors may be contributing to the high frequency of SCFE in this family. While initial genetic testing did not identify a specific underlying diagnosis for this patient, further testing of the patient and her affected family members with whole exome sequencing may lead to new insight regarding the etiology of SCFE in the Amish population and in general.

## 44: Biocompatibility Analysis of 3D Bioprinted Construct for Enhanced Bone Regeneration

Zeena Qiryaqoz BS<sup>1</sup>, Adil Akkouch PhD<sup>2</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Orthopaedic Surgery, Medical Engineering Program, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Three-dimensional (3D) bioprinting, otherwise known as, additive manufacturing, is the layer-by-layer precise positioning of biomaterials, biochemicals and living cells, also called bioink. [1] 3D bioprinting is an emerging technology for the fabrication of complex living constructs for both hard and soft tissue engineering. In bioprinting, the properties of the biomaterials used for bioink formulation as well as the bioprinting process will critically influence the fate of the bioprinted cells. Therefore, there is a need to understand how cells and biomaterials interact during bioprinting. In bone tissue engineering, biomaterials based on collagen, hydroxyapatite, and their composites, have been widely investigated, due to their biocompatibility and osteoconductivity. [2] We proposed in this study the fabrication of a hybrid osteoconductive construct made by mineralized collagen and pre-osteoblast cells using 3D bioprinting and to study the biocompatibility of the fabrication process.

**Methods:** 3D constructs of collagen and hydroxyapatite were prepared without and with cells using 3D bioprinting. We used histology, SEM, and TEM to characterize the structure and morphology. Constructs containing Human Embryonic Palatal Mesenchyme Cells (HEPM) were cultured in DMEM medium for up to 7 days. Cytotoxicity of the bioprinting process on HEPM cells and the effect on inflammatory cytokines and chemokines production were tested using Alamar Blue, LDH and ELISA.

**Results:** SEM analysis showed a porous nanofibrous collagen network with presence of hydroxyapatite particles on the collagen fibers along with incorporation of the HEPM cells into the matrix. The fabrication of the 3D constructs using 3D bioprinting was therefore not toxic and did not alter the viability, proliferation, and cytokines expression of HEPM cells.

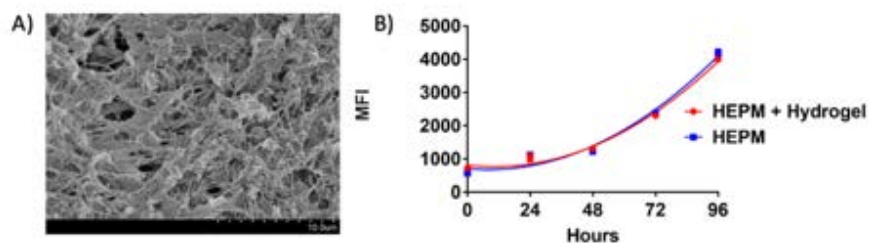


Figure: A) SEM micrograph of the construct. B) Proliferation of HEPM in bioprinted constructs using Alamar Blue.

**Conclusion:** The 3D bioprinting process is safe and did not cause inflammation. This study offers a novel hybrid 3D construct with effective formulation to enhance bone regeneration. This will help to apply bioink-based 3D bioprinting technology into clinical applications in the near future.

**References:** [1] Skardal A, Atala A. (2015), *Ann Biomed Eng.*, 43(3):730-46; [2] Akkouch A. et al. (2011) *J Biomed Mater Res A.* 15;96(4):693-704.

#### ***45: Racial disparity in post-operative pain management following laparoscopic salpingectomies***

Angie Tsuei MD, Emma Swayze MS, Rachel Tomassi BS, Silvia Linares MD

Department of Obstetrics and Gynecology, Western Michigan Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** It has been previously demonstrated that racial biases exist towards patient perception of pain; particularly that Black patients have an increased pain tolerance, compared to White patients [1,2]. Not much is known about the effect of provider bias on prescription of narcotic medications in a post-operative setting. Our primary objective was to determine if there was difference in morphine milligram equivalents (MME) prescribed after laparoscopic bilateral salpingectomies between patients that self-identify as White and Black. Secondary objective was to determine relationship between patient pain score and post-operative MME prescribed.

**Methods:** We conducted a retrospective chart review of patients over the age of 18 who had outpatient laparoscopic bilateral salpingectomies between January 2016 and January 2021 at Bronson Hospital (WMed-2021-0780). Differences in prescribed MME across race were evaluated with an independent sample two-sided t-test. We conducted a logistic regression to evaluate predictors of narcotic prescriptions. A mixed model was used to evaluate the association between provider and discharge dosage. Significance was set at an alpha of 0.05 and SAS v9.4 was utilized for analysis.

**Results:** Out of 399 patients, 74.2% self-identified as White and 35.8% as non-White. Both group's patients were administered a median narcotic dosage of 40mg (IQR 30,45). We found no relationship between race and the odds of getting prescribed more than 30mg of narcotic pain medication (Odds Ratio (OR) 1.20 (95% Confidence Interval (CI) :0.74, 1.95). Both a last post-operative pain score and maximum pain score greater or equal to 5 were not predictive of receiving a larger narcotic dosage, although maximum pain score appears to be trending towards significance; OR 1.15 (95% CI:0.71, 1.87) and OR 1.64 (95% CI:0.98, 2.76) respectively. There were 35 unique providers, ranging from 1 provider-patient encounter to a maximum of 49 provider-patient encounters. A mixed model showed a significant association between provider and discharge dosage ( $p < 0.01$ ).

**Conclusion/Clinical significance:** Race and pain scores were not predictive of post-operative MME prescribed. In contrast, discharge dosage was related to patient provider. This study calls for the development of a standardized post-operative pain control to ensure patients receive prescriptions that meets their specific needs.

## ***49: Influence of age, sex, and environment on the diversity of the murine gut microbiome and expression of pro-inflammatory cytokines***

Sarah Webster Ph.D.<sup>1</sup>, Duncan Vos M.S.<sup>2</sup>, Thomas Rothstein M.D., Ph.D.<sup>1</sup>, Nichol Holodick Ph.D.<sup>1</sup>  
<sup>1</sup>Department of Investigative Medicine, Center for Immunobiology, <sup>2</sup>Department of Biomedical Sciences, Division of Epidemiology and Biostatistics, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** The microbiome and immune system have a unique interplay, which influences homeostasis within the organism. Both the microbiome and immune system play important roles in health and in diseases of the aged including development of cancer, autoimmune disorders, and susceptibility to infection. Various groups have demonstrated divergent changes in gut microbiota during aging, but these studies have largely ignored the compounding factor of biological sex within the context of aging, and little is known about the effect of institutional environment on the composition of gut microbiota in normal healthy laboratory mice.

**Methods:** To better understand the roles of sex, aging, and environment in influencing the gut microbiome, we obtained normal healthy BALB/cByJ from a single source. Male and female mice were aged in two different geographical locations; however, they were housed in comparable AAALAC-approved facilities on the same diet and in identical caging and bedding. Stool and serum samples were collected from both young (2-4mo) and aged (18-26mo) males and females. 16S rRNA sequencing was performed to determine the composition of the microbiome. Cytokine expression was measured using chemiluminescence-based assays.

**Results:** The 16s rRNA microbiome analysis indicated that both age and sex play a role in microbiome composition; additionally, location plays a role in the diversity present as well. Interestingly, these microbiome changes occurred with changes in serum expression of several different cytokines including IL-10 and IL-6, which were also both differentially regulated in context to sex and aging. B-1a cells are known to produce mucosal IgA as well as IL-10 and IL-6, which play roles in regulating the microbiome. Furthermore, we found both IL-10 and IL-6 play a role in the constitutive expression of pSTAT-3 in B-1a cells.

**Conclusions:** Together these results demonstrate sex and age shape the gut microbiome as well as systemic cytokine expression, which can influence, and be influenced by B-1a cells. In addition, location of housing can also influence the microbiome despite common animal sourcing. These results emphasize the importance of sex, age, and housing location in the mechanism of development of the gut microbiome

## 50: *Build It Yourself! Modeling Vessels on Biplane Angiography using Visible Light*

Daniel Byrne<sup>1,2</sup>, Jacob Poliskey PhD<sup>1,3</sup>

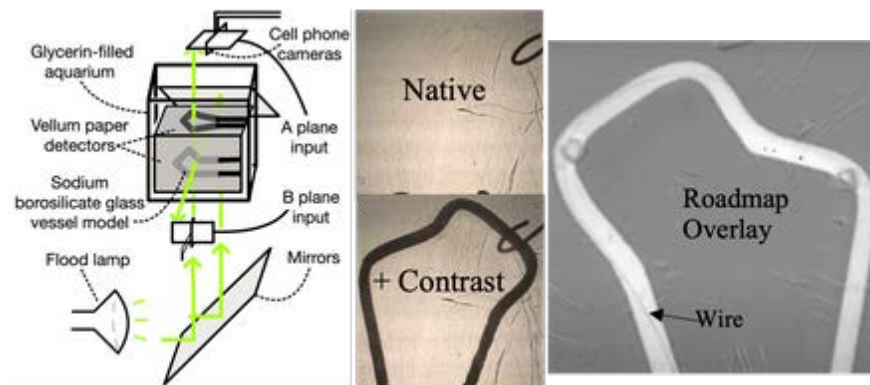
<sup>1</sup>Alverna Innovations, LLC, Kalamazoo, MI. <sup>2</sup>Michigan Technological University, Houghton, MI.

<sup>3</sup>Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Research for imaging in interventional radiology typically requires a C-arm or x-ray biplane to test hypotheses regarding image output modification. Access to these has high barriers for students. To our knowledge, no prior “Do-It-Yourself” angiography systems exist, so we developed a system to view a vascular model on biplane angiography in-house. Our system needed to fit not only in a student’s bedroom but also their budget. Therefore, it was imperative to use visible light (as opposed to x-ray) and to minimize size and cost while accurately modeling an angiography setup.

**Methods:** Our platform consisted of a flood lamp shining through a glass aquarium. The aquarium contained a borosilicate glass tube filled with glycerin in the shape of a vascular model, immersed in a glycerin-table sugar mixture kept at a constant temperature of approximately 70°F. The detectors were vellum paper and two iPhone cameras that recorded the shadow of the vascular model on the vellum. During a run, a 1:1:1 emulsion of water, glycerin, and mineral oil was injected through the model, followed again by glycerin; afterward a wire catheterized the glass tube. Recorded video was sent to an in-house program where a mask frame was selected and then a roadmap was overlaid on the masked image.

**Results:** The apparatus cost approximately \$350 excluding common items and occupied approximately 2’x2.5’ of floor space; the lamp was located 8’ away. Because of refractive index matching, the glycerin-filled tube was nearly invisible until the contrast dye surrogate was run through it. The vellum/iPhone camera setup could detect a standard neurointerventional wire moving through the vascular model, both natively and on a roadmap overlay.



**Conclusion:** The barriers to using an angiography suite as an experimental testbed for new ideas are high for students. Our setup can fit in a small room, uses visible light, and is 5,000-fold cheaper than a real biplane, making it a feasible option for testing basic science questions in the absence of an available biplane. We hope this can serve as a blueprint for other students and researchers who may be facing similar constraints.

### ***53: Immunoglobulin M is Packaged into B Cell-Derived Extracellular Vesicles and can be Transferred to Secondary Cells***

Michael Gutknecht PhD, Nichol Holodick PhD, Tom Rothstein MD, PhD

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

**Introduction:** Extracellular vesicles (EVs) are a heterogeneous population of phospholipid bilayer-enclosed particles secreted by cells in all domains of life, from bacteria to *Homo sapiens*. Uniquely regulated from molecules secreted by the traditional secretory pathway, the bioactive contents associated with EVs can function in an immuno-regulatory capacity. Prior investigation, however, has failed to expressly identify and characterize EV associated-immunoglobulins, molecules secreted by B cells that are essential for antigen recognition and humoral immunity. We hypothesized that immunoglobulin M (IgM) is packaged with EVs and released into the extracellular environment.

**Methods:** Differential ultracentrifugation and sucrose gradient fractionation were utilized to isolate EV populations released by the murine B cell lymphoma WEHI-231 and FACS sorted B cell populations from WT and  $\mu$ sKO C57BL/6 mice, and in mouse peritoneal cavity wash fluid and plasma. EV IgM protein expression was determined by immunoblot, ELISA, and EV adsorption to microbeads/flow cytometry. EV transfer experiments were conducted using both WEHI-231 and S9.6 hybridoma cells (donor) and the human cervical cancer cell line HeLa (recipient).

**Results:** We identified two dominant IgM protein species associated with EVs, a high molecular weight form that was resolved by SDS/PAGE in congruence with pentameric (secreted) IgM and a species that was of similar molecular weight to monomeric IgM. Both forms were present in the microvesicle (IEV, sedimentation 10,000 x G) and exosome (sEV, 100,000 x G) sub-populations. The proportion of each IgM species in IEV and sEV was differentially regulated following *in vitro* stimulation with the gram-negative bacterial cell wall component LPS or the type II cytokine IL-4. Immunoglobulin was detected (immunoblot) and visualized (confocal microscopy) in recipient HeLa cell monolayers following the transfer of isolated IEVs from either WEHI-231 or S9.6 cells.

**Conclusion/Clinical significance:** We demonstrate for the first time that extracellular IgM exists in two forms, pentameric and monomeric, associated with EVs. These results indicate a potential new pathway for distribution of B cell generated antibody, packaged in particles rather than soluble in solution, that may be protective or pathogenic with respect to disease.

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

## ***57: Race, Multiraciality, Income, and Infant Mortality: Markers of Racial Equity***

Catherine Kothari PhD<sup>1</sup>, Katherine Corbit MPH<sup>2</sup>, Joi Presberry MPH<sup>1</sup>, Terra Bautista BA<sup>3,4</sup>, Brenda O'Rourke RN<sup>3</sup>, Deb Lenz MPA<sup>5</sup>, Nia Evans MPH<sup>1</sup>, Marcel Coleman BS<sup>1</sup>

<sup>1</sup>Epi-Biostats Div, Biomedical Sciences, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. <sup>2</sup>Robert Wood Johnson Foundation, Princeton, NJ. <sup>3</sup>Maternal-Child Services, Kalamazoo County Health & Community Services, Kalamazoo, MI. <sup>4</sup>Healthy Babies Healthy Start, Kalamazoo, MI. <sup>5</sup>Kalamazoo County Health & Community Services, Kalamazoo, MI

**Introduction:** Race and income are proxy indicators of social hierarchy; which, in turn, is correlated with health outcomes. Social scientists view multiraciality as a measure of social integration (the “melting pot”). While much is known about the increased proportion of minority race and multiracial families in the U.S. and evidence of socioeconomic integration grows, little is known regarding how these are linked to health outcomes. The goal of this study is to examine the degree to which income interacts with family racial structure to predict infant death outcomes.

**Methods:** This cross-sectional study utilized secondary data analysis of birth records and linked infant birth/death records from 2006 to 2019 from Kalamazoo County. Income was dichotomized into low income and high income based upon insurance type. Race and ancestry data from infant, maternal, and paternal sources were combined into six pan-ethnic categories. We used Generalized Estimating Equation to obtain the associations between a composite raceXmultiracialXincome predictor and outcomes (infant death, weeks gestation), accounting for repeated mother births.

**Results:** Black infants have the worst outcomes (12.34 Infant Mortality Rate, IMR). Multiracial infants tend to have higher family income than monoracial-minority infants, with better outcomes depending on racial group and multiraciality. Multiracial higher-income Black families have substantially better outcomes (2.85 IMR) than single Black race (12.63 IMR) or lower-income multiracial peers (16.16 IMR). Single-race white families also see health gains with higher income (3.60 IMR versus 6.02 IMR). For other minority race families, being single-race rather than multiracial is associated with better outcomes (0.97 IMR versus 5.39 IMR).

**Conclusion/Clinical significance:** Being multiracial is associated with higher income among minority families but lower income among white families. Whether higher income translates into better health depends upon family racial structure: white single-race and Black multirace families see improved health with higher-income. However, non-Black minority families see a “diminishing returns” pattern, where being single-race, rather than higher-income, is associated with better health. Threads of Black oppression run throughout, with the large majority of Black families having substantially worse outcomes.

**WMed IRB# 2017-1079.**



### ***63: Strontium Decreases Mitochondrial Reactive Oxygen Species Production in Chondrocyte Spheroids***

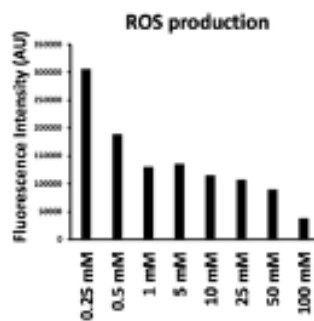
Shelby Chaney<sup>1</sup> MS, Zeena Qiryaqoz<sup>1</sup> BS, Adil Akkouch<sup>2</sup> PhD

<sup>1</sup>Medical student, <sup>2</sup>Department of Orthopaedic Surgery, Medical Engineering Program, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Osteoarthritis prevalence is increasing due to population ageing. Patients with osteoarthritis exhibit overproduction of reactive oxygen species (ROS), which induces chondrocyte senescence, apoptosis, cartilage degradation, synovial inflammation, and dysfunction of the subchondral bone. Strontium ranelate 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. In the United States, strontium ranelate is not approved by the FDA because of serious adverse effects. Alternatively, strontium ion doped scaffolds can be used locally to improve osteogenesis, though the local cytotoxicity level has not been established. It is unknown how strontium exerts its beneficial effects on bone and surrounding tissues such as cartilage. In this study, we are using 3D chondrocytes spheroids to test strontium chloride cytotoxicity and the effect on mitochondrial ROS production. We hypothesize that strontium administration will reduce ROS production which is known to cause tissue damage.

**Methods:** Chondro-spheroids were fabricated using agarose molds. Next, spheroids were cultured in 9 concentrations of strontium chloride (100mM, 50mM, 25mM, 10mM, 5mM, 1mM, 0.5mM, or 0.25mM) and compared to a control in normal culture media. Spheroids were harvested at 1, 3, 5, 7 and 10-days. Cytotoxicity was tested using AlamarBlue and live/dead staining. Spheroids were stained with 2',7'dichlorodihydrofluorescein diacetate to visualize ROS production.

**Results:** Strontium chloride enhanced the proliferation of chondrocytes spheroids in 25mM and 50mM concentrations after 3 days in culture. At 10 days, increased proliferation was only observed in the 10mM concentration. Strontium chloride reduced the production of ROS in a dose-dependent manner (Figure) after 5 days in culture.



**Figure:** Strontium reduced production of ROS in a dose-dependent manner.

**Conclusion/Clinical Significance:** 3D spheroid culturing restores the in-vivo phenotype and function of chondrocytes, which increases the efficacy of in-vitro pharmacotherapy testing. Strontium administration significantly reduces intracellular ROS production. This suggests that strontium chloride could be effectively used for the treatment of osteoarthritis.

## ***67: A Novel Microparticle Immunocapture Assay to Measure Proteostatic Activity***

Darwin Edmond<sup>1</sup>, Kian Mohamadi<sup>1</sup>, Michael Gutknecht PhD<sup>2</sup>, Thomas Rothstein MD, PhD<sup>2</sup>  
<sup>1</sup>Medical student, <sup>2</sup>Department of Investigative Medicine <sup>1</sup>Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** The formation of multimeric protein species, or protein aggregates, is the hallmark of many relentlessly progressive neurodegenerative diseases. Current treatment options are limited and no cures exist. We have recently identified a proteostatic function for Fas Apoptotic Inhibitory Molecule (FAIM), revealing that FAIM opposes aggregation and modulates disaggregation of several aggregation-prone proteins, including amyloid beta 1-42 (Ab42; Alzheimer's Disease) and mutant superoxide dismutase 1 (SOD1; Amyotrophic Lateral Sclerosis). Our project was focused on the application of a novel microparticle immunocapture assay developed in our lab to measure FAIM-mediated proteostasis of Ab42, and alpha-synuclein ( $\alpha$ S), multimerization of which corresponds with Parkinson's disease progression.

**Methods:** Monomeric Ab42 and  $\alpha$ S were kept frozen to prevent aggregation, or incubated with heat and agitation to induce multimerization. Commercially available microparticle formulations were tested for conjugation capacity, blocking efficiency, and antigen binding. Recombinant human FAIM was expressed and purified using the TOP10 bacterial expression system and nickel-charged column chromatography, respectively. Solutions of Ab42 or  $\alpha$ S were incubated with titrated FAIM or control protein (beta lactoglobulin), and the resultant multimerization state was evaluated by acrylamide gel total protein stain, sedimentation, immunoblot, or the bead assay.

**Results:** We first evaluated different microbead platforms for the assay and found critical advantages, including blocking efficiency and binding capacity, for use of aldehyde sulfate super reactive beads over pre-coated antibody capture beads. Sedimentation and immunoblot analysis provided confirmatory evidence that incubation of preformed  $\alpha$ S aggregates with FAIM resulted in the disaggregation of these  $\alpha$ S species. Bead assay measurements indicated that FAIM modulated  $\alpha$ S aggregation state in a dose dependent manner. FAIM proteostatic activity was then tested on Ab42 solutions comprised of progressively larger aggregates. A dose dependent effect of FAIM was observed on both small and large preformed aggregates.

**Conclusion/Clinical significance:** These findings verify the efficacy of a novel microparticle immunocapture assay to evaluate the proteostatic activity of experimental molecules on aggregation prone proteins, and thus may provide an advancement in identifying bioactive agents that oppose the devastating effects of neurodegenerative diseases. Our results suggest that FAIM deserves additional study as such an agent.

## ***70: The Effect of Low-Density Lipoprotein Particles on Osteoblast Differentiation***

Lilly Ruell Masters BS<sup>1</sup>, Hong Phan BS<sup>2</sup>, James Springstead PhD<sup>1</sup>, Adil Akkouch PhD<sup>1,2</sup>

<sup>1</sup>Medical Engineering Program. <sup>2</sup>Medical student. <sup>3</sup>Department of Orthopaedic Surgery, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Oxidized low-density lipoprotein particles (LDL) are known to cause inflammation within the body and contribute to an increased risk of cardiovascular disease. [1] Atherosclerotic calcification and bone mineralization share several common features. Lipoproteins and lipids can accumulate in the subendothelial matrix of human bone vessels as they do in the vascular endothelium. [2] Since osteoblasts are adjacent to the subendothelial spaces, they can be exposed to inflammatory lipoproteins particles. We hypothesize that LDL-particles may play a role in this connection between cardiovascular disease and osteoporosis specifically contributing to the differentiation of osteoblasts. Our study aims to demonstrate the cytotoxicity of oxidized-LDL and non-oxidized-LDL on human osteoblasts and their effect on osteogenic and adipogenic differentiation.

**Methods:** LDL was oxidized using the Fenton-Reaction. Saos-2 human osteosarcoma cells were cultured with increased concentrations of both oxidized-LDL and non-oxidized-LDL of 0, 1, 5, 10, 25, 50, 75, 100, 150, 200 ( $\mu\text{g}/\text{mL}$ ) for up to 7 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, PPAR $\gamma$ ) markers was analyzed via qRT-PCR.

**Results:** Both oxidized-LDL and non-oxidized-LDL show an increase in cell proliferation at 24hr, then a decrease in proliferation after 3 days. There is a dose dependent decrease of proliferation starting at 25  $\mu\text{g}/\text{mL}$  continuing to 200  $\mu\text{g}/\text{mL}$ . At 3 days, oil-droplets are noted at 25  $\mu\text{g}/\text{mL}$  in both oxidized-LDL and non-oxidized-LDL (Figure) indicating adipogenic differentiation.

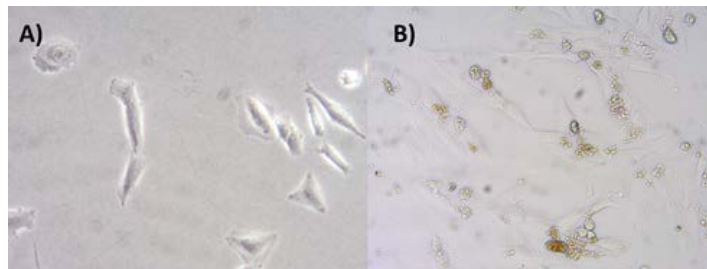


Figure: Saos-2 cells morphology changes and adipogenic differentiation. A) Non-treated control cells at day 0. B) “oil-like” droplets formation when cultured with 200  $\mu\text{g}/\text{mL}$  of oxidized-LDL for 7 days.

**Conclusion/Clinical significance:** We have determined the cytotoxicity and re-differentiation potential of LDL-particles on human osteoblasts. Given this insight, we propose a novel path provided by LDL-particles in the connection between cardiovascular disease and osteoporosis.

**References:** [1] Alekos. NS. et al. (2020) Front Endocrinol, 11, 578194. [2] Burnett. JR. et el. (2002) Ann Clin Biochem, 39, 203-10.

## ***71: Preventing Sleep-related Deaths Using Fetal Infant Mortality Reviews***

Elizabeth Corpuz BA<sup>1</sup>, Brittany Sullivan BS<sup>1</sup>, Emily Beck BS<sup>1</sup>, Emily Carroll BA<sup>1</sup>, Joi Presberry MPH<sup>1</sup>, Debra Lenz MS<sup>2</sup>, Brenda O'Rourke RN, BSN<sup>2</sup>, Terra Bautista BA<sup>2</sup>, Catherine L Kothari PhD<sup>1</sup>  
<sup>1</sup>Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. <sup>2</sup>Kalamazoo County Health and Community Services, Kalamazoo, MI

**Introduction:** Fetal Infant Mortality Review is an evidence-based community-level quality improvement process that reviews infant deaths and produces preventative recommendations.[1] The Center of Disease Control reports 3400 sleep-related infant deaths annually.[2] Kalamazoo County, Michigan historically has high infant mortality among minority groups, including safe-sleep deaths.[1]

**Methods:** Of 98 feto-infant deaths reviewed by Kalamazoo Fetal Infant Mortality Review(2015-2020), 18 were related to unsafe-sleep. Population-level predictors were identified through multivariable analysis (GEE, alpha=.05) estimating unsafe-sleep deaths among birth cohorts (Kalamazoo County, 2006-2019, N=43,485 births). FIMR reviews generated 105 recommendations for improvement. A multistep process was developed for coding and validating recommendations.

**Results:** Fifty-two of 278 infant deaths (18.7%) in Kalamazoo County, Michigan (2006-2019) were associated with unsafe-sleep. Populations at greatest risk of unsafe-sleep death were low-income (6.7OR,CI 3.2-13.9,p<.001) and families of Black race (3.1OR,CI 1.3-7.6,p=.011). Considering multiple risk factors, the families who experience unsafe-sleep deaths were: 3.2aOR (CI1.7-6.2,p<.001) times as likely to smoke prenatally, 3.4aOR(CI 1.4-8.1,p=.006) times as likely to be a single mother, 1.9aOR (CI 1.1-3.3,p=.033) times as likely to have inadequate prenatal care, and likely to have lower birthweight (aOR 1.0, CI .999-1.00, p=.050). The most common recommendations for unsafe-sleep deaths broadly fell into categories of Improving systems of care, Family/provider communication, and Improving provider communication skills. Leading recommendations were: Develop a coordinated, multi-system, community-informed response to safe sleep barriers, Provide content training/panel on emerging risk trends and available resources, and Develop provider skills for shared decision-making & relationship building with patients.

**Conclusion:** Fetal Infant Mortality Reviews underscore that families under stress (isolated, low socioeconomic status, discriminated against) are at greatest risk for unsafe-sleep deaths, necessitating multi-level supports to strengthen knowledge, connectedness, and access to resources. The safe sleep inequities found in this study necessitate targeted interventions aligning with recommendations to ensure improvement in infant-fetal care outcomes.

**Acknowledgments:** Fetal and Infant Mortality Review is funded by Kalamazoo County Health & Community Services, Michigan Department of Health & Human Services, and by United Way of Battle Creek Kalamazoo Foundation

**References:** [1] Kalamazoo County FIMR Recommendations Report (2021) <https://ncfrp.org/wp-content/uploads/Kalamazoo-FIMR-Recommendations-Report-2021.pdf> [2] CDC (2021). <https://www.cdc.gov/>.

**IRB#:** WMed-2017-0179

## ***72: Quality Improvement (QI) Intervention seeking to increase COVID-19 vaccination rates among unvaccinated patients aged 20-64 years in the Emergency Department***

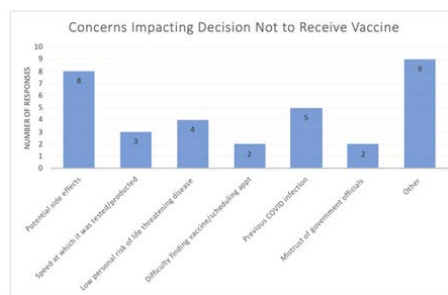
Shelby DeWaard BS<sup>1</sup>, Zachary Dewyer BS<sup>1</sup>, Nelson Hauber MD<sup>1</sup>, Corbin Donham MD<sup>2</sup>, Adam Wuensch MD<sup>2</sup>, Joshua Recknagel MD<sup>2</sup>, Elizabeth Hoffman MD<sup>2</sup>, Rachael Gallup BS<sup>3</sup>, Maureen Ford MD<sup>1</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Emergency Medicine, Western Michigan Homer Stryker M.D. School of Medicine, Kalamazoo, MI. <sup>3</sup>Bronson Methodist Emergency Department, Kalamazoo, MI

**Introduction:** The goal of this study is to determine the effect of a one-time educational intervention on COVID-19 vaccine acceptance in Emergency Department (ED) patients aged 20-64. At the time our QI project was initiated, 55% of the US was fully vaccinated, with 65% having received one dose<sup>1</sup>. In our ED population, fully and partially vaccinated rates were lower at 48% and 53% respectively. We hypothesized that a one-on-one educational intervention, where patients could discuss questions/concerns about the COVID-19 vaccine with physicians and medical students, would increase the rate of patients having received the first dose of a COVID-19 vaccine by 10% among our sample of 100 patients.

**Methods:** Unvaccinated ED patients aged 20 to 64 at Bronson Methodist Hospital were approached and asked if they were willing to discuss COVID vaccines. Consent was obtained, and demographic data collected. Patients were asked about interest in receiving the COVID-19 vaccine and reasons for not doing so. There was then a brief educational intervention/opportunity for the patient to ask questions. Patients are being contacted 4 weeks after their visit to check vaccination status.

**Results:** We have recruited 17/100 participants to date. The seventeen participants have given 33 reasons for not being vaccinated. The most common reasons were potential side effects of the vaccine (8/33) and believing natural immunity after COVID-19 infection made it unnecessary (5/33). Other concerns included: not knowing what is in the vaccine, false claims such as microchipping, and the vaccine being administered in non-healthcare facilities. Eighty two percent (14/17) of participants would be unwilling to receive the vaccine at time of ED visit.



**Conclusion:** To date, the intervention has not appeared to increase patient acceptance of COVID-19 vaccine. Recruitment will continue until we reach our target sample size of 100 and obtain 4 week follow-up data to see if patients choose to get vaccinated. As of February 15th, 2022, the vaccine will be available in the ED, so participants willing to obtain a vaccine can do so during their ED visit; however, initial data suggests acceptance rates will be low.

**References:** [1] US Coronavirus Vaccine Tracker. <https://usafacts.org/visualizations/covid-vaccine-tracker-states/>.

## ***75: No-Shows in a Pediatric Orthopaedic Clinic: Is SCFE a Risk Factor?***

Shaan Manawar MD, Lindsey Young BS, Karen Bovid MD

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

**Introduction:** Slipped capital femoral epiphysis (SCFE) is displacement of the femoral head at the physis and is associated with obesity and low socioeconomic status (SES)<sup>1,2</sup>. Maintaining follow-up is important for SCFE patients to ensure appropriate healing, treat symptomatic impingement, and address contralateral SCFE<sup>2,3</sup>. Factors that influence non-attendance in orthopedic clinics include age, distance from clinic, type of injury, and insurance status<sup>4-10</sup>; low SES is associated with increased no-show rates in medical clinics<sup>11</sup>. Our study aims to determine risk factors for missed appointments in a pediatric orthopaedic clinic, with a focus on the SCFE population.

**Methods:** Retrospective cohort study involving patients aged 7-21 from the WMed Pediatric Orthopaedic Clinic scheduled for an appointment between 5/1/2017 - 7/31/2021. The study group included patients surgically treated for SCFE documented by ICD-9/10 codes. The comparison group included patients who underwent lower extremity surgery for diagnoses other than SCFE with similar follow-up schedules. Data extracted from the medical record included age, race, sex, appointment time/status, length of follow-up, BMI, zip code, Area Deprivation Index (ADI), and insurance provider. IRB granted exempt status WMed-2021-0821.

**Results:** 28 SCFE patients and 85 non-SCFE patients were included in the analysis. Average BMI of SCFE patients (31.65) was significantly higher than non-SCFE patients (26.77) ( $p = 0.022$ ). More SCFE patients had public insurance (65.4%) than non-SCFE patients (38%) ( $p = 0.024$ ) and more SCFE patients were African American (39.3%) than non-SCFE patients (18.8%) ( $p = 0.040$ ). Of 213 post-operative appointments for SCFE patients, 145 were completed and 68 (32%) missed (46 canceled, 22 no-show). Of 620 post-operative appointments for non-SCFE patients, 460 were completed and 160 (26%) missed (126 canceled, 34 no-show). No significant differences were found in missed appointments when accounting for a diagnosis of SCFE, age, sex, BMI, or distance from clinic.

**Conclusion:** Missed post-operative appointments are common in patients with SCFE and other lower extremity diagnoses. Our study did not determine significant risk factors that may result in missed appointments. Future work is needed in ensuring appropriate follow-up care for pediatric orthopaedic patients.

**86: Asthma Education Project at Western Michigan University: A Quality Improvement Initiative to Improve Asthma Control in Children in Southwest Michigan**

Tam Doan BS, Maya Giaquinta BA, BS, Andrew Alfred BS, Sydney Les BS, Wilo Issack MS, Mariam Ischander MBChB

Department of Pediatric and Adolescent Medicine, Division of Pediatric Pulmonology and Sleep Medicine, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Asthma is a chronic inflammatory lung disease characterized by recurrent exacerbations with frequent ED visits/hospitalizations. Over 5.1 million U.S. children suffer from asthma [1]. Asthma adversely affects well-being, decreases life expectancy, increases school/work absences and nighttime awakenings, and impairs exercise tolerance.

**Methods:** In 2019, WMed students initiated an asthma education quality improvement project to improve asthma outcomes in patients seen at pediatric pulmonology clinics. Measured outcomes include decreased frequency of ED/hospital visits, decreased rescue inhaler and systemic steroid usage, improved FEV1/FEF25-75%, and patient satisfaction with the education. Inclusion criteria are patients 6-21 years old without changes in asthma medications. During visits, students provide the initial education session using standardized handouts and bronchial models. Students address allergies, home environment, and medication/spacer usage. Patients are given an American Academy of Pediatrics asthma education booklet and a medication storage case. At approximately 1, 3, 6, and 12 months after the initial visit, students follow up with patients via phone call, MyChart, or in-clinic visit to monitor outcomes.

**Results:** As of January 25, 2022, 67 patients were educated. Table 1 shows the number of patients and date ranges for each visit. Data show a significant reduction in rescue inhaler doses at 1 month (81% reduction,  $p = 0.0056$ ), 3 month (64% reduction,  $p = 0.0455$ ), and 6 month (91% reduction,  $p < 0.0001$ ) follow up when compared to the initial visit. There was also a significant difference for systemic steroid use at 3 months (87% reduction,  $p = 0.0252$ ). Overall, the majority of patients were “very satisfied” with the education provided at initial visit (86.57%) and 1 month follow up (82.35%). Statistical analysis for ED/hospital visits and spirometry data was not performed due to low sample size.

**Table 1:** Characteristics of Outcomes in Asthma Education QI Project

	<b>Number of Patients</b>	<b>Range of Days Elapsed Since Initial Visit</b>	<b>Mean Doses of Rescue Inhaler Taken in the Last Month (Standard Deviation)</b>	<b>Mean Doses of Systemic Steroid Taken in the Last Month (Standard Deviation)</b>	<b>Median Visits to ED, Hospital, Urgent Care, or PCP for Asthma Reasons in the Last Month (Minimum, Maximum)</b>
Initial Visit <sup>a</sup>	67	N/A	11.83 (37.32)	2.60 (15.05)	0 (0, 2)
1 Month Follow Up <sup>a</sup>	34	25 - 63	2.62 (6.16)	0.48 (1.92)	0 (0, 0)
3 Month Follow Up	40	82 - 122	4.53 (8.60)	0.35 (1.17)	0 (0, 3)
6 Month Follow Up	26	137 - 200	1.08 (1.83)	0 (0)	0 (0, 1)
12 Month Follow Up	13	378 - 645	5.85 (20.78)	1.08 (2.81)	0 (0, 0)

<sup>a</sup> 66 patients responded to the rescue inhaler question during the initial visit; 33 patients responded to the systemic steroid question at the 1 month follow up.

**Conclusion:** The data show a significant reduction in rescue inhaler usage at 1, 3, and 6 month follow up when compared to initial visit. There was also a significant difference in systemic steroid usage at 3 month follow up when compared to initial visit. This project is ongoing.

## ***94: Revisiting Trends in the Certification of Choking-related Deaths***

Dakota De Cecco BS<sup>1</sup>, Abigail Grande MPH<sup>2</sup>, Amanda Fisher-Hubbard MD<sup>2</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Pathology, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** It is currently unclear if and how risk factors for choking, including neurological conditions and acute intoxications, are captured on death certificates [1-3]. With feedback from forensic pathologists and public health professionals, the authors expanded upon prior research to examine how choking-related deaths are certified and to discern trends in certification of these deaths.

**Methods:** The authors used a broad strategy to query the electronic database in which cases investigated by the medical examiner's office are recorded. The authors searched the "Cause of death" and "Injury description" fields for "chok\*" and "airway." The authors reviewed results to include cases that fit the type of asphyxial death being investigated (obstruction of internal airways). The decedent demographics, type of examination, cause(s) of death (Part I), manner of death, and other significant conditions contributing to death (Part II) were documented. Contributing causes of death were then divided into categories, including neurological diseases and acute intoxications.

**Results:** A total of 101 cases that met criteria were identified; an additional nine cases will require further investigation due to incomplete information. Decedents ranged in age from 1 to 95 years (average = 63 years). Over 99% of deaths were certified as accidents. In 42% of deaths, a neurological condition was contributory and in 11% of deaths, an acute intoxication was contributory. Thirty-one percent of cases had no other contributory causes and no deaths had both neurological and acute intoxication as contributory causes.

**Conclusion:** The way in which choking-related deaths are certified by forensic pathologists lacks standardization, from terminology to inclusion of risk factors. For public health and vital statistics purposes, further investigation and group review of these deaths to discuss certification should be considered.

**IRB #:** WMed-2022-0876

### **References:**

- [1] Kramarow E, Warner M, Chen L. Food-related choking deaths among the elderly. *Injury Prevention*. 2014;20(3):200.
- [2] Nikolić S, Zivković V, Dragan B, Juković F. Laryngeal choking on food and acute ethanol intoxication in adults--An autopsy study. *J Forensic Sci*. January 2011;56(1):128-31.
- [3] Berzlanovich AM, Muhm M, Sim E, Bauer G. Foreign body asphyxiation--an autopsy study. *Am J Med*. 1999;107(4):351-5.



## ***97: Care Coordination Registry Identifies System Gaps and Strengths***

Joi Presberry MPH<sup>1</sup>, Catherine Kothari PhD<sup>1</sup>, Grace Lubwama DPPD<sup>2</sup>, Terra Bautista BS<sup>3,4</sup>, Brenda O'Rourke RN<sup>3</sup>, Deb Lenz MPA<sup>3</sup>

<sup>1</sup>Epi-Bio Division, Biomedical Sciences, WMed, Kalamazoo, MI. <sup>2</sup>YWCA-Kalamazoo, Kalamazoo, MI. <sup>3</sup>Maternal-Child Health, Kalamazoo County Health & Community Services, Kalamazoo, MI. <sup>4</sup>Healthy Babies Healthy Start, Kalamazoo County Health & Community Services, Kalamazoo, MI

**Introduction.** Kalamazoo County Michigan has a long history of racial disparities in maternal-infant health, with black infants dying at nearly three times the rate of white infants (Relative Rate 2.9, 2017-2019). Home visitation (HV) programs are evidence-based interventions that facilitate access to medical and community resources, improve maternal-infant health and reduce racial disparities. Kalamazoo has plentiful home visitation programs, but referral processes are fragmented and may not be reaching populations at highest risk.

**Methods.** In an effort to coordinate referrals and gather population-level operational data, Cradle-Kalamazoo data backbone implemented a Care Coordination Registry among all six prenatal HV programs in the county. Program-specific data sharing, integration and reporting procedures were developed, piloted and standardized. Regular uploads of all referrals into the registry involve automated and manual steps for data integration and linkage validation. Referral data includes identifiers, referral information, enrollment status, and demographics. WMed IRB# 2016-0123.

**Results.** In the first five years (2016-2020), 4677 prenatal referrals for 3432 pregnant women were deposited into the registry. An estimated 9861 pregnancies were eligible for HV programs, resulting in a referral rate of 47.4%. Referrals were split evenly between nurse-based programs (50.5%) and community health worker (chw)-based programs (49.5%). Sources of the most referrals were hospital obstetric outpatient/inpatient (31.3%), followed by insurance companies (23.7%) and WIC (21.8%).

Enrollment rates averaged 33.8%, were best among low-income women of color (38.0%) and worst among higher-income white women (22.5%) (Pearson Chi Square 36.73, p<.001). The most common referral sources were some of the least effective, particularly insurance company referrals (12.0% enrollment). Although generating a fraction of the referrals, the most effective sources were self-referrals (71.3% enrollment), social service (52.6% enrollment), Cradle-Kalamazoo (51.2% enrollment) and Healthy Start outreach/educators (48.1% enrollment).

**Conclusions.** Cradle data backbone successfully implemented a Care Coordination Registry, which revealed low referral rates, low enrollment rates and an inefficient referral system. Given the potential of HV programs to improve access and health outcomes, this is a critical gap to address. Strengths include the willingness of programs to collaborate and the relatively higher enrollment of low-income women of color.

***109: The Cux1 and Polycystin1 proteins are regulated by the Notch signaling pathway in the developing kidney***

Greg Vanden Heuvel PhD, Kemin Su PhD

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

**Introduction:** Notch signaling is a highly conserved cell-cell communication pathway that is important for the development of most organisms. Transmembrane Notch receptors interact with transmembrane ligands resulting in the cleavage of the Notch receptor and the translocation of the receptor intracellular domain (NICD) to the nucleus where it interacts with the RBPJ/k transcription factor to regulate gene expression. Cux1 is the murine homologue of the Drosophila gene Cut. In Drosophila, multiple genetic interactions between Cut and the Notch signaling pathway occurs during development. Cux1 co-localizes with several components of the Notch signaling pathway during kidney development. Moreover, Cux1 is upregulated in rat kidney epithelial cells expressing a constitutively active Notch1, suggesting this interaction is conserved across species.

**Methods:** To further evaluate whether Cux1 is regulated by the Notch signaling pathway we evaluated mice carrying a targeted deletion of the RBPJ/k transcription factor in the developing kidney. Mice carrying a conditional RBPJ/k allele were crossed with Hoxb7/cre mice to specifically delete RBPJ/k in the developing collecting duct.

**Results:** Newborn RBPJ/k mutant mice exhibited medullary and cortical cystic like dilatations. In addition, there was a complete absence of Cux1 protein specifically in the collecting ducts in which RBPJ/k was deleted, suggesting that Notch signaling is required for Cux1 expression. To evaluate the cystic like dilatations, we analyzed planar cell polarity (PCP) using anti-phospho-Histone H3 antibodies which showed a disruption of spindle orientation in the collecting ducts of RBPJ/k mice. This is similar to the changes in planar cell polarity that occurs in autosomal dominant polycystic kidney disease (ADPKD). To test whether the Notch signaling pathway is involved in PKD, we evaluated the expression of the polycystin1 protein, which is encoded by the PKD1 gene which is mutated to cause ADPKD. Polycystin1 expression was upregulated in the dilated tubules of the Notch mutant mice, but not in the wild type mice.

**Conclusion:** Taken together, these results suggest that Cux1 expression is activated by the Notch signaling pathway and that polycystin1 is repressed by the Notch pathway. These results may lead to new targets for treatment of PKD.

## POSTER PRESENTATIONS

- 4: **Cameron Crasto MD**, Scott Huff MD, Nabil Ebraheim MD  
Girdlestone Procedure: A Viable Alternative for Displaced Femoral Neck Fractures
- 5: **Nicole Fledderman MD**, Lillian Slavin MA, Daniel Dravin PhD, Neelkamal Soares MD  
Mixed Methods Analysis of Reflective Statements of Residents following the  
Developmental-Behavioral Pediatric Rotation
- 6: **Yerie Yang MD**, Syeda Asad MD  
Diagnosis Challenge of Hepatitis C: Extrahepatic Manifestations
- 9: **Julianne Mannix BA**, Laura Bauler PhD, Wesley Turner DO, Joshua Mastenbrook MD  
Gonococcal Meningitis caused by Neisseria gonorrhoea in an Immunocompetent Patient
- 10: **Steven Jones BS**, Laura Bauler PhD  
Encouraging Pre-clinical Scholarship Through a Case Report Writing Elective
- 12: **Allison Balaj BS**, Thomas Rothstein MD, PhD, Hiroaki Kaku PhD  
Small heat shock proteins synergize with FAIM to prevent the characteristic amyloid- $\beta$   
aggregation of Alzheimer's disease.
- 13: **Rachel Zamihovsky BA**, Laura Bauler PhD, Kathryn Redinger MD  
A Cautionary Tale of Costochondritis Mimicking a STEMI
- 14: **Emily Beck BS**, Gregory Vanden Heuvel PhD, Adil Akkouch PhD  
A Role for Cut homeobox 1 in Scoliosis Pathogenesis and Spine Deformity
- 15: **Rosemary Vergara MS**, Sarah Khalil MD, Gitonga Munene MD  
Perioperative Chemotherapy for Hepatic Undifferentiated Embryonal Sarcoma in a Young  
Adult: Case Report and Review of the Literature
- 16: **Robert Sawyer MD**, Mikayla Moody DO  
Is there a community microbial community? A comparison of pathogens between two  
hospital SICUs in a single city
- 17: **Jordan Boivin MD**, James Jastifer MD  
Early results of ankle arthrodesis using an anterior hybrid compression locking plate
- 19: **Abigail Duerst MS**, Anna Vanderschaegen MS, Lisa Graves MD, Juliana Kling MD, MPH  
Exploring the Hidden Curriculum of Sex and Gender-Based Medicine: Medical School  
Faculty Knowledge and Attitudes

- 20: **Justin Mak BS**, Laura Bauler PhD, Krishna Jain MD, Kathryn Redinger MD  
A Case of 36 Cardiac Stents from Recurrent STEMI: Re-examining the Algorithm for Emergent Percutaneous Coronary Intervention
- 21: **Amy Lin MS**, Laura Bauler PhD, Joshua Recknagel MD, Timothy Trichler MD  
Dural Arteriovenous Fistula in a Patient Presenting with Headache
- 22: **Baturay Aydemir MD**, Jon Williams DO, Philip Pazderka MD  
A case of Wellen's syndrome in a patient presenting with chest pain
- 24: **Marian Jirjis MD**, Satish Solanki MD, Lauren Piper DO  
Early manifestation of Granulomatosis with Polyangiitis with gingival limited disease
- 25: **John Bradtke**, Julita Gongolli, Laura Bauler PhD, Mariam Ischander MBChB  
Non-Emphysematous Pulmonary Manifestations of Alpha-1 Antitrypsin Deficiency in Heterozygous Carrier Pediatric Patients
- 26: **Agnieszka Steiner**, Laura Bauler PhD, Mark Schauer MD  
Amiodarone-Induced Thyrotoxicosis in an Athyroid Patient
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**POSTER  
PRESENTATION  
ABSTRACTS**

#### ***4: Girdlestone Procedure: A Viable Alternative for Displaced Femoral Neck Fractures***

Cameron Crasto MD<sup>1</sup>, Scott Huff MD<sup>2</sup>, Nabil Ebraheim MD<sup>1</sup>

<sup>1</sup>University of Toledo College of Medicine, Toledo, OH. <sup>2</sup>Wright State University, Dayton, OH

**Objective:** The Girdlestone procedure (femoral head ostectomy) is a salvage operation that may be used for treatment of infected hip arthroplasty in non-ambulatory patients or those unable to tolerate a two-stage surgery. Infection control is well-established and generally pain is tolerable. The purpose of this study was to evaluate surgical risk associated with Girdlestone procedure as a suitable alternative treatment of displaced femoral neck fracture in very highly-comorbid patients at high-risk for tolerating hemiarthroplasty.

**Design:** A retrospective chart review of 30 non-ambulatory patients over 10 years who underwent Girdlestone procedures for displaced femoral neck fractures due to extremely-high anesthetic and/or infection risk.

**Results:** Girdlestone procedures were reasonably well-tolerated in very high-risk surgical candidates with displaced femoral neck fractures and required lower reoperation rates than closed reduction and percutaneous pinning. Perioperative, 90-day, and 1-year mortality rate were 3% (1/30), 53% (16/30), and 67% (20/30), respectively. Of patients who followed-up after surgery, 33% maintained their previous functional mobility and 66% reported improved mobility after their Girdlestone procedure.

**Conclusion:** Girdlestone procedures serve as a well-tolerated alternative procedure for displaced femoral neck fractures and should be considered when treating a patient who is non-ambulatory.

## ***5: Mixed Methods Analysis of Reflective Statements of Residents following the Developmental-Behavioral Pediatric Rotation***

Nicole Fledderman MD<sup>1</sup>, Lillian Slavin MA<sup>2</sup>, Daniel Dravin PhD<sup>2</sup>, Neelkamal Soares MD<sup>1</sup>

<sup>1</sup>Department of Pediatric and Adolescent Medicine, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. <sup>2</sup>Department of Psychology, Central Michigan University, Mount Pleasant, MI

**Introduction:** We sought to determine the level of reflection of residents completing the developmental-behavioral pediatrics (DBP) rotation and whether level of reflection was correlated with timing of the rotation (earlier or later in training year, before or since the Coronavirus disease 2019 (COVID-19) pandemic and if word count or reading ease moderated the level of reflection.

**Methods:** This retrospective study included deidentified reflection statements of Pediatrics and Medicine-Pediatrics residents after their DBP rotation from 2017-2021. Level of reflection for each of four categories of prompts, leadership, interdisciplinary, family-centered, and equity (LIFE) were coded using a five-point Castleberry rating and analyzed against timing of the rotation, gender, program type, word count and reading ease.

**Results:** Thirty-six residents completed reflections during the time frame studied, 58% completed the rotation prior to the COVID-19 pandemic, and 44% completed the rotation early in the academic year. Mean Castleberry ratings were 3.2 (SD = 0.7), 2.7 (SD = 0.8), 2.6 (SD = 1.0), and 2.6 (SD = 0.8) for LIFE respectively. Simple linear regression showed no differences in ratings based on gender, training program, timing of rotation, or in relation to COVID-19 pandemic. We found statistically significant positive correlations between word count and ratings, though not for reading ease score.

**Conclusions:** Pediatric and Medicine-Pediatrics residents reflect moderately on their DBP rotation, and more on leadership than other aspects integral to DBP practice. Future research is needed to compare reflections on the LIFE framework across different rotations, and thematic/sentiment analysis can reveal opportunities for guiding residents on the reflection process.

## ***6: Diagnosis Challenge of Hepatitis C: Extrahepatic Manifestations***

Yerie Yang MD, Syeda Asad MD

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

**Introduction:** Unlike many other notifiable infectious diseases, the rate of acute Hepatitis C quadrupled from 2010 to 2018 in the United States. Prevalence of Hepatitis C in the United States is estimated to be between 2.5- 4.7 million, of which 80% are chronic. Although mainly attributed to intravenous drug use, this also reflects the diagnosis challenge of Hepatitis C. Hepatitis C has many extrahepatic manifestations, which are thought to be secondary to host immune response to the virus. This case presents an example of extrahepatic manifestation of Hepatitis C that challenged the diagnosis and the importance of its awareness.

**Case Report:** This case presents a 26-year-old male with a history of intravenous drug use and unsafe sexual practices complaining of a pruritic rash on the face and chest that appeared 8 months prior to presentation. It was previously diagnosed as impetigo but did not improve with antibiotics. Associated symptoms included diaphoresis and fatigue only. Patient's liver function test from the previous visit 8 months ago showed elevated liver enzymes. Given his risk factors, hepatitis panel and sexually transmitted disease testing were ordered, which returned positive for Hepatitis C.

**Discussion:** Extrahepatic manifestations of Hepatitis C can often be nonspecific, creating diagnostic challenges. For example, clinicians may not be aware that pruritus is present in about 15% of patients with chronic Hepatitis C. This case demonstrates the importance of recognizing extrahepatic manifestations to diagnosis Hepatitis C. With increasing awareness, extrahepatic manifestations can be used as an aid to diagnose Hepatitis C.



**Figure: Pruritic Rash on Patient's Anterior Chest.**

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## ***9: Gonococcal Meningitis caused by Neisseria gonorrhoea in an Immunocompetent Patient***

Julianne Mannix BA<sup>1</sup>, Laura Bauler PhD<sup>2</sup>, Wesley Turner DO<sup>3</sup>, Joshua Mastenbrook MD<sup>3</sup>

<sup>1</sup>Medical Student, <sup>2</sup>Department of Biomedical Sciences, <sup>3</sup>Department of Emergency Medicine, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** *Neisseria gonorrhoea* is a leading cause of sexually transmitted infection (STI) among young adults. *N. gonorrhoea* classically infects and colonizes the mucosal endothelium of the urogenital tract manifesting as cervicitis in women and urethritis in men. *N. gonorrhoea* has the potential to spread hematogenously from the site of infection to cause a disseminated gonococcal infection (DGI). Hematogenous spread occurs in 0.5% - 3% of primary gonorrhoea infections, and may manifest with polyarthrititis, skin lesions, or more rarely, meningitis or endocarditis. Gonococcal meningitis may have a slower onset and more mild symptoms than typical bacterial meningitis, including headache, fever, and nuchal rigidity.

**Case History:** This report presents a case of disseminated gonococcal meningitis in an immunocompetent patient with the initial presentation of diffuse headache with photophobia. While in the Emergency Department (ED), the patient developed fever, mild nuchal rigidity, and subsequently underwent lumbar puncture with results suggestive of bacterial meningitis. The patient was ultimately diagnosed by a cerebral spinal fluid (CSF) polymerase chain reaction (PCR) that was positive for *N. gonorrhoeae*, and was treated with a 14-day course of intravenous ceftriaxone which resolved the infection.

**Clinical Significance:** Disseminated gonococcal infection (DGI) is characterized by a classic symptom triad of dermatitis, tenosynovitis, and migratory polyarthrititis. This disease process is thought to occur more commonly in women due to less symptomatic mucosal STIs, leading to delayed treatment and infection progression. Gonococcal meningitis is a rare consequence of DGI, but maybe more common for certain strains, necessitating public health notification. Patients presenting to the ED with acute headache, fever, nuchal rigidity, maculopapular rash, or altered sensorium, should trigger suspicion for meningitis. Diagnosis is made by lumbar puncture. However, a negative CSF PCR Meningitis/Encephalitis Panel does not rule out bacterial meningitis and treatment should continue in the presence of a suggestive initial CSF and hematology analysis. Additional data should be gathered from the patient including a more thorough social history to identify risk factors for meningitis to allow for narrowing of treatment and additional confirmatory studies. DGI, as a disseminated sexually transmitted infection, requires extended antibiotic treatment and identification and treatment of sexual partners.

## ***10: Encouraging Pre-clinical Scholarship Through a Case Report Writing Elective***

Steven Jones BS<sup>1</sup>, Laura Bauler PhD<sup>2</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Biomedical Sciences, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Starting January 2022, the USMLE will transition to a pass/fail outcome for the Step 1 exam. Historically, the Step 1 exam score has been used extensively by residency programs in their selection of applicants, this change necessitates alterations to how residencies review applications. In light of this, medical schools are finding ways to make their graduates more competitive, and one way is by providing easier access to research and publication opportunities. Here we describe the outcomes of a case report writing elective offered at WMed intended to familiarize students with academic medical writing, case reports, and the publication process. While similar electives have been offered to first-year residents, the outcomes of this type of curriculum for preclinical students has not been documented in the literature.

**Methods:** The one-week elective has been offered to second-year medical students since 2018. All students (n=38) who participated in the elective between February 1, 2018 and February 1, 2021 were sent an anonymous survey to evaluate their motivations for taking the elective, previous experience with research and publication, and experience with the elective. Data was also collected regarding the scholarly output for each student project conducted during the elective including conference presentations and publications.

**Results:** The survey results showed students were primarily motivated to enroll based on the goal of learning how to write a case report. Students reported high student satisfaction with the elective, as well as positive learning outcomes and increased comfort with medical research and publication. Furthermore, the case report writing elective was an effective tool to increase student scholarly output, with 76% producing a completed draft, 84% presenting at a conference, and 45% publishing manuscripts.

**Conclusion:** Together this data indicates that this type of curriculum is an effective way to encourage publication and increase students' comfort with clinical research and writing. Students benefit from increased exposure to the medical literature, in-depth discussions with clinical faculty, and scholarly products including conference abstracts and publications. This elective is a curricular component that can be used to increase student driven research and scholarship that could be implemented at other institutions.

## ***12: Small heat shock proteins synergize with FAIM to prevent the characteristic amyloid- $\beta$ aggregation of Alzheimer's disease***

Allison Balaj BS<sup>1</sup>, Thomas Rothstein MD, PhD<sup>2,3</sup>, Hiroaki Kaku PhD<sup>2,3</sup>

<sup>1</sup>Medical student, <sup>2</sup>Center for Immunobiology, <sup>3</sup>Department of Biomedical Sciences, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI.

**Introduction:** Cells are subject to environmental insults, such as heat shock and oxidative stress, that cause accumulation of aggregated proteins. We previously found that Fas Apoptosis Inhibitory Molecule (FAIM) protects cells from stress-induced cell death by preventing generation of protein aggregates similar to heat shock proteins (HSPs) [1]. Protein aggregates are associated with neurodegenerative diseases, including Alzheimer's disease (AD). In this study, we sought to determine how FAIM protein dynamics change during cellular stress, and whether FAIM can prevent the formation of amyloid- $\beta$  aggregates, a pathological hallmark of AD [2].

**Methods:** Using HeLa and HLE B-3 cell lines, we analyzed FAIM expression levels and cellular location during cellular stress by western blotting. We also investigated the possibility that FAIM is recruited to a complex containing HSPs by co-immunoprecipitation followed by western blotting and in situ proximity ligation assay (PLA). To examine whether FAIM inhibits amyloid- $\beta$  aggregation similar to HSPs, we used Thioflavin T (ThT), a dye that only fluoresces when incorporated into amyloid fibrils.

**Results:** We found that the majority of FAIM protein shifted to the detergent-insoluble fraction in response to cellular stress, which was especially noticeable after heat shock. A similar shift to the insoluble fraction was observed in small heat shock protein (sHSP) family molecules after stress. The similarity between FAIM and sHSPs in subcellular distribution after stress suggests that FAIM might prevent protein aggregation with sHSPs. We then observed the synergistic effect of FAIM and HSP27 on the prevention of protein aggregates using an amyloid- $\beta$  aggregation model.

**Conclusion/Clinical significance:** Our work provides new insights into the interrelationships among FAIM, sHSPs, and amyloid- $\beta$  aggregation that one day may help treat and understand neurodegenerative diseases. This has potential to lead to species-compatible, rationally designed, preventative and therapeutic interventions.

**Acknowledgments:** Work supported by Public Health Service grant AG072148 awarded to HK by the National Institutes of Health.

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### ***13: A Cautionary Tale of Costochondritis Mimicking a STEMI***

Rachel Zamihovsky BA<sup>1</sup>, Laura Bauler PhD<sup>2</sup>, Kathryn Redinger MD<sup>3</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Biomedical Sciences, <sup>3</sup>Department of Emergency Medicine, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo Department, MI

**Introduction:** Chest pain is one of the leading complaints seen by Emergency Department (ED) providers and must be rapidly evaluated to rule out an acute coronary syndrome. Patients with evidence of ST-segment myocardial infarction (STEMI) are typically treated with percutaneous coronary intervention (PCI) with stenting to rapidly re-perfuse the myocardial tissue. However, stenting may also lead to subsequent chest pain, causing patients to return to the ED post-discharge. ED physicians must also be aware of non-ischemic causes of chest pain that may mimic STEMI, particularly in patients who have had prior myocardial infarctions (Deshpande, Engel).

**Case History:** A 59-year-old male with an extensive medical history including severe coronary artery disease, multiple STEMI, over 30 stents, and 4 coronary artery bypass grafts (CABG) presented to the ED with 3 weeks of crushing chest pain. The patient's electrocardiogram (ECG) and clinical findings correlated with chronic STEMI however, the patient's cardiologist deemed the patient ineligible for future stenting due to insufficient space for additional stents. Several weeks later, the patient presented to the ED with findings concerning for STEMI, triggering emergent PCI protocols. However, the ECG readings were deemed to be lingering from previous damage and intervention, as a physical exam determined his chest pain was secondary to costochondritis.

**Clinical significance:** Differentiating an acute STEMI from other mimickers such as left ventricular hypertrophy is a crucial step in working up a patient with chest pain (Agrawal). Once a STEMI is identified, the standard of care is often PCI. However, after having over thirty stents, PCI may no longer be an option. Additionally, underlying cardiac pathology may complicate the accurate diagnosis of a STEMI, particularly in patients who experience chronic non-ischemic chest pain. While suspicion of acute STEMI should trigger PCI protocols, ED physicians should complete a thorough physical exam in addition to conducting an ECG, especially in cases with recent PCI, as the underlying cause of chest pain may be complicated by lingering ST-segment elevation on ECG. Early consultation with interventional cardiology and admission for observation may be an acceptable alternative to emergent and repeated PCI.



## 14: A Role for Cut homeobox 1 in Scoliosis Pathogenesis and Spine Deformity

Emily Beck BS<sup>1</sup>, Gregory Vanden Heuvel PhD<sup>2</sup>, Adil Akkouch PhD<sup>3</sup>

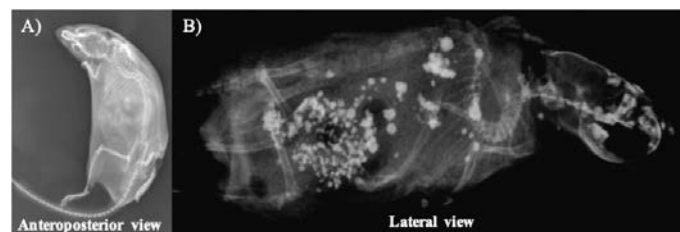
<sup>1</sup>Medical student, <sup>2</sup>Department of Biomedical Sciences, <sup>3</sup>Department of Orthopaedic Surgery, Medical Engineering Program, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** More than 29 million children worldwide have adolescent idiopathic scoliosis. <sup>[1]</sup> This is the most frequent musculoskeletal disorder in children, which dissimilar to adult scoliosis, occurs without associated degenerative changes. The etiology of idiopathic scoliosis is unknown. Recent research has suggested that variations in cartilage composition of the intervertebral disc can increase susceptibility for scoliosis through multiple mechanisms, including impacting bone quality and an asymmetric response to biomechanical loading. <sup>[1,2]</sup> Cut homeobox 1 (Cux1) is a nuclear transcription factor involved in cell proliferation, migration and invasion. <sup>[3]</sup> In developing limb, Cux1 regulates the onset of joint formation by mediating conversion of chondrocytes into non-chondrogenic cells. <sup>[4]</sup> Our goal is to determine the role of Cux1 in scoliosis pathogenesis.

**Methods:** Transgenic mice ectopically expressing Cux1 develop multiorgan hyperplasia and growth abnormalities. <sup>[3]</sup> Anteroposterior and lateral x-ray images were obtained, and Cobb angles were measured utilizing PowerPoint following Jones, et al. methods. <sup>[5]</sup> Bone and cartilage samples were obtained from apices of spine curvatures. H&E, Safranin-O, and Alcian-blue stains were used for histological analysis. Paired t-test analysis was used to compare Cux1 transgenic mice x-ray measurements to wild-type.

**Results:** 52% of the Cux1 transgenic mice were found to have scoliotic curvature ( $>10^\circ$  Cobb angle on anteroposterior view), compared to a 3% prevalence of adolescent idiopathic scoliosis in humans.

<sup>[1]</sup> Significant spine deformity was observed for select Cux1 transgenic mice on lateral view, with most severe phenotype exhibiting a  $159^\circ$  lordotic curvature and  $121^\circ$  kyphotic curvature.



**Figure:** CUX1 transgenic mice exhibiting A) scoliotic phenotype, B) severe lordotic and kyphotic curvatures.

**Conclusion:** To our knowledge, this is the first report of a scoliotic phenotype in Cux1 transgenic mice. Further investigation into the molecular role of Cux1 in spine development may yield better understanding of scoliosis pathogenesis.

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## ***15: Perioperative Chemotherapy for Hepatic Undifferentiated Embryonal Sarcoma in a Young Adult: Case Report and Review of the Literature***

Rosemary Vergara MS<sup>1</sup>, Sarah Khalil MD<sup>1</sup>, Gitonga Munene MD<sup>1,2</sup>

<sup>1</sup>Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. <sup>2</sup>West Michigan Cancer Center, Kalamazoo, MI

**Introduction:** Hepatic undifferentiated embryonal sarcoma of the liver (UESL) is a rare hepatic malignancy found more commonly in pediatric patients. It has been associated with poor outcomes in adults and the role and timing of systemic therapy is unclear. Although there are a few case reports detailing the use of adjuvant therapy to improve patient outcomes, there has been no case report of perioperative therapy for hepatic undifferentiated embryonal sarcoma in adults.

**Case History:** In this report, a 22-year-old male admitted with right upper quadrant pain was diagnosed with a 20 x 10 x 10 cm well-circumscribed, highly vascularized hepatic mass in the entirety of the left lobe. Biopsy confirmed the diagnosis of UESL. PET/CT showed no evidence of metastatic disease and he received four cycles of Doxorubicin and Ifosfamide with demonstrated reduction in size and decrease in PET avidity. He underwent left hepatectomy with periportal lymphadenectomy, cholecystectomy, and partial gastrectomy with negative margins and received adjuvant Doxorubicin, Ifosfamide and Mesna. At 48 months, the patient was alive without evidence of disease.

**Clinical significance:** We hereby emphasize the potential advantages of perioperative chemotherapy in the management of UESL in adults.

## 16: Is there a community microbial community? A comparison of pathogens between two hospital SICUs in a single city

Robert Sawyer MD, Mikayla Moody DO

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

**Introduction:** Nosocomial and healthcare-associated infections drive increased healthcare costs and negatively affect patient outcomes. The human microbiome has been heavily explored in recent years with incomplete data regarding hospital-specific and community-specific microbial communities. Although bacterial species differ between intensive care units in the same hospital, it is unclear if they differ between similar units in similar hospitals in the same community. Our hypothesis is that pathogens in surgical intensive care units are distinct between hospitals, even in the same community.

**Methods:** From 2017-2021, data were prospectively collected from the SICUs of two 500 bed hospitals located 3 miles apart in the same city (Hospital A and Hospital B). Infections defined using CDC criteria were recorded for trauma and general surgery patients, as well as patient demographics, APACHE II score, and causative organism. Means were then compared using the Student t-test, and proportions were compared with Chi-square or Fisher's exact test. \*\*IRB approval in progress. \*\*

**Results:** Overall, *Escherichia coli* was the most commonly isolated pathogen in Hospital A, while *Staphylococcus aureus* was most commonly isolated at hospital B (Table, \* =  $p \leq 0.05$  between hospitals). Enterococci were more common in Hospital A, and *Haemophilus influenzae* and *Enterobacter* spp. were more common in Hospital B. After stratification between trauma and non-trauma patients, however, these differences disappeared, with the exception of more overall Gram-positive organisms and fewer Gram-negative organisms among Hospital A trauma patients compared to Hospital B. There were no differences in rates of isolation of either fungi or resistant bacteria between hospitals. APACHE II scores were also similar when stratified by diagnosis.

Pathogen	Hosp A Overall	Hospital A Trauma	Hosp A Non-Trauma	Hosp B Overall	Hosp B Trauma	Hosp B Non-Trauma
All	190	52	138	369	232	137
<i>S. aureus</i>	22 (12%)	15 (29%)	7 (5%)	58 (16%)	50 (22%)	8 (6%)
MSSA	16 (8%)	11 (21%)	5 (4%)	40 (11%)	37 (16%)	3 (2%)
MRSA	6 (3%)	4 (8%)	2 (1%)	18 (5%)	13 (6%)	5 (4%)
Enterococci	26 (14%)*	6 (12%)	20 (15%)	25 (7%)	13 (6%)	12 (9%)
<i>E. faecalis</i>	19 (10%)	4 (8%)	15 (11%)	19 (5%)	9 (4%)	10 (7%)
VRE	6 (3%)	2 (4%)	4 (3%)	2 (1%)	2 (1%)	0 (0%)
<i>Strep. spp.</i>	16 (8%)	4 (8%)	12 (9%)	(7%)	11 (5%)	16 (12%)
All GPC	77 (41%)	28 (54%)*	49 (36%)	141 (38%)	89 (38%)	52 (38%)
<i>E. coli</i>	29 (15%)	9 (17%)	20 (15%)	41 (11%)	24 (10%)	17 (12%)
<i>Enterobacter</i>	5 (3%)*	2 (4%)	3 (2%)	24 (7%)	16 (7%)	8 (6%)
<i>P. aerug.</i>	13 (7%)	2 (4%)	11 (8%)	20 (5%)	13 (6%)	7 (5%)
<i>H. influenzae</i>	3 (2%)*	2 (4%)	1 (1%)	20 (5%)	19 (8%)	1 (1%)
<i>Klebs. spp.</i>	14 (7%)	1 (2%)	13 (9%)	37 (10%)	21 (9%)	16 (12%)
All GNR	81 (43%)	19 (37%)*	62 (45%)	183 (50%)	123 (53%)	60 (44%)
Fungi	14 (7%)	0 (0%)	14 (10%)	19 (5%)	7 (3%)	12 (9%)

**Conclusion:** At a species level, admission diagnosis appears to be a greater determinant of pathogen isolation than hospital when comparing similar intensive care units, but a larger body of data is needed to flesh out a distinct microbial map of the organisms occupying a certain geographic region. Further areas for investigation include comparison between hospital units, specific anatomic sites, and ICU versus floor patients.

## ***17: Early results of ankle arthrodesis using an anterior hybrid compression locking plate***

Jordan Boivin MD, James Jastifer MD

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

**Introduction:** Tibiotalar arthrodesis for osteoarthritis has been shown to be an effective surgical treatment due to consistent pain relief, a low reoperation rate, and the ability to correct significant deformities.<sup>[1]</sup> Many techniques have been described to achieve fusion of the ankle joint with a lateral, medial or arthroscopic approach to the ankle joint. Various constructs have been used including interfragmentary screws, compression plating, locking plate augmentation, and intramedullary nail.<sup>[1,2]</sup> The purpose of the current study is to assess the early clinical outcomes of a novel anterior hybrid compression locking plate using an anterior approach.

**Methods:** We retrospectively reviewed a single-surgeon case series of consecutive patients who underwent tibiotalar arthrodesis using an anterior hybrid compression locking plate (Stryker AxSOS 3 Anterior TT CP plate). Data collected included age, gender, body mass index (BMI), smoking status, diabetic status, surgical indication, length of follow-up, radiographic outcome, complications, visual analog score (VAS) pre- and post-operatively.

**Results:** Twelve patients were identified for retrospective review from 2021. Average patient age is 59 years old. Average follow-up is seven months. Average BMI is 32.2. One patient was a smoker and one patient was diabetic. On radiographic examination, one patient had a partial union on computerized tomography (CT). Additional complications included one hardware removal and one periprosthetic fracture. VAS decreased from  $6.3 \pm 2.6$  to  $1.6 \pm 2.4$  ( $P < 0.001$ ).

**Conclusions:** Early results using an anterior hybrid compression locking plate demonstrate it as a viable surgical treatment option for ankle arthrodesis. The complications and fusion rates appear to be comparable or better to previous fusion constructs, however this is a limited series of patients.<sup>[1,2]</sup>



**Figure:** Case representation of periprosthetic fracture complication. A) demonstrates preoperative CT. B) demonstrates intraoperative imaging. C) demonstrates radiographic evidence of periprosthetic fracture. D) demonstrates post-operative radiographs after fixation of the fracture. E) demonstrates final post-operative radiographs with successful fusion.

**References:** [1] Coughlin M, Saltzman C, Anderson R. Mann's Surgery of the Foot and Ankle. 9th ed. Philadelphia, PA: Elsevier Saunders; 2014. [2] Nihal A, Gellman RE, Embil JM, Trepman E. Ankle Arthrodesis. Journal of Foot and Ankle Surgery. (2008);14:1-10.

**IRB #:** WMed-2021-0790

## ***19: Exploring the Hidden Curriculum of Sex and Gender-Based Medicine: Medical School Faculty Knowledge and Attitudes***

Abigail Duerst MS<sup>1</sup>, Anna Vanderschaegen MS<sup>1</sup>, Lisa Graves MD<sup>2</sup>, Juliana Kling MD, MPH<sup>3</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Family and Community Medicine, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. <sup>3</sup>Division of Women's Internal Medicine, Mayo Clinic, Scottsdale, Arizona

**Background:** A person's sex and/or gender may influence the pathogenesis, presentation, and therapeutic response to disease; yet, the impact of sex and gender is not routinely evaluated in medical research, nor adequately emphasized in medical school curricula. Additionally, little is known about medical school faculty knowledge and attitudes regarding sex and gender based medicine (SGBM). This information could help provide insight into how to incorporate sustainable faculty development that incorporates SGBM to influence medical school curriculum.

**Objective:** To evaluate faculty knowledge, perceptions and attitudes about SGBM within a single medical school.

**Methods:** An online survey was administered to 158 faculty members at Western Michigan Homer Stryker M.D. School of Medicine via Redcap. The survey was 39 questions adapted from two prior surveys used in medical student and resident populations and modified for faculty participants that included knowledge questions about sex and gender differences. The hidden curriculum theory, which proposes students learn through formal curriculum as well as through passive perceptions of faculty and institutional attitudes, was used as a theoretical lens.

**Results:** Of 158 surveys, 38 were completed (24%). Respondents answered an average of 48.53% of the knowledge questions correctly, and percent correct did not differ significantly between male and female faculty members ( $p=0.2732$ ). Seventy one percent of respondents indicated it was important or very important to consider sex and gender when providing patient care. Only 24% indicated they had some formal or continuing education on the topic. Respondents indicated interest in educational opportunities for SGBM in the form of online modules or lectures.

**Conclusions:** Though faculty respondents endorsed SGBM as important, few have had formal education related to the topic. Faculty education on SGBM may close knowledge gaps and facilitate integration of this curriculum at medical institutions.

**IRB #:** WMed-2021-0764

## ***20: A Case of 36 Cardiac Stents from Recurrent STEMI: Re-examining the Algorithm for Emergent Percutaneous Coronary Intervention***

Justin Mak BS<sup>1</sup>, Laura Bauler PhD<sup>2</sup>, Krishna Jain MD<sup>3</sup>, Kathryn Redinger MD<sup>4</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Biomedical Sciences, <sup>3</sup>Department of Surgery, <sup>4</sup>Department of Emergency Medicine, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Approximately 1.5 million myocardial infarctions (MI) occur in the United States annually, with many of these patients presenting to the Emergency Department (ED). Due to the success of expeditious percutaneous coronary intervention (PCI) in treating MI, protocols have been established to reduce the time between acute ST-segment elevation myocardial infarction (STEMI) diagnosis and cardiac catheterization protocol activation. However, not all patients with acute STEMI may benefit from emergent PCI, as recent ACC/AHA guidelines for PCI in acute coronary syndromes acknowledge certain populations are underrepresented in the literature and their recommendations for such populations are based instead on clinical judgment.

**Case History:** A 59-year-old male presented to the ED for exacerbation of baseline chest pain. He had an extensive history of cardiac disease and 36 prior cardiac stent placements, with four stents placed within the past 11 days. An electrocardiogram (ECG) was positive for inferior wall STEMI, triggering rapid activation of the cardiac catheterization protocol. Interventional cardiology was consulted prior to cardiovascular laboratory (CVL) transfer and elected against further PCI due to lack of PCI-salvageable heart tissue.

**Discussion:** Rapid CVL activation followed by PCI is the current standard of care for acute STEMI, with the Joint Commission on Accreditation of Healthcare Organizations establishing a goal door-to-balloon time of less than 90 minutes. The pursuit of streamlined care to meet time-based benchmark metrics sometimes comes at the expense of a thorough diagnostic evaluation. This may have been the case for our patient too many times, as he had previously received 36 stents, completely lining the vessels of the heart. The physician, after diagnosing STEMI via ECG, should pause to ask whether these are new dynamic changes and whether there is an alternative diagnosis for the ECG changes. If so, like was done in this case, a conversation with interventional cardiology prior to CVL transfer may be beneficial.

**Conclusion:** We suggest there should be clear exclusion criteria or a systematic checklist for consideration for PCI to better identify patients who may not benefit from acute emergent intervention.

## ***21: Dural Arteriovenous Fistula in a Patient Presenting with Headache***

Amy Lin MS<sup>1</sup>, Laura Bauler PhD<sup>2</sup>, Joshua Recknagel MD<sup>3</sup>, Timothy Trichler MD<sup>3</sup>

<sup>1</sup>Medical student, <sup>2</sup>Department of Biomedical Sciences, <sup>3</sup>Department of Emergency Medicine, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Dural arteriovenous fistulas (DAVFs) are abnormal vascular connections in the brain that can be life-threatening. DAVFs may lead to serious complications such as neurological injury, intracranial hemorrhage, and death. However, DAVFs can be difficult to identify since clinical presentation of DAVFs vary widely, and standard imaging such as computed tomography or magnetic resonance imaging are insufficient to visualize DAVFs. Additionally, DAVFs are an extremely rare subtype of intracranial arteriovenous malformations. Early recognition, diagnosis, and appropriate management of DAVFs is essential to improving patient outcomes.

**Case Description:** We report a case of a 65-year-old patient that presented to the Emergency Department with initial complaint of a chronic headache. History and focal neurological exam revealed that patient experienced pulsatile tinnitus, sensory disturbances, and vision changes. Brain CT angiography (CTA) confirmed presence of a DAVF, and coil embolization of the fistula was performed.

**Discussion:** DAVFs are often challenging to identify, as they can present with a wide range of symptoms such as headache, pulsatile tinnitus, visual impairment, or other ocular symptoms. Angiographic studies are needed to make a definitive diagnosis. Since DAVFs have potentially serious and life-threatening complications, it is important that they be diagnosed early and appropriately managed. Recognition of key presenting symptoms is important to develop clinical suspicion of a potential DAVF. This case highlights the importance of considering angiographic imaging to evaluate for DAVF in patients with pulsatile tinnitus or other focal neurological complaints including headaches and visual disturbances, so that a potentially life-threatening diagnosis is not missed.

## 22: A case of Wellen's syndrome in a patient presenting with chest pain

Baturay Aydemir MD, Jon Williams DO, Philip Pazderka MD  
Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Wellens syndrome is a disease associated with significant coronary artery stenosis characterized by specific ECG changes. Classically, Wellens syndrome is diagnosed in patients with a resolved chest pain on presentation, with either biphasic or deeply inverted T waves on leads V2 and V3 [1]. This pattern is highly specific for a critical left anterior descending (LAD) artery stenosis.

**Case Description:** We present a case of Wellens-type ECG changes in a patient with chest discomfort. We obtained history directly from the patient and performed chart review to acquire clinical follow up information. A 57-year old patient with possible prior myocardial infarction history presented with 1 week of intermittent left sided chest pain. Although he did not meet ST-elevation-myocardial-infarction (STEMI) criteria, he had Wellens-type ECG changes. Patient underwent cardiac catheterization, and his proximal LAD was found to be 90% stenosed and his first obtuse marginal (OM1) was found to be 80% stenosed. He underwent stent placement in both LAD and OM1. He was chest-pain free and was discharged in good condition.

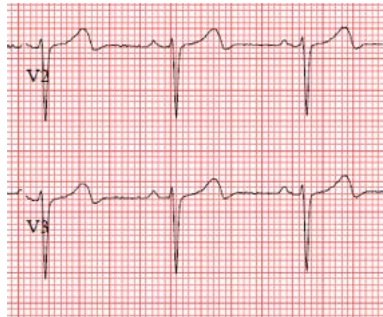


Figure: Leads V2 and V3 exhibiting the biphasic t-waves characteristic of Wellens pattern.

**Discussion:** Here we present a case of a patient who presented with intermittent chest pain with an ECG not meeting STEMI criteria, and yet was subsequently found to have a significant stenosis of his LAD and OM1 coronary arteries. Most commonly, the decision for cardiac catheterization is based on the STEMI criteria, but as this case shows, there are other important ECG patterns that should prompt cardiac catheterization. Classically, the Wellens syndrome is diagnosed only when the ECG pattern is present in a chest pain-free state. However, as our case shows, a Wellens-type ECG pattern in a patient experiencing chest pain is still concerning and should warrant a consideration for cardiac catheterization.

**References:** [1] Rhinehardt J. et al. (2002) Am. J. Emerg. Med., 20(7), 638-43.



## 24: Early manifestation of Granulomatosis with Polyangiitis with gingival limited disease

Marian Jirjis MD<sup>1</sup>, Satish Solanki MD<sup>2</sup>, Lauren Piper DO<sup>1</sup>

<sup>1</sup>Department of Family Medicine, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. <sup>2</sup>Bronson Rheumatology Specialist, Battle Creek, MI

**Introduction:** Granulomatosis with Polyangiitis (GPA) is thought to be an autoimmune disease, associated with c-ANCA. GPA causes tissue necrosis, granulomatous inflammation and vasculitis, consequently leading to end organ damage, specifically affecting the upper and lower respiratory tract (paranasal sinuses, nose, airways, lungs) and kidneys. Classical findings can include any of the following: ulceration/ polyps in nasal mucosa, lung nodules/ cavities/ infiltrates, hemoptysis, urinary sediments, and hematuria.<sup>1</sup> Initial onset of symptoms is variable, and GPA is rapidly progressive. The purpose of this case report is to illustrate gingival manifestation of GPA as an early onset of disease.

**Case Description:** 56-year-old male without past medical history presented to rheumatology clinic for evaluations of buccal/ lingual strawberry gingivitis (figure 1). He has a one-month history of rapidly progressive diffuse gum swelling, bleeding, and pain. His dentist trialed antibiotics with no improvement. He was referred to a periodontist who biopsied the gingival mucosa. Biopsy revealed heavy mixed inflammation including eosinophils, multinucleated giant cells, and prominent areas of erythrocyte extravasation, suggestive of GPA. Patient denied nosebleed, dyspnea, hemoptysis, cough, decreased urination and hematuria. Subsequent rheumatological lab work up revealed positive c-ANCA. Renal function, CT of head, sinus, and chest were all unremarkable. Methotrexate plus folic acid, and high dose prednisone were initiated for non-organ threatening GPA. After 6 weeks of treatment, patient noted a significant improvement in symptoms with gingival hyperplasia resolving.



Figure 1.1 and 1.2: diffuse gingival hyperplasia in upper and lower gingiva.

**Discussion:** Gingival involvement is a rare presentation of GPA. In a systematic review it was shown that 68.4% of cases reported that gingival manifestation was the first symptom of the GPA, and lesions resolved once treatment was initiated.<sup>1</sup> This case highlights that GPA should be considered as a differential diagnosis in patients presenting to primary care settings with concerns of gingivitis. This prompts appropriate work up and leads to earlier medical management, which prevents rapid progression of GPA and damage to vital organs.

**References:** [1] Apoitá-Sanz M., Blanco-Jauset P., et al. (2020) Granulomatosis with Polyangiitis (Wegener's Granulomatosis): Orofacial Manifestations. Systematic Review and Case Report. Oral Health Prev Dent.18(1):929-943.

## ***25: Non-Emphysematous Pulmonary Manifestations of Alpha-1 Antitrypsin Deficiency in Heterozygous Carrier Pediatric Patients***

John Bradtke<sup>1</sup>, Julita Gongolli<sup>1</sup>, Laura Bauler PhD<sup>1</sup>, Mariam Ischander MBChB<sup>2</sup>

<sup>1</sup>Department of Biomedical Sciences, <sup>2</sup>Department of Pediatric and Adolescent Medicine, Division of Pediatric Pulmonology and Sleep Medicine, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Background:** Alpha-1 antitrypsin deficiency (AATD) is an autosomal codominant disorder that manifests as pan-acinar emphysema of the lower lobes in mid-adulthood but can also present as liver disease and non-emphysematous pulmonary disease.<sup>1</sup> While research has shown more severe manifestations in homozygous individuals (Pi\*ZZ), less is known regarding the breadth and severity of disease manifestations in heterozygous carriers (Pi\*MZ and Pi\*MS). Carriers have been shown to be susceptible to developing emphysema but less so than homozygous individuals, with increasing risk associated with environmental factors such as smoking.<sup>1</sup> Non-emphysematous pulmonary manifestations of AATD have also been documented in adult carriers, but are rarely reported among pediatric patients.<sup>2,3,4</sup>

**Case History:** This case series examines three pediatric patients who are carriers for AATD presenting with non-emphysematous lung manifestations. Case 1 involves a 7-year-old male carrier (Pi\*MS) who presented with left-lower-lobe pneumonia and bronchiectasis. He tested negative for environmental allergies, primary ciliary dyskinesia (PCD), immunodeficiency, and cystic fibrosis (CF). Case 2 involves a 15-year-old female carrier (Pi\*MZ) who presented with severe persistent asthma, recurrent hospitalizations, recurrent respiratory infections, cardiac arrest, atopic dermatitis, allergic rhinitis and multiple food and environmental allergies. Case 3 details a 21-year-old male carrier (Pi\*MS) who presented with severe persistent asthma, plastic bronchitis, and bronchiectasis. His sweat chloride test showed CF was unlikely and PCD was negative, however his IgA was low (33mg/dl).

**Discussion:** Together these observations suggest that pediatric patients who are AATD carriers may be predisposed to non-emphysematous lung manifestations in childhood not just in adulthood as has previously been documented. Alpha-1 antitrypsin has anti-inflammatory and immunomodulatory effects by inhibiting TNF- $\alpha$  and IL-1 $\beta$ , which may predispose patients to prolonged inflammation and recurrent infections.<sup>5</sup> Acute and chronic unresolved inflammation may lead to bronchiectasis secondary to neutrophilic driven lung damage, but the pathophysiology is not well understood.<sup>6</sup> This case series aims to increase awareness about the potential for AATD carrier status to predispose to severe pulmonary manifestations in children. We recommend increased screening for pediatric patients with severe pulmonary conditions to allow for early interventions, including lifestyle modifications to prevent or delay future progression to non-emphysematous lung disease.

## ***26: Amiodarone-Induced Thyrotoxicosis in an Athyroid Patient***

Agnieszka Steiner<sup>1</sup>, Laura Bauler PhD<sup>2</sup>, Mark Schauer MD<sup>3</sup>

<sup>1</sup>Medical Student. <sup>2</sup>Department of Biomedical Sciences, <sup>3</sup>Department of Medicine, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Amiodarone is among the most frequently used antiarrhythmic medications, despite significant adverse effects. Among these is amiodarone-induced thyrotoxicosis, which occurs in 7-15% of patients on amiodarone. This can occur through either an inflammatory mechanism (Type 2) or due to amiodarone's iodine content (Type 1). Therefore, it is common practice to monitor thyroid hormone levels in all patients on amiodarone and investigate signs of hyperthyroidism promptly. When a patient is athyroid, however, such signs may seem misleading. We present here the intersection of the well-known thyrotoxic effects of amiodarone with the rare incidence of "forgotten" goiter.

**Case history:** An 80-year-old man with 13 years of levothyroxine-controlled hypothyroidism post-thyroidectomy for benign substernal thyroid developed recurrent atrial arrhythmias and was treated with amiodarone. His chronic heart failure worsened over the following three months and lab studies revealed low thyroid stimulating hormone (TSH 0.11 u [iu]/mL) and elevated thyroxine levels (free T4 2.7 ng/dL) despite a constant levothyroxine dose. This indicated hyperthyroidism consistent with endogenous hormone production on top of levothyroxine supplementation. The source was theorized to be a substernal mass, which had been visualized at the time of amiodarone initiation. Iodine uptake studies had confirmed it to be inactive tissue of thyroid origin. In response to the new onset hyperthyroidism, levothyroxine was discontinued and thyroid hormone levels normalized.

**Conclusion/Clinical significance:** Cases of "forgotten" goiter have historically been extremely rare, which may in part be explained by their relatively asymptomatic nature. However, thyroidectomies are on the rise, as is the use of amiodarone. Taken together, these trends increase the importance of vigilance for amiodarone activation of "forgotten" goiters. Due to the morbidity and mortality associated with amiodarone induced thyrotoxicosis, early recognition of the signs and symptoms is essential. This novel case of amiodarone-induced euthyroid function in "forgotten" goiter tissue serves as a reminder of the critical importance of monitoring thyroid levels in all amiodarone patients, regardless of underlying thyroid status.

## 29: Necrotizing Pneumonia Associated With Vaping Use in a Previously Healthy Young Male

Marian Jirjis MD, Lamiya Z. Raghid MD, Andrew Luciano MD

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

**Introduction:** Use of electronic cigarettes, or vaping, has been gaining popularity due to the misconception that it is safer than cigarettes or with the belief that it aids in tobacco cessation. Since the vaping epidemic started in 2019, there have been many reported cases of e-cigarette-vaping product use associated lung injury (EVALI). E-cigarettes contain toxic chemicals which may damage lung tissue<sup>1</sup>. Upon literature review, there is only one case report about necrotizing pneumonia associated with vaping<sup>2</sup>. Our case aims to illustrate the association of vaping with necrotizing pneumonia in a healthy young adult.

**Case Description:** A 27-year-old healthy male presented with complaints of right-sided chest pain, dyspnea, fatigue, worsening productive cough, intermittent fevers and diarrhea. History of 12 pack-years of smoking, quit 10 months ago, switched to vaping of nicotine/THC products. Exposure risks include cattle, chemicals during marijuana farming and use of vaporized products. Imaging was consistent with necrotizing pneumonia (Figure 1). Patient was admitted, started on broad-spectrum IV antibiotics and discharged on Augmentin. On follow-up with infectious disease, he demonstrated resolution of symptoms and Augmentin was discontinued.

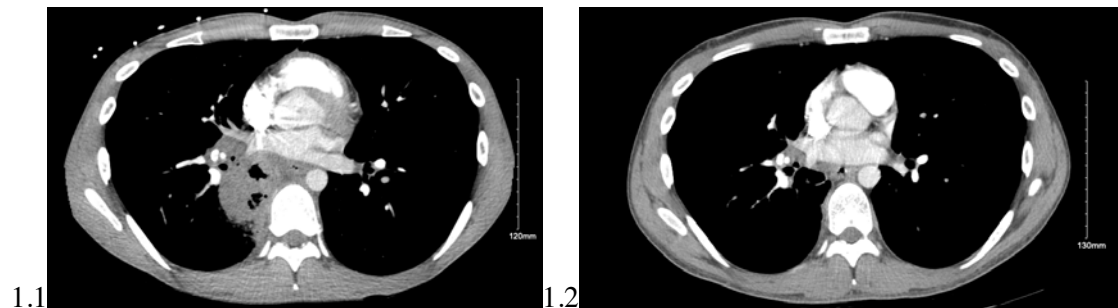


Figure 1: Figure 1.1: CT-Chest revealed a right lower lobe cavity. Figure 1.2: Repeat CT after 8-weeks showed improvement.

**Discussion:** The most commonly reported vaping products used by patients hospitalized for EVALI are THC- containing products. 80% of patients reported use of these products in the 3 months preceding symptoms<sup>3</sup>. Although there is no clear pathophysiological mechanism of vaping associated with lung disease, it is likely the toxic products contained in e-cigarettes that injure lung tissues. It is important to counsel patients on the association between vaping and lung injury.

**References:** [1] Griffiths A, et al. (2020) Lung Injury Associated with E-Cigarette or Vaping Product Use. *Pediatr Ann.* 1;49(2):93-98. [2] El Chebib, Hassan, et al. (2020) Anaerobic Necrotizing Pneumonia: Another Potential Life-Threatening Complication of Vaping? *Pediatrics* 145: 4. [3] Ellington, Sascha, et al. (2020) Update: Product, Substance-Use, and Demographic Characteristics of Hospitalized Patients in a Nationwide Outbreak of e-Cigarette, or Vaping, Product Use–Associated Lung Injury. *MMWR. Morbidity and Mortality Weekly Report* 69(2): 44–49.

### ***30: An unusual presentation of sacral Varicella-zoster virus (VZV) encephalitis***

Elizabeth Corpuz BA, Mahmud Abdeljaber PharmD, Kylie Hendges MD, Mark Schauer MD  
Department of Medicine, Western Michigan University Homer Stryker M.D. School of Medicine,  
Kalamazoo, MI

**Introduction:** Herpes zoster is a reactivation of the latent varicella zoster virus from peripheral ganglia, most commonly involving the skin of the thoracic, cervical, or cranial distributions.<sup>[1,2]</sup> Less commonly, it presents in the sacral dermatomal distribution.<sup>[3]</sup> Neurologic sequelae, such as encephalitis, rarely complicate the disease course. We present a case of herpes zoster of sacral distribution complicated by encephalitis, which illustrates the importance of skin examination in cases of altered mental status to facilitate expedient diagnosis and treatment.

**Case Presentation:** An 88-year-old man presented to the emergency department with generalized weakness and altered mental status with occasional bouts of urinary incontinence. Examination was notable for penile and sacral vesicular lesions consistent with herpes zoster in the S3 dermatomal distribution. CSF examination was positive for varicella zoster virus PCR. Based on these characteristic lesions and lab results, a diagnosis of varicella zoster encephalitis was made. A fourteen-day course of intravenous acyclovir was initiated with subsequent improvement of his condition.

**Discussion:** The incidence of herpes zoster is estimated at 3.4-4.82 per 1000 persons per year for the general population and greater than 11 per 1000 person years in people aged 80 years or older.<sup>[4]</sup> The most common dermatomes involved are thoracic and cervical segments, with sacral dermatomes involved in less than 4% of cases.<sup>[2]</sup> Recent studies have found that cutaneous lesions are frequently absent in cases of VZV encephalitis.<sup>[5]</sup> Whereas meningitis presents with headache and nuchal discomfort, encephalitis often presents with marked changes in brain function, manifesting as altered mental status.<sup>[6]</sup> In patients presenting with altered mental status, this case demonstrates that a skin examination may uncover viral lesions suggestive of the etiology.

**References:** [1] Kennedy PGE, Gershon AA. (2018) *Viruses*, 10, 609. [2] Aggarwal SK, Radhakrishnan S (2016) *Med J Armed Forces India*, 72, 175-177. [3] Chiriac A, et al. (2019) *J Pain Res*, 12, 1475–1477. [4] Johnson RW, Alvarez-Pasquin MJ, Bijl M, et al. (2016) *Ther Adv Vaccines*, 3, 109-120. [5] Alvarez JC, Alvarez J, Tinoco J, et al. (2020) *Cureus*, 12, e11583. [6] Greenberg SB. (2003) *Office Practice of Neurology*, 466-469.

### ***35: Detection Of G-quadruplex DNA Structures Within Human PKD1***

Shane Handelsman B.S., Nikoli Nickson B.S., Kemin Su PhD, Eric Larson PhD  
Department of Biomedical Sciences, Western Michigan University Homer Stryker M.D. School of  
Medicine, Kalamazoo, MI

**Introduction:** Inactivating mutagenesis of the *PKD1* gene leads to polycystic kidney disease, an inherited disorder resulting in kidney cysts and end-stage renal disease. The mechanisms responsible for *PKD1* inactivation are unknown. We have discovered that human *PKD1* encodes widespread guanine-rich sequences, each of which has the potential to form a four-stranded DNA structure called G-quadruplex. G-quadruplexes at various other loci stall replication and create DNA breaks, suggesting that this structure may also directly contribute to *PKD1* instability.

**Methods:** We have tested the model that G-quadruplex forms within the *PKD1* gene in the cellular environment. Human genomic DNA was probed with a G-quadruplex-specific antibody in a modified Chromatin Immunoprecipitation approach both in vitro and in vivo. We are also developing a novel method for directly visualizing *PKD1* loci within a cell using catalytically inactivated and fluorescently labeled CAS9, thereby permitting the immunodetection of G-quadruplex at that locus.

**Results:** We found that Chromatin Immunoprecipitation assays reliably enriched for *PKD1* sequences that could form G-quadruplexes, but not for regions that were missing guanine repeats. Transferring that protocol to crosslinked cells, we likewise enriched for G-quadruplex-sequences within *PKD1*, albeit at a modest level. We have also purified and tested a modified CAS9 protein for fluorescence labeling, an advance that will allow for the detection of specific loci inside nuclei under non-denaturing conditions.

**Conclusions:** The identification of G-quadruplexes within *PKD1* supports the model that this structure forms within the gene under cellular conditions. Further, enrichment of crosslinked *PKD1* chromatin with a G-quadruplex antibody argues that this structure forms within the gene during transcription or replication. Since G-quadruplex DNA is known to cause DNA breaks and mutagenesis, our results connect G-quadruplex structures with the events leading to *PKD1* inactivation and cyst formation. It also identifies a target for drug development. Ligands that prevent or slow the formation of G-quadruplexes would reduce *PKD1* mutagenesis and prolong renal functionality in at-risk individuals.

### ***36: Repeated Self- and Peer-Evaluation Reduces Gender Disparity Seen in Self-Evaluations***

Simran Singh BA<sup>1</sup>, Laura Bauler PhD<sup>2</sup>, Sara Allison PhD<sup>2</sup>, Maria Sheakley PhD<sup>2</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Biomedical Sciences, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Peer-evaluation offers a venue for honest, meaningful feedback in a professional environment. Feedback from peers helps students improve their communication and interprofessional skills in a team setting. However, pre-existing bias may influence the feedback an individual gives. This study seeks to determine if students improve the accuracy of their self-evaluations after multiple rounds of feedback.

**Methods:** WMed M1 medical students (n = 86) participated in peer-evaluation in their Team Based Learning (TBL) groups comprised of 5-6 students per group. Evaluation rounds 1 and 2 took place 6 months apart, within the TBL groups. Students evaluated 8 teamwork skills (collaboration, communication, knowledge, consideration, participation, timeliness, authenticity, leadership) for themselves and each of their peers. A self- and a peer-given teamwork score was calculated for each student by averaging the scores of the 8 skills. The difference between self- and peer-given teamwork scores was used to determine if students tended to over or under rate themselves. The differences between self- and peer- given skill and teamwork scores were compared across gender using unpaired t-tests.

**Results:** In round 1, females were more likely to under-rate themselves in the participation skill (p = 0.017) and authenticity skill (p = 0.001), while males were more likely to overrate themselves. There was a significant association between gender and the difference in self- and peer-given overall teamwork scores, where females had a greater tendency to under-rate themselves, while males tended to overrate themselves (p = 0.007). In round 2, there was no significant difference in self versus peer ratings in the participation skill (p = 0.508), authenticity skill (p = 0.469), or overall teamwork score (p = 0.386) when compared across gender.

**Conclusion:** This study suggests that medical students, through multiple rounds of evaluations, were able to incorporate feedback from peers to better evaluate themselves. Reduction in the difference between self- and peer-given scores between rounds, as compared across gender, indicates increased accuracy of self-scores and decreased gender bias when evaluating oneself. Peer-evaluation is an easy and simple tool that can be used to improve self-evaluation and may increase the confidence of female students.

### ***37: Effect of a Mandatory Study Regimen on ITE Scores in a Family Medicine Residency***

Brandon Manderle MD<sup>1</sup>, Andy Jan BA<sup>2</sup>, Joseph Billian MS<sup>3</sup>, Kristi Vanderkolk MD<sup>1</sup>

<sup>1</sup>Department of Family Medicine, <sup>2</sup>Medical student, <sup>3</sup>Division of Epidemiology and Biostatistics, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Background:** The In-training Exam (ITE) has been in use as a tool for assessing resident knowledge throughout Family Medicine residency since 1980. Research has been conducted on the ITE's validity and reliability and as a tool for predicting performance on the American Board of Family Practice certification exam. Little data exists on how study programs implemented during residency may affect ITE scores. There have been no published studies involving long-term (6+ month) study plans and their effect on ITE scores in Family Medicine residents.

**Hypothesis/Purpose:** The purpose of this study was to evaluate the effects of required and regimented study protocols on ITE scores in family medicine residents.

**Study Design:** This was a retrospective study during the academic years of 2017-2018, 2018-2019, 2019-2020, 2020-2021 and 2021-2022. The ITE data within a single residency program at a Midwest academic institution was evaluated. The primary objective of the study was to evaluate the efficacy of a mandatory reactive study program implemented in residents that were identified as at-risk for low board scores (those who scored <50th%ile on the ITE). The second component of this study evaluated the efficacy of implementing a prophylactic study program for all PGY1 residents to prevent scores below the national mean from occurring.

**Results:** Regarding the reactive study regimen, we are 97.5% confident that residents in the reactive study regimen improve their score by 9.3-98.1 points, and we are 97.5% confident that residents without the reactive study regimen improve their score by -57.8- 58.3 points. Negative improvement indicates worsening ITE score. Regarding the prophylactic study regimen, due to group sizes, scores and standard deviations of scores there was insufficient power to justify testing for a difference between the treatment and control group.

**Conclusion:** Implementation of a reactive study regimen for those residents who scored below the national mean on the ITE appears to result in subsequent increases in ITE scores compared to those without such a required study program. Several confounders limit the broad application of these results and the use of required study programs for residents should continue to be evaluated for effectiveness and burden.



#### ***40: Treating Nausea in the Emergency Department: A Randomized-controlled Non-inferiority Trial of Haloperidol vs. Ondansetron***

Jessica McCoy MD, Koby Buth, Mark Canner, Jessica Edwards, Logan Mills, Benjamin Root, Raechel Warchock, Jeanna Yu, Stephen Godfrey MD, Jason Helbig DO  
Department of Emergency Medicine, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Nausea and vomiting are common complaints in the emergency department (ED). Ondansetron is a first-line antiemetic in the ED due to perceived efficacy and safety. Haloperidol is a D2 antagonist approved as an antipsychotic, but low-dose haloperidol has been effective for the emergent treatment of nausea and vomiting associated with cannabis hyperemesis syndrome, diabetic gastroparesis, and migraines. The objective is to compare the effectiveness of haloperidol and ondansetron for nausea and vomiting in ED patients. Secondary outcomes include time to symptom improvement, efficacy in cannabis users, adverse effects, and QT prolongation.

**Methods:** This study was a randomized, double-blind, non-inferiority trial of patients aged 18-55 from April 2021 to December 2021. 381 patients were evaluated for inclusion, 225 were excluded due to screening criteria, and 48 patients completed the study. Patients received either 2.5mg IV haloperidol or 4 mg IV ondansetron. The primary and secondary outcome measures were mean change in nausea and abdominal pain severity from enrollment to 30, 60, and 90 minutes. Patients were contacted after 24 hours to collect follow-up data.

**Results:** There is not sufficient statistical power to detect demographic differences between the treatment groups. At baseline, pain and nausea scores were insignificantly different between groups. Changes from baseline nausea are insignificant. Pain was significantly reduced at 60 and 90 minutes post-treatment for haloperidol when compared to ondansetron. There is no significant difference in QT change between the treatment groups. In cannabis users, haloperidol demonstrates significant improvement in nausea and pain scores at 60 and 90 minutes post-treatment when compared to ondansetron. Resolution of nausea occurred in 62% of the Haloperidol group and 33% in the ondansetron group. Resolution of pain occurred in 86% of patients in the haloperidol group and in 29.6% of the ondansetron group. The differences between resolution of symptoms are not statistically significant at current group sizes.

**Conclusions:** Haloperidol has shown a role in treating nausea and vomiting in various conditions. This study supports a broader application of its use as a noninferior treatment option to ondansetron in the management of generalized nausea and abdominal pain in the ED.

IRB#: WMed-2020-0690

## ***42: Increased NICU Admission Rate for Infants of Chlamydia-Infected Mothers***

Wilo Issack MS<sup>1</sup>, Laura Bauler PhD<sup>2</sup>, Catherine Kothari PhD<sup>3</sup>, Jack Loveland<sup>4</sup>

<sup>1</sup> Medical student. <sup>2</sup>Department of Biomedical Sciences, <sup>3</sup>Department of Biomedical Sciences; Division of Epidemiology, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI.

<sup>4</sup>Undergraduate Biology Major, Kalamazoo College, Kalamazoo, MI

**Introduction:** Chlamydia trachomatis is one of the most common sexually transmitted infections. Risk of infection is higher for individuals with lower socioeconomic status, women of color, and those less than 20-years. Chlamydia infection during pregnancy can significantly impact birth outcomes including increasing the risk of preterm delivery and having an infant of low birth weight. Both of these birth outcomes increase an infants' likelihood of being admitted to the neonatal intensive care unit (NICU). Additionally, infants can become infected during birth leading to ocular and pulmonary complications. This study seeks to determine if chlamydia infection of mothers during pregnancy is an independent risk factor for admission of an infant to the NICU, and to determine if that risk varies by race.

**Methods:** This study was a retrospective cohort analysis consisting of 35,755 pregnant women who lived in Kalamazoo County at the time of their birth. The birth and death records between 2008 and 2019 were obtained from the Michigan Department of Health and Human Services. Women with multiple gestation births, infants with a birthweight of <500g or >7000g, and records lacking chlamydia infection or NICU admission data were excluded. Data were analyzed using Pearson's chi-square and binary logistic regression models.

**Results:** Results of the study illustrated a significant increase in the NICU admission rate for infants of mothers with chlamydia (7.2% vs. 3.8%,  $p < 0.001$ ). Multiple factors can contribute to an increased NICU admission rate, but after adjusting for all other variables, chlamydia remained an independent risk factor for NICU admission (OR 1.47(1.20-1.79),  $p < 0.001$ ). When the data were stratified by race, chlamydia remained a risk factor for poor birth outcomes in both women of color (OR 1.58(1.21-2.06),  $p < 0.001$ ) and white women (OR 1.39 (1.02-1.88),  $p = 0.037$ ).

**Discussion & Conclusions:** C. trachomatis infection in women is often asymptomatic, which allows it to be transmitted between individuals unknowingly. Since NICU admission is associated with long-term developmental complications, decreasing risk is important. The findings of this study illustrate the importance of regular and repeated chlamydia screening in expecting mothers since infection can adversely impact the health of both the mother and the infant.

## ***46: The Effects of Exercise on Tissue Levels of GDNF and Estrogen in Male and Female Rats***

Juliana M. VanGyseghem, John M. Spitsbergen

Department of Biological Sciences, Western Michigan University, Kalamazoo, MI

**Introduction:** Premenopausal women display lower incidence and severity of neurological diseases compared to men of the same age, yet they are often treated similarly. Decline in neuromuscular function is associated with aging and this may be partially explained by decline in neurotrophic factor expression with age. It is possible that increased expression of target-derived neurotrophic factors, like glial cell line-derived neurotrophic factor (GDNF), may help protect against the age-related decline in neuromuscular function. Previous studies performed only in male rats have shown GDNF in skeletal muscle increases with exercise. Exercise has been shown to increase estrogen receptor levels in skeletal muscle, and GDNF and estrogen signal through similar intracellular pathways with estrogen enhancing intracellular GDNF signaling. Our hypothesis is that levels of GDNF expression in skeletal muscle will be higher in young female rats than in age-matched male rats. We also hypothesize that exercise will cause a greater increase in skeletal muscle GDNF content in females compared to males.

**Methods:** Male and female Sprague-Dawley rats were allowed to exercise in voluntary running wheels for 2-weeks, 4-weeks, or 6-months. Following exercise, hindlimb muscles were removed and processed for protein extraction or immunohistochemical analysis. GDNF protein content in skeletal muscle was determined by western blot and enzyme-linked immunosorbent assays. Immunohistochemical analysis was performed to examine the structure of the neuromuscular junction and for localization of GDNF protein in muscle tissues.

**Results:** We identified differences in GDNF protein content in muscle of sedentary and exercised male and female rats, with higher GDNF levels in both exercised and sedentary females compared to age-matched males. 6-week female GDNF (pg/mol) was 45.75, which was significantly higher than age-matched male at 1.55. For both sexes, exercised animals had higher levels of skeletal muscle GDNF protein content than their age-matched sedentary counterparts. Exercised 12-week males GDNF (pg/mol) of 98.20 was significantly higher than the sedentary of 5.25.

**Conclusion/Clinical significance:** Understanding the role that neurotrophic factors play in neuroprotection as we age and understanding the impact of gender and exercise these processes may help guide novel therapeutic strategies to protect against age-related neurological decline.

## ***47: Debt and Personal Financial Well-being of Family Medicine Residents: A CERA Study***

Stephanie Ellwood DO<sup>1</sup>, Jamie Weathers PhD<sup>2</sup>, Jim DeMello DBA<sup>2</sup>, Lisa Graves MD<sup>3</sup>, Jumana Antoun MD<sup>4</sup>, Neelkamal Soares MD<sup>5</sup>

<sup>1</sup>Family and Community Medicine, Western Michigan Homer Stryker M.D. School of Medicine, Kalamazoo, MI. <sup>2</sup>Western Michigan University, Haworth College of Business, Kalamazoo, MI. <sup>3</sup>Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. <sup>4</sup>American University of Beirut, Beirut, Lebanon. <sup>5</sup>Pediatrics, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Background and Objectives:** Personal financial wellness is a milestone in graduate medical education. Previous surveys addressing financial wellness have not included family medicine (FM) residents and no literature thus far has explored the relationship between their debt and perceived financial well-being. Our study sought to understand how FM residents' debt level, year of training, and medical school location affect their personal financial well-being.

**Methods:** Our survey was included in the Council of Academic Family Medicine Educational Research Alliance (CERA) survey sent to 5000 FM residents. The Consumer Financial Protection Bureau (CFPB) financial well-being scale was part of our survey questions. Descriptive statistics, associations using Chi square tests, and ordered logit regression were obtained to evaluate probability of impact of debt on financial well-being.

**Results:** 266 residents responded with a mean CFPB score of 55.7 (SD 12.1) that generally increased with year of residency. Median debt level range of FM residents was \$225,000 - \$299,000 in the first two years of residency and decreased in the third year. There was a strong association between debt and household income and personal financial well-being reported by FM residents.

**Conclusions:** FM residents' debt levels were aligned with recent studies of other specialties and CFPB scores were in the medium wellness range. Personal financial well-being was significantly associated with both household income and debt. CFPB scores can be a useful tool in documenting personal financial wellness in FM residents. Future studies should evaluate personal finance curriculum in residency and effects on financial well-being.

## ***48: Blood Clots Formed In Vitro as a Therapeutic Vehicle During Bone Healing***

Victor Hung BS<sup>1</sup>, Peter Awad BS<sup>1</sup>, Erica Myrick MS<sup>1</sup>, Kristi Bailey BS, HTL<sup>2</sup>, Jered Cornelison PhD<sup>2</sup>, Christine Pink PhD<sup>2</sup>, Haiying Pan MS<sup>3,4</sup>, Yong Li MD, PhD<sup>3,4</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Pathology, <sup>3</sup>Department of Orthopaedic Surgery, <sup>4</sup>Medical Engineering Program, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Biologically active components in blood clots secrete factors that aid with the natural healing process of bone injuries. Previous studies demonstrate that mesenchymal stem cells (MSCs) have the potential of promoting bone healing when loaded onto various scaffolds to effectively treat cranial bone defects. The aim of this study was to investigate the healing effects of implanted isogenic blood clots loaded with MSCs into skull bone defects.

**Methods:** Blood was drawn from isogenic C57/BL6J mice and allowed to clot at room temperature to form blood clots *in vitro*. Blood clots were either loaded with primary bone marrow-derived murine MSCs or had nothing added (for vehicle control). Bilateral 3-mm cranial skull defects were surgically induced on isogenic mice under sterile conditions, and different treatments were administered to each defect for comparison *in vivo*. Treatment conditions of the skull defects included blood clots loaded with MSCs, blood clots alone (vehicle control), or negative control (no treatment). After 3, 6, and 8 weeks of healing, the mice were sacrificed and their skulls were dissected for gross, radiographic, and histological analyses of skull bone healing with each treatment. This protocol was approved by WMed IACUC.

**Results:** The surgical procedure for creating bilateral skull bone defects and implantation of blood clots loaded with MSCs (formed *in vitro*) was successfully performed *in vivo*. The skull bone defects treated with blood clots containing MSCs showed a higher degree of healing and bone formation compared to the vehicle and negative controls. The vehicle controls showed a higher degree of bone healing when compared to the negative controls. This was demonstrated grossly, on histological staining, and also with radiographic imaging.

**Conclusions:** Our results align with other studies indicating improved bone healing with MSCs and with blood clots. Considering that the use of *in vitro* blood clots as a vehicle to deliver the MSCs is novel, our future studies will aim to elucidate the mechanism behind the isogenic blood clot in tissue repair, including bone healing.

## ***51: Kalamazoo Maternal/Child Health Universal Access Form Investigation***

Catherine Kothari PhD<sup>1</sup>, Joi Presberry MPH<sup>1</sup>, Matthew Gray BS<sup>2</sup>, Jeanna Yu BS<sup>2</sup>, Jaide Woods-Dawson MS<sup>2</sup>, Rosemary Vergara MS<sup>2</sup>, Komal Razvi MPH<sup>3</sup>, Mary DeMoss BS<sup>3</sup>, Brenda O'Rourke RN<sup>4</sup>

<sup>1</sup>Department of Biomedical Sciences, Division of Epidemiology and Biostatistics, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. <sup>2</sup>Medical student. <sup>3</sup>YWCA-Kalamazoo, Kalamazoo, MI. <sup>4</sup>Kalamazoo County Health & Community Services, Kalamazoo, MI

**Introduction:** The Maternal/Child Health Universal Access Project is designed to address racial health disparities between infants in Kalamazoo County. The Universal Access Form, a focal point of this project, can be completed by families to indicate areas of need, after which a Community Health Worker can facilitate referrals to available social and medical resources based on the family's requests.

**Methods:** A REDCap survey was administered to a group of Kalamazoo mothers, the Community Voice Panel. Forty-five of the 74 members responded; ages 21 to 40, with 1 to 9 children, 35.6% women of color (n=16), and 28.9% (n=13) with household incomes \$40,000 or less. The questionnaire comprised 22 close-ended and five open-ended questions for feedback on structure, content, and implementation strategies for the Universal Access Form. Pearson Chi Square analysis (alpha=.10) was used to compare responses by race and income.

**Results:** Respondents indicated that the form was easily understandable (97.8%, n=44), and that they would be willing to complete it. A strong majority noted the importance of convenience (88.7%, n=39) and wanted more information about "next steps" on the form (90.9%, n=40). 59.1% noted concerns about privacy (n=26). Of the five proposed scenarios, approximately two-thirds of respondents preferred to complete the form during their WIC appointment, via link before their WIC appointment, or via tablet at their doctor's appointment, as opposed to via QR code on a public flyer or with a community health worker's assistance at the doctor's office. However, women of color were more open to the latter option than white women. Women of color were also significantly more concerned about privacy than white women. There were no differences by socio-economic status.

**Conclusion/Clinical significance:** Using the response data, recommendations for the Universal Access Form's implementation strategy were created to help ensure it becomes an effective tool for addressing the project's overall goal of improving infant mortality and reducing racial health inequities.

**Acknowledgments:** This project was supported through a Michigan Health Endowment Fund grant awarded to the YWCA Kalamazoo for the Kalamazoo Maternal/Child Health Universal Access Project.

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## ***54: Teaching HINTS+: Designing a curriculum to teach Emergency Medicine physicians to apply and interpret the HINTS+ exam in dizzy patients***

Maureen M. Ford MD<sup>1</sup>, Colleen Howing MD<sup>1</sup>, N. Charity Nguyen<sup>2</sup>, Kathryn Redinger MD<sup>1</sup>, Henry Higby MD<sup>1</sup>, Rachel Wilson<sup>3</sup>

<sup>1</sup>Department of Emergency Medicine, Western Michigan University Homer Stryker M.D. School of Medicine. <sup>2</sup>Medical student. <sup>3</sup>Western Michigan University, Kalamazoo, MI

**Introduction:** Dizziness is a common complaint in the Emergency Department (ED) and can reflect benign or severe etiologies. Acute vestibular syndrome (AVS) is defined as dizziness associated with gait instability, nystagmus, nausea/vomiting, and head motion intolerance. Ten to twenty percent of dizzy patients presenting to the ED are experiencing AVS. Twenty-five percent of those patients are suffering from a posterior circulation stroke. A combination of bedside physical exam maneuvers, the HINTS+ exam, has been developed to help differentiate benign from serious causes of dizziness. The exam has been shown to be more sensitive than MRI for posterior circulation strokes in AVS patients when performed by otoneurologists on a cohort of admitted patients. Despite its proven sensitivity, the HINTS+ exam is not highly utilized by ED physicians. Its sensitivity, when applied to ED patients, is unknown.

**Methods:** Kern's six-step approach to curriculum development was used to develop 'Teaching HINTS+' a physician focused research study. This curriculum includes instruction about dizziness/AVS, when applying the HINTS+ exam is appropriate, and instructions on how to perform and interpret findings of the exam. Physicians then practice the exam and are given direct feedback. Physicians are also provided with EPIC smart lists and Cerner macros to assist with documenting and interpreting the exam.

**Results:** HINTS+ performance and interpretation scores of participants in this prospective observational study are being obtained. The data will be analyzed to determine if this formal curriculum improves physician knowledge of appropriate application and interpretation the HINTS+ exam.

**Clinical Significance:** Patients with posterior circulation stroke are misdiagnosed 37% of the time on their initial ED visit. Misdiagnosis is more likely in the young (age < 50), women, and minorities. Mastery of the HINTS+ exam by EM physicians has the potential to aid in recognition of dangerous central causes of AVS and decrease the use of low yield, expensive tests commonly ordered on patients with AVS, such as non-contrast head CTs. The sensitivity and specificity of the exam when performed by ED physicians cannot be determined until more physicians are applying the exam to appropriate patients and performing and interpreting it correctly.

## ***55: Barriers to Postpartum Care: A Mixed Methods Study of Midwestern Postpartum Women***

Kathryn Tighe<sup>1</sup>, Emily Miller<sup>1</sup>, Katherine Tierney PhD<sup>2</sup>, Nicole Pearce<sup>1</sup>, Agnieszka Steiner<sup>1</sup>, Joi Presberry MPH<sup>2</sup>, Catherine Kothari PhD<sup>2</sup>

<sup>1</sup>Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. <sup>2</sup>Department of Sociology, Western Michigan University, Kalamazoo, MI

**Introduction:** Despite the importance of postpartum care in providing support to new mothers, women of color and women with lower socioeconomic status (SES) attend postpartum visits less often. This paper seeks to classify and explore barriers to postpartum care and to identify potential policy and practice changes that could improve accessibility.

**Methods:** The data used in this study was collected in two phases. First, survey data and medical record abstraction of 244 postpartum women in Kalamazoo County Michigan was collected. Second, focus groups were conducted with a socioeconomically and racially diverse subset of the study participants (n=17, 3 focus groups). The data was analyzed with an iterative and reflective mixed methods approach. Quantitative analyses included logistical regression of the survey and medical records data. Team-based inductive qualitative analyses were conducted on the focus group transcripts.

**Preliminary Results:** Bivariate logistic regression of the data confirmed lower attendance at postpartum visits among women of color and women with lower socioeconomic resources. In the qualitative analyses, four primary barriers were identified: patient-provider relationship, time and scheduling of visits, childcare-related barriers, and, least frequently, material and insurance related barriers. We found that some of these barriers, operationalized with the representative survey, do mediate or suppress the associations between demographic factors (SES and race) and postpartum care attendance.

**Conclusion/Clinical significance:** This study demonstrates the need for a deeper understanding of factors underlying decreased attendance at postpartum visits among women of color and women with lower socioeconomic status. Identification of time and scheduling issues as a common barrier provides a concrete mechanism for improvement of attendance that could be taken by providers. Importantly, the study also identifies patient-provider relationship as a critical component of quality of care received at postpartum visits.

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## ***58: Eosinophilic Enteritis Following Moderna COVID-19 Vaccine Administration***

Mahmuod Abdeljaber<sup>1</sup>, Yvonne Hojberg<sup>1</sup>, Joseph Prahlow MD<sup>2</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Pathology, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Eosinophilic disorders following COVID-19 vaccination have been reported sparsely in the literature. <sup>[1-3]</sup> However, eosinophilic enteritis has not been previously reported. We report a case of a natural death related to eosinophilic enteritis following Moderna COVID-19 vaccination.

**Case presentation:** A 76-year-old man with a medical history significant for obesity died at home. He had received the Moderna COVID-19 vaccine nine days prior to death and experienced abdominal distension and pain within one day of vaccination, and progressive abdominal distension and discomfort, to include shortness of breath in the days preceding death. He did not seek medical attention for these symptoms. Autopsy examination revealed cardiomegaly, mild to severe coronary and aortic atherosclerosis, pulmonary emphysema, diabetes mellitus, and obesity. Also present were abdominal cavity adhesions and 1500 mL of serosanguinous fluid within the peritoneal cavity. Histological examination revealed abundant eosinophils in tissues, including the small intestines, epicardium, and lungs. An independent Centers for Disease Control and Prevention examination concurred with the autopsy findings of eosinophilic enteritis. The cause of death was ruled as hypertensive and atherosclerotic cardiovascular disease, with contributing causes of pulmonary emphysema, diabetes mellitus, obesity, and eosinophilic enteritis with possible systemic eosinophilia.

**Discussion:** Eosinophilic enteritis is a subtype of eosinophilic gastrointestinal disorders.[4] Symptoms may include abdominal pain, distension, and ascites. Typically, eosinophilic enteritis is a chronic relapsing condition, though our patient did not have a history of eosinophilic enteritis or previous symptoms that hint towards an undiagnosed condition. The temporal relationship of vaccination, onset of abdominal symptoms, and death increases suspicion that the patient's condition, and thus death, was secondary to COVID-19 vaccination. Although a conclusive determination regarding the association between the vaccination and death could not be made with certainty, the case was referred to the Vaccination Adverse Event Reporting System. Clinicians should be aware of the possibility of eosinophilic disorders following certain vaccinations.

**References:** [1] Lospinoso K, et al. (2021) JAAD Case Rep, 13, 134–137. [2] Miqdadi A. and Herrag M. (2021) Cureus, 13, e18959. [3] Ibrahim H, et al. (2022) Cureus 14: e21176. [4] Memon R. J. and Savliwala M. N. (2021) In: StatPearls.

## ***59: Motivation or Regulation: Comparison of Alterations in Glutamate Signaling between Nucleus Accumbens and Prefrontal Cortex in Obesity-Prone Rats***

Victoria Addis, Keenan Boulnemour, Peter J Vollbrecht PhD

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

**Introduction:** Obesity is a global epidemic and leads to long-term negative impacts on one's health. Despite this, rates continue to rise even in individuals that want to lose weight. Recent studies show that alterations within the nucleus accumbens (NAc), a brain region involved in motivation, likely make it more difficult to lose weight and keep it off. In addition, alterations have been observed in the prefrontal cortex (PFC) of obese patients, possibly leading to difficulty in controlling feeding behaviors such as over-consumption of calorie-dense foods. Finally, both obesity and stress cause a state of chronic inflammation that negatively affects brain function. Here we examine key proteins in glutamate signaling and immune response in both the NAc and PFC to examine how these regions are affected by obesity.

**Methods:** Four selectively bred obesity-prone (OP) and five obesity-resistant (OR) adult rats were monitored for weight gain across five weeks before being anesthetized using isoflurane. Microdissection of the brain was performed to isolate the NAc and PFC and tissue was flash frozen. Western blot analysis was performed using antibodies to glutamine synthetase (GS), microglial marker IBA-1, glial glutamate transporter (GLT-1), and glucose transporter 1 and 3 (GLUT-1/3) in duplicate. Images were developed and analyzed using a C-DiGit Blot Scanner and ImageStudio.

**Results:** Both GS and GLT-1 were significantly lower in the NAc of OP rats compared to OR rats ( $p=0.0313$  and  $p=0.0247$  respectively). IBA-1 trended towards a decrease in OP rats NAc tissue ( $p=0.0518$ ). Examination of PFC tissue is ongoing.

**Conclusion:** These data demonstrate lower expression of IBA-1, GS, and GLT-1 in NAc of OP compared to OR rats. Lower IBA-1 levels could be an indication of microglial dysfunction within the NAc. Lower GS and GLT-1 expression in the NAc of OP rats helps to explain previously observed elevations in NAc glutamate levels and may ultimately lead to excitotoxicity and loss of dendritic spines. Taken together, these results indicate that obesity-related changes in glutamate signaling are present in the NAc and possibly in the PFC that may be leading to changes in motivational drive for food and regulation of food consumption.

## ***60: A Quality Improvement Evaluation of Spectrum Health Inpatient Antipsychotic Use Post-ICU Initiation***

Ashley Ingison PharmD<sup>1,2</sup>, Dane Shiltz PharmD<sup>1,2</sup>, Calvin Ice PharmD<sup>2</sup>

<sup>1</sup>Ferris State University College of Pharmacy, Grand Rapids, MI. <sup>2</sup>Spectrum Health Pharmacy Department, Grand Rapids, MI

**Introduction:** Intensive care unit delirium can produce negative outcomes. Despite limited and conflicting evidence regarding efficacy for inpatient delirium, antipsychotics are often used when agitation interferes with clinical care. However, equivocal evidence supports antipsychotics to alter the course of delirium and use is associated with adverse effects. Regardless, new prescribing occurs in 8-42% of ICU patients and post-ICU continuation into the general medical ward ranges between 26-28%. At discharge, antipsychotics initiated in the ICU continues at discharge in 4-55% of patients. Furthermore, up to 64% of these individuals are inappropriately discharged on an antipsychotic. This quality improvement evaluation reviewed antipsychotic continuation from the ICU into the general medical unit setting for delirium; to evaluate continuation from the general medical unit setting into the discharge setting; to evaluate psychiatry consultation supporting antipsychotic continuation at transitions of care; and to evaluate side effects attributed to antipsychotics in the general medical unit setting.

**Methods:** As a quality improvement study, an honest broker identified a retrospective dataset for 232 patients admitted to an ICU and newly initiated on an antipsychotic for delirium between January 1, 2021 and June 30, 2021 at Spectrum Health Butterworth and Blodgett Hospitals. A student pharmacist collected multiple demographic and clinical variables and documented in REDCap®.

**Results:** Eighty-three patients remained after exclusion. Among this group, 25 (30.1%) continued into the general medical ward setting. Of these 25 patients, antipsychotic therapy continued at discharge for 8 (32% of general medical ward; 9.6% of all) patients. Psychiatry initiated antipsychotic therapy for 2 (2.4%) ICU patients, both orders continued into the general medical ward setting, and 1 order continued at discharge. Seventeen (68%) patients experienced one or more side effects potentially attributed to antipsychotic therapy.

**Conclusion:** Antipsychotic continuation across the timeframe from admission to discharge and beyond remains significant. The notable incidence of side effects potentially associated with antipsychotic therapy could be avoided by vigilant evaluation at time of care transitions from ICU to general medical ward and general medical ward to discharge. Additionally, psychiatry consultation could be utilized to assist in appropriate initiation and closer monitoring to justify (dis)continuation when warranted.

## 61: COVID-19 Pandemic, Social Change, and a Rise in Overdose Deaths

Chloe Bielby MPH<sup>1</sup>, Catherine Kothari PhD<sup>2</sup>, Kori Mecklenburg BS<sup>3</sup>, Joyce deJong DO<sup>1</sup>

<sup>1</sup>Department of Pathology, <sup>2</sup>Department of Biomedical Sciences, <sup>3</sup>Medical Student; Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** The number of fatal drug overdoses increased dramatically during the early months of the COVID-19 pandemic compared to deaths in 2018 and 2019. Well established risk factors for fatal overdose include those who are unemployed [1], recently released from jail [2], and using substances containing fentanyl [3]. These risk factors were exacerbated by the increase in unemployment, reduction in jail populations for social distancing, and fentanyl prevalence in illicit substances. This research aims to explore the association of overdose deaths with employment status, jail release, and fentanyl use.

**Methods:** Data was abstracted from the Medical Examiner's Office database of deaths reported where drugs were listed as the immediate cause of death. The variables analyzed include demographics, recent incarceration, employment status, substance use history, circumstances of overdose, and substances contributing to death. The authors compared characteristics of decedents who overdosed pre-pandemic (January 1st, 2018 to March 13th, 2020) to decedents who overdosed post-pandemic (March 14th, 2020 to December 31st, 2020). Bivariate analyses were conducted (Pearson chi-square, one-way ANOVA) using SPSSv27 with an alpha level of .05.

**Results:** There was a statistically significant increase in the number of decedents in the post-pandemic time frame who were recently released from jail, unemployed at time of death, and had fentanyl or methamphetamine contribute to their death. When employment status and jail release were put in a multivariate analysis, those who were unemployed and recently released from jail were twice as likely to have an overdose death post-pandemic compared to pre-pandemic.

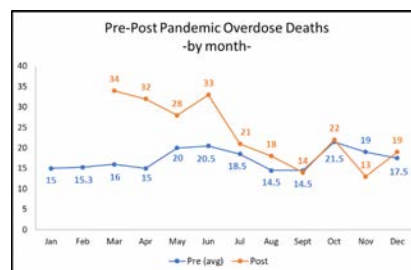


Figure: Note: Pre-pandemic numbers averaged across multiple months: three years for January-mid March (2018-2020), and two years for mid-March through December (2018-2019). Post-pandemic numbers are raw counts for mid-March through December, 2020.

**Conclusion:** Screening for substance use disorders during jail intake, providing treatment during incarceration, and providing resources for recovery at release can lower the risk for fatal overdose. Securing stable employment can provide financial security, a consistent schedule, and safe housing. Finally, providing fentanyl testing strips can lower the number of overdoses especially to those who are returning to substance use after a period of being substance free.

## 62: Hypoxia and HIF-Induction Increase Expression of Anti-Apoptosis Protein XIAP

Jefferson DeKloe<sup>1</sup>, Joseph Preziosi<sup>1</sup>, Haiying Pan<sup>2</sup>, Yong Li MD, PhD<sup>2</sup>

<sup>1</sup>Medical Student, <sup>2</sup>Department of Orthopaedic Surgery, Medical Engineering Program, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Myoblast transplantation has been beneficial in replacing diseased or injured skeletal muscles (1, 2). A large share of the transplanted cells die within the first 24 hours (2). Here we show that hypoxic pre-conditioning leads to expression of the anti-apoptosis protein X-linked inhibitor of apoptosis (XIAP) and promotes cell survival to severe hypoxia. Treatment with Cobalt Chloride and deferoxamine (DFX) can increase levels of HIF-1 $\alpha$ , the major internal cell signal for hypoxia (3). Treatment with these chemicals also increases XIAP expression, suggesting HIF-1 $\alpha$  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 100 $\mu$ M Cobalt Chloride or 100 $\mu$ M DFX. After 12-, 24- and 48-hours western blot were performed for XIAP.

**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**.

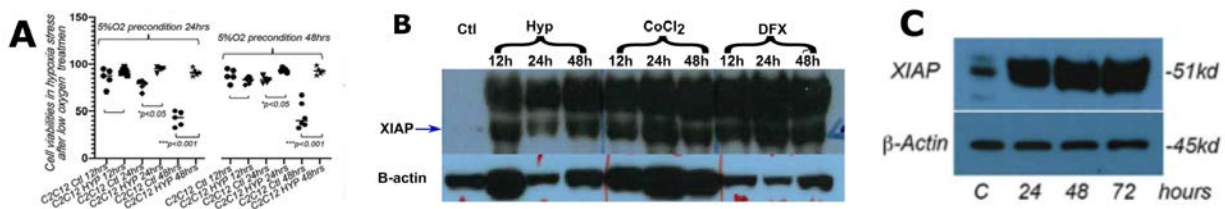


Figure: Cell survival rates of pre-conditioned cells in 1% oxygen compared to controls (A) XIAP expression increased after, Cobalt Chloride and DFX (B) and hypoxic pre-conditioning (C).

**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.

**Acknowledgments:** This study partially supports from Dr. Li's grants and WMed pilot grants.

**References:** [1] Skuk D, et al. *Neuromuscular Disord.* 2007;17(1):38-46. [2] Beauchamp, J.R et al. 1999. *J Cell Biology*, 144(6):1113-1122. [3] Woo, Kyung Jin, et al. *Biochemical and biophysical research communications* 343.1 (2006): 8-14.

## 64: Mechanisms of Formate Binding Proteins

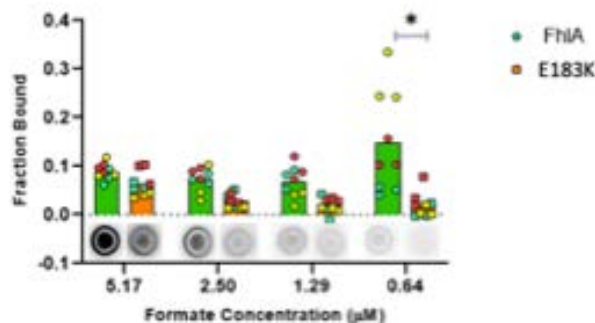
Abrar AlFardan, Benjamin Koestler

Department of Biological Sciences, Western Michigan University, Kalamazoo, MI

**Introduction:** *Shigella* is a human pathogen that causes shigellosis, a diarrheal disease with symptoms ranging from mild to severe watery or mucoid/bloody diarrhea accompanied with fever and abdominal cramp. *Shigella* is a serious health threat because there is no vaccine and treatment has become more challenging due to the increase in antibiotic resistance. *Shigella* is transmitted via the fecal oral route and is able to invade the colon epithelium and uses the host's nutrients to replicate within the host cell cytosol. During this time, *Shigella* is able to sense and adapt to the changing conditions in the host cytoplasm. Previous studies concluded that *S. flexneri* uses glycolysis and mixed acid fermentation for metabolism of the host cytosolic carbon. Previous research concluded that formate regulates *S. flexneri* pathogenesis, acting as a signaling molecule in the host cell cytoplasm; however, this mechanism is not fully understood. There are no studies that have identified formate binding proteins, but in the closely related bacteria *Escherichia coli*, there is a transcriptional regulator called FhlA that regulates the expression of formate hydrogenlyase complex (FHL) in response to formate. To study formate binding proteins in *S. flexneri*, we used a method called differential radial capillary of action ligand assay (DRaCALA). This is a high throughput assay where a small volume of protein mixed with radiolabeled ligand in a binding buffer is applied to a dry nitrocellulose membrane, then radionuclides bound to the membrane are visualized using a phosphor screen.

**Methods:** We performed DRaCLA using  $^{14}\text{C}$ -labeled formate. We compared the known formate binding protein FhlA from *E. coli*, and FhlA with a E183K mutation, which is predicted to be deficient in formate binding.

**Results:** We observed an interaction to formate in FhlA and FhlA E183K mutant (Figure A). However, FhlA fraction bound was higher than FhlA E183K mutant.



**Figure A:** Formate binding protein FhlA was mixed with  $^{14}\text{C}$ - formate. The mixture was spotted on a nitrocellulose membrane and viewed using phosphor screen.

**Conclusion:** FhlA binds more to formate when compared to FhlA E183K mutant, which indicate that this residue plays an essential role in formate binding.

## 65: Preconditioning with Hypoxia stimulates PD-L1 Expression in Myoblasts

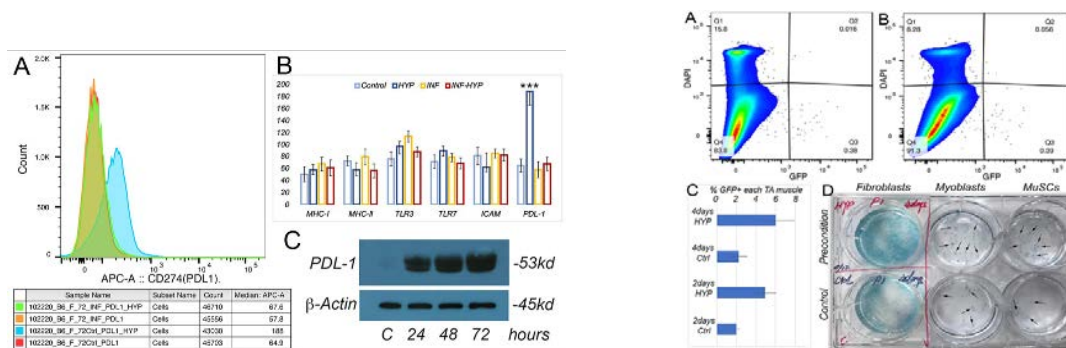
Juliana Overbey<sup>1</sup>, Delour Haj<sup>1</sup>, Kevin Chen<sup>1</sup>, Justin Lee<sup>1</sup>, Yong Li MD, PhD<sup>2</sup>, Haiying Pan<sup>2</sup>

<sup>1</sup>Medical Student. <sup>2</sup>Departement of Orthopaedic Surgery, Medical Engineering Program, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Transient exposure to low oxygen levels in tissue (e.g., hypoxia) and host immune response often leads to rapid cell death of transplanted cells. Hypoxia has been found to increase the activity of hypoxia-inducible factor (HIF)-1 $\alpha$  which then results in altered transcription and surface protein expression. Programmed Death Ligand1 (PD-L1) is a pro-survival surface protein that reduces the cytotoxicity of innate immune cells which has been found to be upregulated following hypoxia exposure in several cell types. This correlation leads us to hypothesize that PD-L1 expression is increased following myoblast culture in a hypoxic condition to promote survival rate of transplanted cells.

**Methods:** C2C12 myoblasts were cultured in 5% O<sub>2</sub> for times ranging from 15 minutes to 72 hours. Flow cytometry was performed to identify surface expression of PD-L1, MHC-1, MHC-2, TLR3, TLR7, and ICAM with IFN $\gamma$  pre-induction, as well as by Western Blot. Then cells were pre-labeled with LacZ and injected intramuscularly into the right TA muscles of adult C57BL6J mice, and the control non-hypoxic myoblasts were injected into the left TA muscles. After 2-4 days, the survival of transplanted myoblasts (LacZ+) was analyzed.

**Results:** We discovered that surface PD-L1 expression increased significantly in after hypoxia pre-treatment in as early as 6 hours of culture (Fig. 1A&B). This discovery was confirmed by Western Blot (Fig 1C). We also detected that preconditioning hypoxia significantly improved the survival rate of LacZ+ myoblasts in vivo by flow cytometry (Fig. 2A-C) as well as by re-isolation of muscle cells with LacZ staining and analysis (Fig. 2D).



**Discussion:** The reduction in the inflammatory response of the host tissue, in addition to the improved survival of transplanted cells, could justify the use of a hypoxia preconditioning culture treatment prior to the transplant of donor progenitor cells into tissues for the use of cell-based therapies. Our study suggests that transient, hypoxia-mediated induction of PD-L1 expression results in increased survival of myoblasts after transplanted into the limb muscles in mice. Furthermore, PD-L1 promotion may be used as a strategy to improve donor cells to escape the host immune system, e.g., immune-privilege, thus improve cell transplantation.

## 66: Risk Factors for Manipulation Under Anesthesia Following Total Knee Arthroplasty: A Systematic Review and Meta-analysis

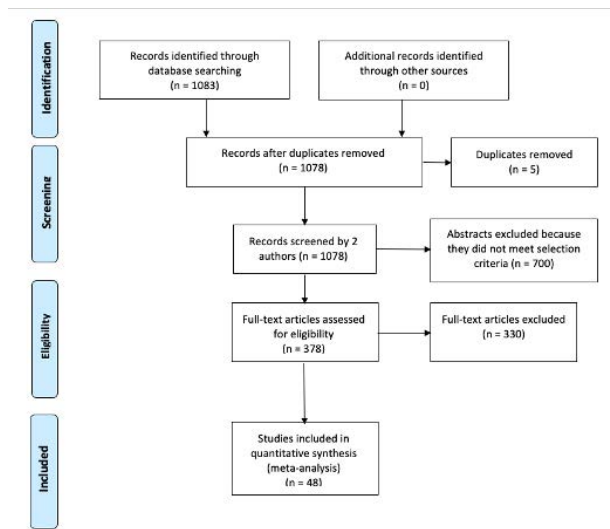
Son Tran<sup>1</sup>, Juliana Overbey<sup>1</sup>, Andre Ksajikian<sup>1</sup>, Sumit Patel MD<sup>2</sup>, Yong Li MD, PhD<sup>2</sup>

<sup>1</sup>Medical Student. <sup>2</sup>Department of Orthopaedic Surgery, Medical Engineering Program, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Arthrofibrosis of the knee following total knee arthroplasty (TKA) is a potential postoperative complication that can lead to debilitating results, poor patient satisfaction, and revision surgery. Frequently, arthrofibrosis is treated with manipulation under anesthesia (MUA), which increases the risks of morbidity and mortality to patients. This study aims to compile and evaluate risk factors for MUA following primary TKA.

**Methods:** Five databases were searched from inception to October 1st, 2021. Abstracts and full-text articles were screened for those that included risk factors predictive of MUA following TKA. Results were summarized as forest plots of individual studies and pooled random effect results. Statistical significance was set at  $P < 0.05$ .

**Results:** Database search yielded 48 studies involving 2,958,055 patients. 15 demographics and 8 potential risk factors were analyzed for MUA after primary TKA, of which 4 were found to be significant. Meta-analysis indicated younger age (OR: -4.23; 95% CI: -8.17-(-0.29)), black race (OR: 1.81; 95% CI: 1.43-2.29), preoperative ASA score  $< 2$  (OR: 0.64; 95% CI: 0.55-0.76), prior knee procedure (OR: 2.00; 95% CI: 1.49-2.69) as significant risk factors after TKA. There was moderate evidence for smoking as a risk factor (Odds Ratio [OR]: 1.35, 95% CI [0.96 – 1.89],  $p = 0.09$ ) and limited evidence for gender, obesity, and diabetes as possible risk factors for arthrofibrosis requiring MUA.



**Discussion:** The results of our meta-analysis indicate that black race, younger age, and preoperative ASA scores  $< 2$  have strong evidence as risk factors for post-operative arthrofibrosis. Surgeons should be aware of these risks when considering management of patients with the aforementioned risk factors in order to ensure patient satisfaction and operative success.



***67: A Novel Microparticle Immunocapture Assay to Measure Proteostatic Activity***

Darwin Edmond<sup>1</sup>, Kian Mohamadi<sup>1</sup>, Michael Gutknecht PhD<sup>2</sup>, Thomas Rothstein MD, PhD<sup>2</sup>  
<sup>1</sup>Medical student, <sup>2</sup>Department of Investigative Medicine <sup>1</sup>Western Michigan University Homer  
Stryker M.D. School of Medicine, Kalamazoo, MI

**Accepted for oral presentation**

## ***68: Arthrofibrosis in Rheumatoid Arthritis Patients after Primary Total Knee Arthroplasty***

Andre Ksajikian<sup>1</sup>, Juliana Overbey<sup>1</sup>, Son Tran<sup>1</sup>, Sumit Patel MD<sup>2</sup>, Yong Li MD, PhD<sup>2</sup>

<sup>1</sup>Medical Student, <sup>2</sup>Department of Orthopaedic Surgery, Medical Engineering Program, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Rheumatoid Arthritis (RA) a systemic autoimmune disease and is the most prevalent inflammatory disease of synovial joints. In patients with RA, degeneration of the knee may lead to total knee arthroplasty (TKA) to alleviate the significant pain and range of motion (ROM) limitations associated with RA. Rarely, arthrofibrosis of the joint after TKA results in suboptimal surgical outcomes requiring manipulation under anesthesia (MUA) to correct ROM limitation. There is limited understanding of the incidence of this rare complication; we hypothesize that the autoimmune environment of RA may result in increased risk of arthrofibrosis after TKA.

**Methods:** All publicly available databases were reviewed to identify papers that analyzed RA as a risk factor for stiffness following TKA. Given the variable definition of stiffness following TKA, the use of manipulation under anesthesia was used as a surrogate marker for arthrofibrosis. Studies that did not provide descriptive data for their patient populations or were not available in English language were excluded.

**Results:** 4 papers out of the 1,083 reviewed included RA as a risk factor for MUA after TKA. In these papers, the incidence of MUA in RA patients ranged from 0-3.1% 1-4. In the general population, the incidence of MUA is approximately 4.2%.

**Discussion:** Despite the significant synovial inflammation associated with RA, clinicians should be confident that current literature indicates RA is not a significant risk factor for arthrofibrosis following TKA. However, further retrospective reviews in diverse populations may provide a better understanding of the underlying mechanisms that cause post-surgical arthrofibrosis.

## ***69: A rare case of cholecystocolonic fistula***

Samantha Woolery MS<sup>1</sup>, Laura Bauler PhD<sup>2</sup>, Lisa Miller MD<sup>3</sup>, Kristofer Nava MD<sup>3</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Biomedical Sciences, <sup>3</sup>Department of Surgery, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Background:** Cholelithiasis, or gallstones, is a common phenomenon in Western populations. Treatment and management are well described, and progression is typically predictable. Disease severity and complications can however be quite varied. Left untreated cholelithiasis can commonly progress to acute cholecystitis, choledocholithiasis with or without acute cholangitis, and gallstone pancreatitis. More rare complications include gall bladder cancer, cholecystoenteric fistulas, gallstone ileus, and Mirizzi syndrome. Cholecystoenteric fistulas occur in 0.5-0.9% of patients with cholecystolithiasis, and cholecystocolonic fistulas are even more rare accounting for less than 20% of the incidence of cholecystoenteric fistulas second only to cholecystogastric fistulas. Diagnosis of cholecystoenteric fistulas present a challenge as signs and symptoms often mimic classic acute cholecystitis. Imaging may not reveal the erosion of the gallbladder into adjacent structures and most diagnoses to date have been incidental findings intraoperatively.

**Case History:** Here we present a case of a 50-year-old male who presented with acute on chronic cholecystitis who was later found to have gall bladder empyema and a cholecystocolonic fistula. Initial imaging showed cholelithiasis with gall bladder wall thickening and a positive Murphy's sign. Lack of resolution of symptoms lead to subsequent imaging which showed progression of his cholelithiasis and inflammation. The patient was taken to the operating room for a laparoscopic cholecystectomy. Intraoperatively the patient was found to have an early developing fistula between the fundus of the gallbladder and the transverse colon. The gallbladder was fibrosed and firm, with no identifiable plane along the infundibulum. As a result, the procedure was converted to an open laparotomy and a subtotal cholecystectomy was performed. The patient did well postoperatively and was subsequently discharged without any complications.

**Discussion/Conclusions:** Rare complications of gall stone disease can be associated with higher mortality and morbidity. Clinicians must take into consideration the possibility of these complications afflicting patients presenting with acute gall stone disease, especially for patients with an unknown history of gall stones, as the severity of the disease may not become clear until surgical intervention.

### ***73: Use of Allograft Bone Matrix in Clinical Orthopaedics***

Erica Myrick MS<sup>1</sup>, Peter Awad BS<sup>1</sup>, Victor Hung BS<sup>1</sup>, Shaan Manawar MD<sup>1,2</sup>, Yong Li MD, PhD<sup>1,2</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Orthopaedic Surgery, Medical Engineering Program, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Background:** Degenerative disease, severe infection, trauma, and the excision of tumors can result in bone defects beyond the threshold size for spontaneous healing. The gold standard for treatment of defects measuring 2-5 centimeters is the use of autologous bone graft. This treatment has significant shortcomings including harvest site pain and the inability to obtain large amounts of graft for sizable critical bone defects [1]. Bone allografts, such as demineralized bone matrix (DBM) and decellularized bone matrix (dECM), serve as alternatives that may alleviate the burden and limitations presented by this current method of treatment. In this study, we review existing literature on DBM and dECM and summarize the applications of these interventions in the field of orthopaedics.

**Methods:** We performed a PubMed search from the years 2000 to 2021. We used MESH terms "demineralized bone matrix ", "decellularized bone matrix", and "clinical application"

**Results:** Studies reveal the use of DBM to treat spinal fusions in the pediatric population to be as effective as autografts and more effective than allograft cancellous cortical chips alone [2-5]. Additional studies demonstrated adequate rates of bony fusion and enhanced speed of fusion in long bone non-union defects of children [6-7]. One study found that adults treated with DBM had significantly reduced incidence of post-operative pseudoarthrosis after pedicle subtraction osteotomy compared to patients treated with autologous bone graft [8]. Finally, our literature search revealed that dECM has not been studied in human trials, though its use in animal models has demonstrated its effectiveness as a medium for bone growth in critical size defects [9-11].

**Conclusion:** This literature review suggests that DBM may demonstrate similar effects on bone healing as autologous bone grafts while reducing its limitations. There is not enough literature demonstrating the effects of dECM on bone healing to adequately compare its effect to the current gold standard, however, future studies should explore this topic in more depth. Finally, further studies with higher levels of evidence are warranted to assess the effectiveness of DBM as a substitute for cancellous autograft.

## 74: Impact of Acetylcholine on Osteoblast Differentiation and Activity in vitro

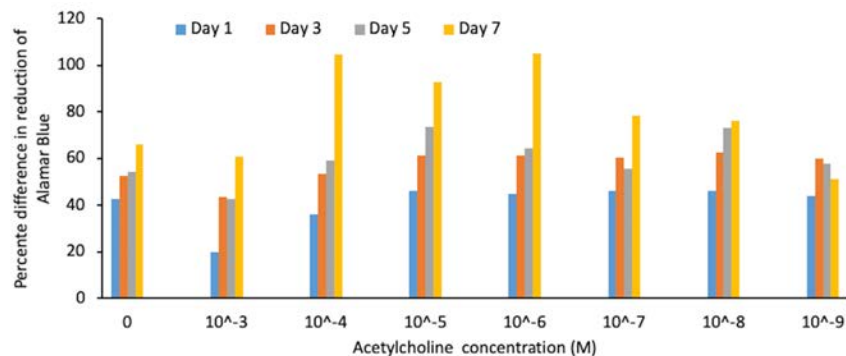
Ravi Trivedi BS<sup>1</sup>, Keith Kenter MD<sup>2</sup>, Adil Akkouch PhD<sup>2</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Orthopaedic Surgery, Medical Engineering Program, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Improper restoration of the tendon-to-bone-interface 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 tendon-to-bone-interface by introducing both bioactive compounds and micro-architecture that is conducive to tendon adhesion [1]. Recent studies in murine models showed that local supplementation of acetylcholine to the tendon-to-bone-interface can enhance the early stage of bone-tendon insertion healing by reducing inflammation [2]. Acetylcholine is a neurotransmitter that is liberated at nerve endings to facilitate cellular communication. However, the effect of acetylcholine on bone cells and bone formation remains largely unknown. This study aims to elucidate the effect of acetylcholine on osteoblasts proliferation and differentiation. By doing so we hope to identify the concentration of acetylcholine that leads to the most osteoblast activity and least toxicity.

**Methods:** A cell line of human-like osteoblasts (Saos-2) were cultured with Opti-MEM growth media (10% Fetal Bovine Serum and 1% Penicillin/Streptomycin) in 24-well plates at a concentration of  $3 \times 10^4$  cells/well. After an incubation period of 24h, Saos-2 were treated with solutions of acetylcholine-containing media at concentrations ranging from  $10^{-3}$  M to  $10^{-9}$  M. Cells cultured in growth media were used as control. Cell viability, proliferation and differentiation were analyzed over the following 14 days using Alamar Blue assay, osteogenic mediators expression (Osteocalcin, Runx-2) by qRT-PCR, collagen staining, and alkaline phosphatase activity assay.

**Results:** At the lowest dose of  $10^{-9}$  M, acetylcholine did not affect the growth of osteoblasts. However, we appreciate an increase for cellular proliferation at concentrations ranging from  $10^{-8}$  and  $10^{-4}$  M. 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.



**Figure:** Alamar Blue proliferation assay of Saos2 cultured with increased concentrations of acetylcholine.

**Conclusion/Clinical significance:** This pilot study will allow us to determine the effective doses of acetylcholine to be integrated in scaffolds for rotator cuff repair.

**References:**[1] Liu Q. et al. (2018), J Tissue Eng Regen Med., 12(7):1690-1701. [2] Wang Z. et al. (2021), Am J Sports Med., 49(4):909-917.

## ***76: Inhibitors of HDAC and MCL-1 synergistically reduce proliferation in cultured human melanoma cells***

Chester Gauss<sup>1</sup>, William Azkoul II<sup>2</sup>, Abby Knudson<sup>2</sup>, Jordan Zuckerman<sup>2</sup>, Yue Xi<sup>2</sup>, Andrew Fribley<sup>2</sup>

<sup>1</sup>Medical student, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI.

<sup>2</sup>Wayne State University School of Medicine, Detroit, MI

**Introduction:** Melanoma is a malignant cancer of the melanocytes. It is regarded as the most aggressive skin cancer due to a high rate of recurrence and distant metastatic potential. The standard of care treatment for melanoma is surgical excision however management of post-surgical margins remain variable among health care providers. Due to the excessive degree of relapse following resection, developments in adjuvant care have been greatly expanded over recent years. Despite advances in melanoma treatment with BRAF inhibitors such as Vemurafenib, approximately 7,100 people died in the U.S. last year and the number is expected to increase in 2022. This demonstrates an urgent need for supplementary treatment options.

**Methods:** The current study employed a panel of melanoma cells representative of multiple anatomical sites. Two new drugs, with different mechanisms of action, were employed to determine the antiproliferative effects on melanoma cells in culture. AZD5991 is a novel pre-clinical drug candidate, currently in phase 3 clinical trials which induces apoptosis through inhibition of Myeloid cell leukemia (MCL-1). Panobinostat (LBH589) is a newly FDA approved histone deacetylase (HDAC) compound that is active in a variety of human malignancies.

**Results:** AZD5991 and Panobinostat both reduced proliferation in each melanoma cell line examined at low (micromolar) concentrations. Furthermore, isobologram analysis revealed the combined effects of the two drugs was synergistic. Analysis of cDNA libraries generated from whole-cell lysates utilizing RT-qPCR revealed that the combined treatment of AZD5991 and Panobinostat increased the expression of a panel of cell death transcripts. Interestingly, TRIB3, DR5 and GADD45A were significantly increased suggesting that endoplasmic reticulum (ER) stress may contribute to the observed antiproliferative effects of these compounds. Considered together, these data confirm that MCL-1 and HDAC inhibition could individually and synergistically reduce proliferation in cultured melanoma cells. The reduction in proliferation was accompanied by increased expression of genes associated with ER stress-induced apoptosis.

**Conclusions:** Studies currently underway will further elucidate the role of ER stress and more thoroughly characterize the features (gene and protein expression) induced following exposure to AZD5991 and Panobinostat. These current preliminary studies suggest the combined targeting of MCL-1 and HDAC may be a novel approach to treat melanoma.

## 77: Fabrication of 3D Electroconductive Scaffold for Bone Regeneration

Kunal Ranat BS<sup>1</sup>, Mitchell Kenter MS<sup>2</sup>, Keith Kenter MD<sup>2</sup>, Adil Akkouch PhD<sup>2</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Orthopaedic Surgery, Medical Engineering Program, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Bone-related injuries continue to be a growing concern within the healthcare community. These issues are exacerbated in elderly populations since the incidence of bone-related issues increases along with decreased healing capacity. To resolve this problem, we propose fabricating three-dimensional (3D) scaffolds made by electroconductive polymers to promote bone regeneration. Electrical stimulation has been shown to upregulate growth factor expression, which enhances synthesis of extracellular matrix proteins and accelerates tissue repair. [1] As such, we aim to synthesize an “electroconductive polymer ink” by combining polycaprolactone (PCL) with Poly(3,4-ethylenedioxythiophene) (PEDOT) to create 3D scaffolds using melt-electrowriting. Melt-electrowriting is a novel high-resolution technology for creating predefined micrometric fibers where geometries can be customizable. [2] Osteoblast cell lines will be used to determine if effective bone cell proliferation is possible on the scaffold.

**Methods:** PEDOT nanoparticles were synthesized by oxidative polymerization of the 3, 4-ethylenedioxythiophene monomer (EDOT) in the presence of ferric. The morphology and chemical composition of resulting PEDOT was determined using SEM and XPS. PCL was mixed with PEDOT at 5, 10 and 20% weight ratio and melted in a microwave. Composites were loaded into the Axo-A3 3D bioprinter (Axolotl Bio) and melt-electrowriting was conducted using an electrical field of 5 kV. Human osteoblasts were used to test cell adhesion, proliferation, and osteogenic differentiation.

**Results:** PEDOT nanoparticles were successfully synthesized using oxidative polymerization. A typical compact and globular morphology of PEDOT was observed under SEM. XPS analysis of the C(1s) core spectrum revealed the typical peaks from three distinct types of carbon present in the chemical structure of PEDOT. The 3D fabricated electroconductive scaffold is non-cytotoxic and effectively improved osteoblasts adhesion and proliferation.

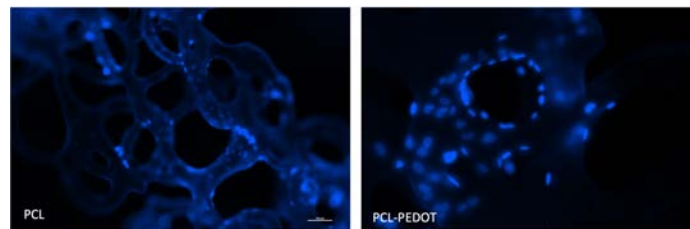


Figure: Osteoblasts adhesion on 3D printed scaffolds. DAPI staining after 5 days in culture.

**Conclusion/Clinical Significance:** Ultimately, prospective scaffolds will be installed within devices that permit electrical stimulation, which, when implanted into an animal or human model, may conceivably promote bone regeneration.

**References:** [1] Clark D. et al. (2017), Curr Osteoporos Rep. [2] Aleem IS. et al. (2021), Scientific Reports.

**Acknowledgment:** This study was supported by the Pilot Research Program from WMed.

## 78: Effects of Pirfenidone on Fibroblast Proliferation and Gene Expression

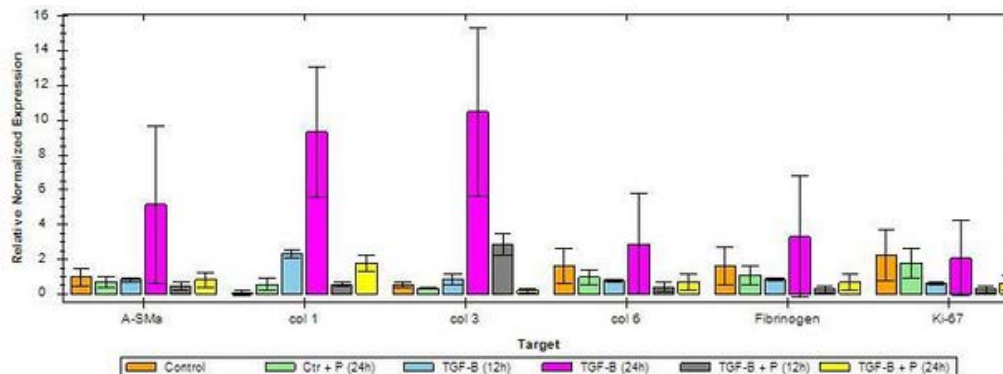
Andre Ksajikian BS<sup>1</sup>, Juliana Overbey BS<sup>1</sup>, Son Tran BS<sup>1</sup>, Sumit Patel MD<sup>2</sup>, Yong Li MD, PhD<sup>2,3</sup>

<sup>1</sup>Medical student, <sup>2</sup>Department of Orthopaedic Surgery, <sup>3</sup>Medical Engineering Program, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Fibrosis is a complication of regular healing that is often debilitating. The process of tissue insult and healing involves inflammation, various cytokines, cell signaling markers, and the production of a new extracellular scaffold by proliferating cells and their secretions. To mitigate collagen overproduction, excess inflammation, and excess cell proliferation at the site of injury, Pirfenidone, a drug that is approved for lung fibrosis, will be tested in vitro on 3T3 mouse embryonic fibroblasts.

**Methods:** 3T3 mouse embryonic fibroblasts were used in three different preparations and at two time points. The control group was cultured in DMEM with 10% FBS. The second preparation was 3T3 cells with the addition of TGF- $\beta$ , which was used to induce fibroblast proliferation and collagen production to mimic tissue fibrosis. The third included both TGF- $\beta$  and pirfenidone. All preparations were cultured for 12 and 24 hours. After collection, analysis was done via qPCR to quantify levels of gene expression.  $\alpha$ -smooth muscle actin (SMA), Col1, Col3, Col6, fibrinogen, and Ki-67 were used as markers for the q-PCR.

**Results:** As seen in the figure 1 below, cell expression for  $\alpha$ -SMA, Col1, and Col3 drastically increased in the 3T3 cells that were given TGF- $\beta$  and incubated for 24 hours. Conversely, the culture of cells that were incubated with both TGF- $\beta$  and Pirfenidone showed a marked decrease in the expression of those same biomarkers. Although not as drastic, levels of col6, fibrinogen, and Ki-67 also showed a slight increase in the cells given TGF- $\beta$  for 24hrs as compared to the levels of these biomarkers in the pirfenidone treated group. No noteworthy changes were observed in the 12-hour timepoint groups.



**Discussion:** Based on these results, it is suspected that the hypothesized effect of pirfenidone is true. We hope to transition to an in vivo model to assess Pirfenidone's effect on post-operative skin, soft tissue, and joint fibrosis. With the prevalence of iatrogenic skin, soft-tissue, and joint fibrosis after various types of procedures, Pirfenidone may potentially be used to decrease scarring, joint stiffness, inflammation and improve patient satisfaction after surgery.



## ***79: CMML-2 with Syncopal Episodes as Initial Presentation: A Case Report and Review of the Literature***

Hayley Barker BS<sup>1</sup>, Maya Giaquinta BS, BA<sup>1</sup>, Matthew Kennedy DO<sup>2</sup>, Melissa Olken MD, PhD, FHM<sup>3</sup>  
<sup>1</sup>Medical student, <sup>2</sup>Psychiatry Residency, <sup>3</sup>Department of Medicine, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Chronic myelomonocytic leukemia 2 (CMML-2) has features of both myelodysplastic and myeloproliferative disorders and results from the abnormal production of monocytic cells. CMML-2 is partially distinguished from CMML-0 and CMML-1 based on the number of blasts seen on bone marrow biopsy. 1-4 The following case report follows the case of a 67-year-old woman who presented to the ED after two syncopal episodes and was subsequently diagnosed with CMML-2 with transformation to acute myeloid leukemia (AML).

**Methods:** This is a case report and literature review.

**Results:** Initially, the patient's presentation was thought to be due to a GI bleed from antral erosive gastritis with mild ulcerations noted on EGD. However, due to increasing need for pRBC and platelet transfusions, Heme/Onc was consulted, and a bone marrow biopsy obtained that showed CMML-2. The patient was treated with five days of Dacogen with no clinical improvement. Her hospital course was prolonged due to transfusion dependency before being discharged to Hospice where she passed away a few days later.

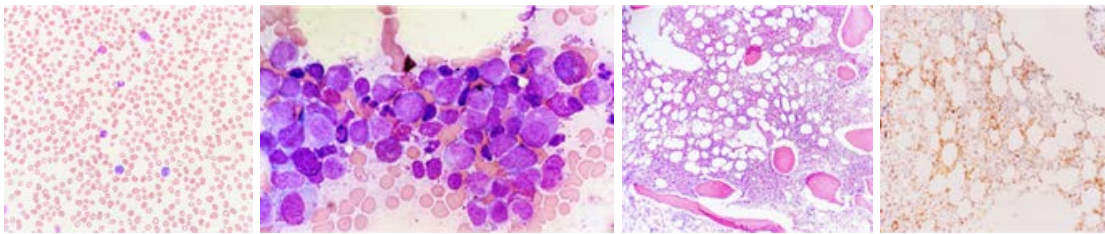


Image acknowledgements to Agatha Board MD

**Conclusion/Clinical significance:** To our knowledge, this is the first case report showing CMML-2 initially presenting with syncopal episodes; when considering the underlying cause of syncope, it is important to keep differentials broad and consider all systems.

**References:** [1] Patnaik MM and Lasho T. (2020) Hematology Am Soc Hematol Educ Program, 2020, 460–464. [1] Patnaik MM and Tefferi A. (2018) Am J Hematol, 93, 824-840. [3] Sangiorgio VFI, Arber DA, & Orazi A. (2020) Int J Lab Hematol, 42, 101-108. [4] Valent P, Orazi A, Savona MR, Patnaik MM, Onida F, van de Loosdrecht AA, Haase D, Torsten H, Elena C, Pleyer L, Kern W, Pemovska T, Vladimer GI, Schanz J, Keller A, Lübbert M, Lion, T, Sotlar K, Reiter A, De Witte T, Pfeilstöcker M, Geisser K, Padron E, Deininger M, Orfao A, Horny H-P, Greenberg PL, Arber, DA, Malcovati L, & Bennett JM. (2019) Haematologica, 104, 1935-1949.

**80: Risk factors for Complex Regional Pain Syndrome Type I after distal radius fracture repair:  
A systematic review and Meta-analysis**

Son Tran BS<sup>1</sup>, Jessica Duong BS<sup>1</sup>, Brandon Pham BS<sup>2</sup>, Sumit Patel MD<sup>3</sup>, Craig Raberding MD<sup>4</sup>

<sup>1</sup>Medical student. <sup>2</sup>Michigan State University College of Osteopathic Medicine, Lansing, Michigan.

<sup>3</sup>Department of Orthopaedic Surgery and Biomedical Sciences, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. <sup>4</sup>Department of Orthopaedic Surgery, Surgery of the hand, Ascension Borgess Hospital, Kalamazoo, MI

**Introduction:** Complex Regional Pain Syndrome Type I (CRPS I) is a rare, but serious complication of distal radius fracture. It is characterized as a chronic, uncontrollable pain that develops after distal extremity trauma in the absence of direct nerve damage and that rarely spontaneously resolves. Currently, there is no curative treatment for CRPS I, making this complication much more difficult to manage. We seek to identify risk factors that predispose patients to developing CRPS I following any distal radius fracture (DRF) repair.

**Methods:** Five databases were searched from inception to December 12th, 2021. Abstracts and full-text articles were screened for those that included risk factors predictive of CRPS I following any DRF repair. Results were summarized as forest plots of individual studies and pooled random effect results. Statistical significance was set at  $P < 0.05$ .

**Results:** Forty-six articles were evaluated for full-text screening, of which twenty-eight articles were excluded. CRPS I was found in 0.3% of patients following any DRF repair. Patients who developed CRPS I had distal ulnar fractures that accompanied the DRF, had open fractures, and were female.

**Discussion:** Our findings suggest that patients who suffer from distal radius fractures with concomitant ipsilateral ulnar fractures or those who have open distal radius fractures are more likely to develop CRPS I. This is likely due to the complexity of the trauma and its complex repair process, ultimately leading to the development of CRPS I.

## 81: Time to Treatment and Outcomes of Gastric Cancer Between 2004 and 2017 from the National Cancer Database

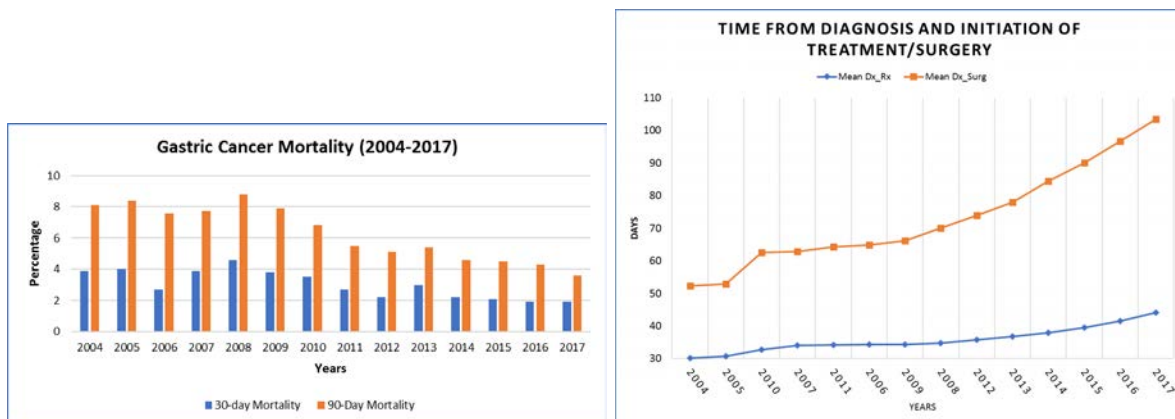
Kent Grosh MD<sup>1</sup>, Mohamed Kamel MD<sup>2</sup>, Faiz Tuma MD<sup>1</sup>, Saad Shebrain MD<sup>1</sup>

<sup>1</sup>Department of General Surgery, Kalamazoo, MI. <sup>2</sup>Surgery, Cincinnati, OH

**Background:** Gastric cancer is an aggressive malignancy that commonly presents as advanced disease. We hypothesized that advances in diagnosis have led to earlier treatment and improved survival.

**Methods:** We identified clinical stages I-III gastric cancer patients in the National Cancer Database (NCDB) who underwent gastrectomy between 2004 and 2017. We created three groups based on waiting time (WT) from diagnosis to treatment initiation [KG1] :  $\leq 21$  days, 22-42 days, and  $> 42$  days. Trends in WT, mortality, and the association between the WT and demographic variables were evaluated.

**Results:** There were 15,169 (34.1%) patients in group 1; 15,249 (34.3%) patients in group 2; and 14089 (31.%) patients in group 3 (45,998 total). There was a progressive increase in median (IQR[KG2] ) of WT from 25 (9.75, 41) days in 2004 to 37 (23, 55) days in 2017 ( $p < 0.001$ ). The WT to surgery[KG3] for the same period increased from 32 (11, 82.25) days to 107 (37, 147) days ( $p < 0.001$  vs 102). There was no correlation between WT and sex, race, stage of cancer, insurance status, or rural/urban status. WT correlated positively with the distance of patient's residence and the treating hospital (\*\*\*) . The 30-, and 90-day mortality decreased over time (3.9%, 8.8% in 2004, to 1.9%, 3.6% in 2017).



**Conclusions:** Among patients undergoing gastrectomy for stage I-III gastric cancer, this study shows increased WT from diagnosis to initiation of treatment between 2004 and 2017 though mortality has decreased. Increased patient travel distance was identified as a possible contributor to increased WT.

### ***83: Biomimetic Scaffolds for Bone Regeneration Using 3D Melt Electrowriting***

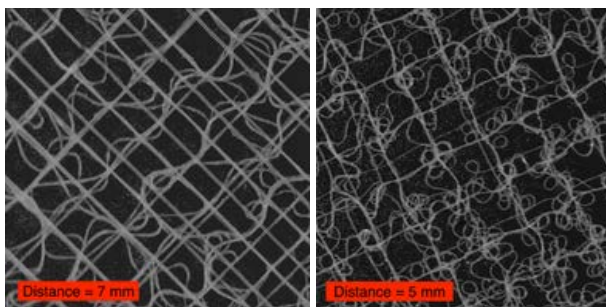
Maninder Randhawa BS<sup>1</sup>, Kunal Ranat BS<sup>1</sup>, Adil Akkouch PhD<sup>2</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Orthopaedic Surgery, Medical Engineering Program, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** The treatment of critical-sized bone defects poses a major clinical problem. Autografts are the gold standard for healing bony defects. However, graft implantation has many problems, including a high rate of complications during the harvesting procedure such as infection, and nerve/vascular lesions. The amount of bone that can be harvested is also limited, which becomes problematic when treating larger defects. For this reason, it is important to consider the use of synthetically engineered biomimetic scaffolds in the treatment of bony defects. Using 3D printing technology, specific parameters of the scaffold such as shape, porosity, and composition can be adjusted which allows for better customization when treating defects. The goal of this study is the fabrication of well-defined scaffolds for bone defects using 3D melt electrowriting; a novel technology that allows for the extrusion of nanofibers during the printing process, providing extreme precision in the fabrication process.

**Methods:** Multiple biomimetic scaffolds were designed using computer aided design (CAD) software Axo-A3. Scaffolds were fabricated using medical-grade polycaprolactone (PCL) and the Axo-A3 3D bioprinter (Axolotl Bio). Printing parameters such as voltage, speed of the printer head, distance (mm) between the nozzle and platform, infill and shape of the scaffold, and pressure were adjusted between each print. The type of fibers produced (i.e. nanofibers) and the alignment of the fibers were then recorded as well as the texture of the scaffold produced.

**Results:** Multiple scaffolds were produced using a voltage of 5 kV, pressure of 5.0 psi, and printer head speed of 50 m/s. When adjusting for distance, fiber orientation was noted to change, with larger distances resulting in more aligned fibers and smaller distances resulting in more coiled fibers.



**Conclusion:** These results will help determine specific parameters to fabricate a range of scaffolds with desired properties to match the specific needs of different patients. By characterizing the effects that certain variables have on scaffold properties, customized grafts can be made to treat a variety of bone defects.

**References:** [1] Von Witzleben. M, et al. (2021) *Advanced Healthcare Materials* 10.10:2002089.

## ***84: Modified Component Separation Technique For Repair Of Giant Ventral Hernias With Loss Of Abdominal Domain***

Andrew Alfred BS<sup>1</sup>, Dakota De Cecco BS<sup>1</sup>, Saad Shebrain MD, MMM<sup>2</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Surgery, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Repair of giant ventral hernias with loss of abdominal domain is challenging as there is no single standard repair technique. Component separation offers a newer option that facilitates more natural tissue coverage in these patients.

**Case Presentation:** Case 1: 65-year-old female with significant surgical history presented with abdominal pain, increasing abdominal bulge, and difficulty with colostomy. Physical exam showed a large ventral incisional hernia. A CT scan of the abdomen and pelvis showed a huge hernia containing significant portions of abdominal contents. Extensive adhesions complicated the procedure. A subtotal colectomy was performed (transverse and left colectomy) with defunctionalized rectal stump. The contents of the hernia were reduced.

Case 2: 60-year-old female presented with a three-year history of increasingly symptomatic abdominal bulge and anemia requiring transfusion. Physical exam showed a 25 x 30 x 20 cm ventral hernia with ulcerations and bleeding. Skin biopsy ruled out cancer. CT of the abdomen and pelvis showed a large hernia which contained significant abdominal viscera. The ulcerated skin was excised, and the fascial edges were identified. Hernia contents were reduced to the abdomen.

In both cases, the fascial defects were 15-20 cm transversely. The component separation technique facilitated reduction by 8-10 cm. To close the remaining defects, a XENMATRIX™ was used in the first case and a PHYSIOMESH™ in the second. The gap in the external oblique aponeurosis was enforced using XENMATRIX™ in both cases. A colostomy was created through the right rectus muscle in the first case. Redundant skin and subcutaneous tissues were excised and then closed over drains.

Neither patient developed compartment syndrome. Drains were removed after 3-4 weeks in the subsequent clinic visits.

**Discussion:** Component separation technique provides more natural tissue coverage for closing large fascial defects. However, in cases of giant ventral hernia, an extra prosthetic material is still required.

## **85: 30-day Outcomes of Extremity and Non-extremity Necrotizing Soft Tissue Infections (NSTI) in ACS-NSQIP Data**

Jessica Duong BS<sup>1</sup>, Neal Ferrin DO<sup>2</sup>, Saad Shebrain MD<sup>2</sup>, Robert Sawyer MD<sup>2</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Surgery, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Despite advances in surgical care, necrotizing soft tissue infection (NSTI) remains a serious surgical problem associated with high mortality if not treated aggressively and timely. The study aims to evaluate the 30-days postoperative outcomes in patients with NSTI using ACS-NSQIP.

**Methods:** Using the ACS-NSQIP database (2015-2017), patients with ICD-9/ICD-10 diagnosis of NSTI who underwent surgical interventions were identified and divided into extremity (E-NSTI) and non-extremity (NE-NSTI) groups. 30-day postoperative mortality, morbidity, length of hospital stay (LOS), return to the operating room (OR), and readmission rates were analyzed. Proportions were compared using Chi-squared test, or Fisher exact test, and continuous variables were compared using t-tests or Mann Whitney test. A  $p < 0.05$  was considered statistically significant.

**Results:** Of 2233 patients identified, 1907 (85.4%) had necrotizing fasciitis, and 326 (14.6%) had Fournier gangrene. 356 (16%) patients were in the E-NSTI group and 1877 (84%) were in the NE-NSTI group. Both groups had similar baseline characteristics. However, the E-NSTI group had a higher proportion of patients who were male (70.8% vs. 59.5%,  $p < 0.001$ ), and who had a history of diabetes, DM, (56.7% vs. 50.9%,  $p < 0.001$ ) and renal failure, RF (10.7% vs. 5.6%,  $p < 0.001$ ). Overall, the amputation rate was 10.6%. There were no significant differences in 30-day mortality (11.8% vs. 9.9%), serious morbidity (64.4% vs. 61.5%), overall morbidity (68.3% vs. 65.2%), return to the OR (13.5% vs. 12.8%), and readmission rate (11% vs 9%) between both groups. No differences were noted in mean LOS and operative time. More than half of the patients in the E-NSTI group (54.3%) were discharged to rehab/skilled care centers, compared to 37% in the NE-NSTI group ( $p < 0.001$ ). On subgroup analysis, 237 patients in the E-NSTI group (66.6%) underwent amputation/dislocation to control sepsis.

**Conclusion:** No differences in 30-day outcomes between the E-NSTI and NE-NSTI groups were noted. However, pre-surgically, the E-NSTI group had a higher percentage of predisposing factors such as DM and RF, and postoperatively, the E-NSTI group had a higher percentage of discharges to non-home places. The amputation rate is extremely high in patients with E-NSTI and further actions must be taken to address this outcome.

## 87: Effect of Strontium and Niobium on Bone Proliferation and Differentiation

Suhaib Ellythy BA<sup>1</sup>, Shelby Chaney MS<sup>1</sup>, Keith Kenter MD<sup>2</sup>, Adil Akkouch PhD<sup>2</sup>

<sup>1</sup>Medical student. <sup>2</sup>Department of Orthopaedic Surgery, Medical Engineering Program, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Strontium and Niobium are two elements that have shown immense therapeutic potential in bone trauma recovery and degenerative bone diseases like osteoporosis. Strontium is thought to have both anabolic and anti-resorptive effects through inducing the proliferation of pre-osteoblast as well as inhibiting the proliferation of osteoclasts.[1] On the other hand, Niobium is thought to aid in osseointegration of implants and scaffolds.[2] The purpose of this study is to further explore the mechanism of action of both elements, find the effective minimal dose of both strontium and niobium for use in-situ, and investigate their cytotoxic effects. This allows us to improve scaffold engineering to enhance bone regeneration and treatment of degenerative bone diseases. We hypothesize that low doses of these elements will show no effect on osteoblasts while high doses can result in adverse effects and ultimately cell death.

**Methods:** Human-like osteoblasts were treated with niobium concentrations of 0.01, 0.025, 0.05, 0.1, 0.25, 0.5, 1, and 5mM; or strontium at 0.25, 0.5, 1, 5, 10, 25, 50, 100mM. We also tested their combinatory effect at 0.25 mM niobium and 25mM strontium, 0.167 mM niobium and 33.3mM strontium and 0.125 mM niobium and 37.5 mM strontium. Cells in growth media were used as control. Cell viability, proliferation and differentiation were analyzed over the following 14 days using Alamar Blue assay and alkaline phosphatase activity.

**Results:** Strontium at above 50 mM reduced the proliferation of osteoblasts after 24h culture. Niobium also inhibited cell proliferation starting at 0.1mM. Remarkably, the combination of niobium at 0.25 mM and strontium at 25 mM resulted in higher proliferation rate.

**Conclusion/Clinical Significance:** The study of the combinatory effect of strontium and niobium on osteoblast proliferation and growth will increase the efficacy of their use in bone regeneration applications.

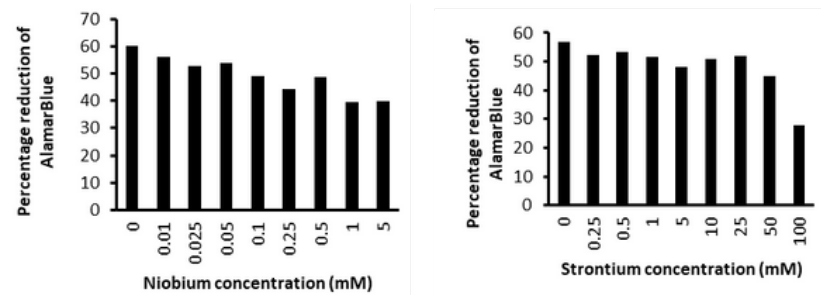


Figure: Osteoblast metabolic activity when treated with increased concentrations of niobium and strontium at 24h.

**References:** [1] Kołodziejaska B. et al. (2021) Int J Mol Sci. [2] Marins NH. et al. (2019) Colloids Surf Biointerfaces.

## 88: The Effect of Low-Density Lipoproteins on miRNA Expression in Osteoblasts

Hong Phan BS<sup>1</sup>, Lilly Ruell BS<sup>1</sup>, James Springstead PhD<sup>2</sup>, Adil Akkouch PhD<sup>2,3</sup>

<sup>1</sup>Medical student, <sup>2</sup>Medical Engineering Program, <sup>3</sup>Department of Orthopaedic Surgery, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Low-density lipoproteins (LDL) are known to cause inflammation via upregulation of genes involved in the inflammatory responses and are associated with development of atherosclerotic cardiovascular disease [1]. Previous studies have shown that increasing LDL levels are negatively associated with bone marrow density and is correlated with increasing age-related bone loss through the production of proinflammatory cytokines that inhibit signaling pathways important in bone metabolism and remodeling [2]. microRNAs, however, also play a role in modulating these signaling pathways to mediate age-related bone loss [3]. We hypothesize that microRNAs, therefore, can modulate the inflammatory response associated with LDL particles, specifically to reverse the progression of bone loss and adipogenesis within the bone marrow. Our study aims to further understand the role of miRNAs to counteract the role of LDL in mediating the age-related switch between adipogenesis and osteogenesis in osteoblasts.

**Methods:** Saos-2 human osteosarcoma cells were cultured with increased concentrations of oxidized-LDL particles of 0, 1, 5, 10, 25, 50, 75, 100, 150, 200 ( $\mu\text{g/mL}$ ) for up to 7 days. Cell cytotoxicity was performed using lactate dehydrogenase, and Alamar Blue assay. Expression of a panel of miRNAs related to inflammation was analyzed via qRT-PCR.

**Results:** Osteoblast proliferation increased over time with all tested concentrations, with higher values at 100  $\mu\text{g/mL}$ . Despite a decrease in proliferation at higher concentrations, it still higher than the non-treated group (Figure).

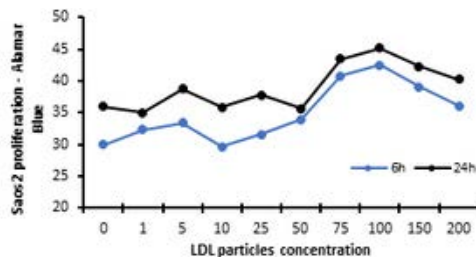


Figure: Saos-2 cells cytotoxicity assay when cultured with LDL particles.

**Conclusion/Clinical significance:** The profiling of miRNAs changes induced by oxidized-LDL particles will help the discovery of new therapeutics for the treatment of chronic inflammation mediated by higher levels of lipoproteins in elderly and obese population.

**References:** [1] Yin, W. et al. (2019) *Nutrients*, 11(6), 1394. [2] Tintut, Y., & Demer, L. L. (2014). *Trends in endocrinology and metabolism: TEM*, 25(2), 53–59. [3] Zhang, Y. L., et al., (2021). *International journal of molecular sciences*, 22(13), 7210.



## ***89: Etiology of Cardiopulmonary disease during the pandemic. A challenging case***

Muhammad Armughan Ali MD, Marium Rehman MD, Dilpat Kumar MD, Mark Schauer MD  
Internal Medicine Residency, Western Michigan University Homer Stryker M.D. School of Medicine,  
Kalamazoo, MI

**Introduction:** Multitude of cases with cardiovascular manifestations and sequelae associated with Coronavirus disease-19 (COVID-19) have been reported. We report a case of myopericarditis, pulmonary embolism, and neurological symptoms manifesting after resolution of acute episode.

**Case Presentation:** An 81-year-old woman presented with anginal chest pain on exertion, lasting for 20 minutes. She had history of hypertension and prior tobacco use. She was sick 2 weeks before presentation and endorsed fatigue with low grade fevers, dry cough, dysgeusia, and anosmia. She had a negative SARS-CoV-2 PCR test on admission. On presentation, she was tachycardic to 102 beats/min. Troponins were elevated at 1169 and 963 ng/L with EKG showing diffuse ST-segment elevation in inferolateral leads. Computed Tomography (CT) of chest revealed patchy ground glass opacities in the right middle and lower lobes. Transthoracic echo revealed ejection fraction of 35%, severe hypokinesis of distal wall and apical akinesis suggestive of TCM. She was started on colchicine for pericarditis. Lexiscan stress test did not reveal any evidence of inducible ischemia. COVID-19 antibody test was positive for IgG antibody, indicating previous infection. Patient was discharged on colchicine, beta-blocker and apixaban. Patient reported confusion and word finding difficulty on follow-up office visit suggestive of post COVID “Brain Fog” and has a pending TTE to reassess improvement in EF.

**Discussion:** Our case emphasizes the importance of the use of COVID-19 antibodies as a surrogate test to indicate infection in the setting of a negative PCR test, especially in symptomatic patients. Whether patients, who develop severe extra pulmonary/cardiac manifestations in the absence of overt pulmonary disease have certain preexisting risk factors, remains a question that needs to be further explored.

**Conclusion:** Acute infection or sequelae of COVID-19 should be kept in hindsight while evaluating a patient presenting with cardiac manifestations of COVID-19 even in the setting of negative PCR test.

## ***90: How to Teach Regional Anesthesia to Emergency Medicine Residents***

Philip Pazderka MD, Wael Hakmeh DO, Kelsey Burson DO, Jessica Thornton DO, Nathan Welham MD  
Department of Emergency Medicine, Western Michigan University Homer Stryker M.D. School of  
Medicine, Kalamazoo, MI

**Introduction:** Ultrasound-guided regional anesthesia (UGRA) is a safe and efficient tool to achieve adequate pain control for patients in the emergency department (ED). Use of UGRA can provide an alternative approach to procedural sedation and opioid analgesia, both of which entail risks. UGRA may be underutilized due to limited training opportunities needed to achieve procedural competence and confidence. Currently, use of cadaver models in ultrasound education is very limited. The objective of this study was to develop and implement a structured educational intervention in UGRA using cadaveric models and to assess its effect on the participants' self-perceived level of procedural confidence.

**Methods:** Nerve blocks performed include the fascia iliaca, serratus anterior, interscalene, posterior tibial, median, radial, and ulnar nerve blocks. Residents performed each of the aforementioned procedures. Pre- and post-intervention surveys were administered to emergency medicine residents of post graduate year (PGY) 1-3. The survey contained 11 Likert-type and two demographic items (gender and year of training). Likert-type items are measured on a five-point scale (1=Strongly Disagree, 2=Disagree, 3=Neutral, 4=Agree, and 5=Strongly Agree).

**Results:** There were 66 pre-intervention and 58 post-intervention survey respondents. Responses from a total of 32 participants (n=32) with matched pre- and post-intervention responses were analyzed. Unmatched surveys (pre-intervention surveys lacking a post-intervention survey, or vice versa) were excluded, as were post-survey responses which were submitted prior to the pre-survey response. 100% of respondents felt empowered to perform some regional anesthesia nerve blocks ( $p < .0001$ ). 90.6% felt that they had a good understanding of the medications used in regional anesthesia ( $p < .0001$ ). 90.6% felt confident in their ability to perform these nerve blocks. 93.8% felt confident in their ability to teach patients the side effects of regional anesthesia ( $p < .0001$ ).

**Conclusion:** Emergency medicine residents' perceived confidence in performing regional anesthesia nerve blocks improved after the educational intervention utilizing fresh cadaver training models. These results present further evidence and support for the use of fresh cadavers as a cost-effective and efficient training model to enhance resident confidence in performing regional anesthesia.

## ***91: Eastern Massasauga Rattlesnake Envenomation in Southwest Michigan: A Case Report***

Alexandra Dinello MD, Lindsay Nausin DO

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

**Introduction:** Michigan and Ontario, the regions with the largest populations of eastern massasauga rattlesnakes, only report one or two envenomations annually [1]. This case report reviews the management of these rare envenomations via a nine-year-old male with a history of Hypoplastic Left Heart Syndrome (HLHS) who presented to an ED in southwest Michigan after being bitten.

**Case Presentation:** A nine-year-old male with a history of HLHS presented to the ED after he was bitten by an eastern massasauga rattlesnake. The patient had marked swelling and ecchymosis to the leg surrounding two small puncture marks over the medial malleolus. Four vials of CroFab were given initially and the patient was admitted to the pediatric floor where he continued to have daily measurements of pre-marked sites. Baseline and serial labs were obtained including INR, aPTT, platelets and fibrinogen. On day two, orthopedic surgery was consulted due to concern for compartment syndrome but ultimately, this was excluded given his soft compartments and ability to tolerate passive ROM. On day three, the patient again had a marked increase in swelling and received an additional four vials of CroFab. The patient's symptoms gradually improved, and on day five he was discharged home.

**Discussion:** Antivenom is indicated in patients with worsening local injury, thrombocytopenia, coagulopathy, other concerning systemic effects, or those with certain comorbidities. In this case, a patient with a history of HLHS presented with significant leg swelling with rapid progression. The patient received a total of eight vials of CroFab including a second dose on day three and eventually improved. In children, the dose for CroFab is the same as adults. For pediatric patients <10 kg or those with underlying cardiopulmonary or renal disease, the total volume of diluent can be reduced. The initial recommended dose is 4-6 vials however patients in shock or with serious bleeding can get 8-12 vials. Even with redosing, some patients will have refractory coagulopathy. Patients receiving antivenom should be admitted for observation for at least 18-24 hours with serial exams, wound care, monitoring for delayed immunologic reactions, and serial blood draws to ensure normalization [2].

## ***92: The Effect of Gross Anatomy Tutorials Using Near-Peer and Reciprocal Peer Teaching on Students' Confidence and Performance***

Jonathan Tse BS<sup>1</sup>, Victoria Addis BS<sup>1</sup>, Simranjeet Cheema BS<sup>1</sup>, Sungjik Cha BS<sup>1</sup>, Victor Hung BS<sup>1</sup>, Sara Allison PhD<sup>2</sup>

<sup>1</sup>Medical Student. <sup>2</sup>Department of Biomedical Sciences, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** At WMed, medical students have their first significant component of anatomy during the Musculoskeletal System course. Previous studies have shown that students' first experience learning anatomy, especially in the context of cadavers, can be an incredibly stressful and challenging experience. High levels of stress have been shown to be detrimental to student learning and performance. However, near-peer teaching and reciprocal peer teaching have recently demonstrated much promise in boosting student confidence and performance. The current study sought to design student-led tutorials incorporating these two teaching strategies in order to improve students' learning and build confidence in the anatomy lab.

**Methods:** Eighty-four first-year medical students were invited to participate in two anatomy tutorials detailing the lower and upper extremities. Immediately prior to the tutorial, participants completed a pre-quiz which consisted of five anatomy-based questions that also required students to rate their confidence in their answer choices. During the tutorials, students rotated through five stations where near-peer tutors provided a brief overview of limb musculature. Following the initial instruction from tutors, students rotated through an additional five stations and were asked to teach each other what they learned on a new set of cadavers. A post-quiz was administered to assess changes in student knowledge and confidence. This included five different anatomy-based questions of a similar difficulty level.

**Results:** Forty-eight students participated in the lower extremity anatomy tutorial. Data is currently being collected and will be analyzed upon the completion of the upper extremity anatomy tutorial. The researchers hypothesize that the application of peer-teaching and reciprocal peer teaching will demonstrate a significant increase in student learning and confidence.

**Conclusion:** Medical student confidence and performance may have various implications for the future practice of the medical students. Identifying effective teaching strategies that can improve both is important for medical educators seeking to develop successful students and clinicians.

**IRB Reference Number:** WMed-2021-0848

## 93: Quality Improvement Initiative in Sweat Chloride Testing at the WMed Health Cystic Fibrosis Program and Bronson Methodist Hospital

Jessica Ziccarello BS<sup>1</sup>, Paul Guthrie MLS, Ian Parrott MLS, Bethany Peak MBA, MLS, Carolina Herrera RRT<sup>3</sup>, Debra Wells-Schmidt RN<sup>3</sup>, Sally Bonnema RD<sup>3</sup>, Sheryl Lozowski-Sullivan MPH, PhD<sup>3,4</sup>, Kristi Homan CPhT<sup>3</sup>, Nichole Vess RN<sup>3</sup>, Teresa Bailey PharmD, BCPS, BCACP, FCCP<sup>3,4</sup>, Julie Hovey MA<sup>3</sup>, Andrea Caskey LMSW<sup>3</sup>, Mariam Ischander MBChB<sup>3,4</sup>

<sup>1</sup>Medical student. <sup>2</sup>Bronson Methodist Hospital, Kalamazoo, MI. <sup>3</sup>Health Cystic Fibrosis Program, <sup>4</sup>Department of Pediatric and Adolescent Medicine, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Sweat chloride testing is widely recognized as the gold standard for Cystic Fibrosis (CF) diagnosis. In order to maintain the accuracy of the test, the amount of sweat collected must reach a minimum threshold, or the sample is designated quantity not sufficient (QNS). This necessitates repeat sweat chloride collection at a later date, which causes stress for parents and, if the child does have CF, a delay in the initiation of therapy. In December of 2020, a multidisciplinary team from the WMed Health Cystic Fibrosis Program commenced a Quality Improvement (QI) project in conjunction with the Bronson Methodist Hospital (BMH) laboratory to decrease the QNS rate and thereby maintain accreditation through the Cystic Fibrosis Foundation (CFF). The goal was to achieve the CFF-recommended QNS rate of less than 5% for patients older than 3 months of age, and less than 10% for patients 6 weeks to 3 months of age by November 30, 2021.

**Methods:** This quality improvement project identified seven unique areas for process improvement. Initiatives included stopping inpatient sweat chloride testing unless permission is granted by the lab medical director or CF program director; education for providers ordering sweat chloride testing; updating BMH lab procedure and reference values that appear on the lab report to reflect new CFF guidelines; and in-service training under expert guidance for the BMH lab team to review and perfect sweat chloride analysis techniques.

**Results:** At the beginning of the QI Project, QNS for patients >3 months was 5.4%, and for patients 6 weeks to 3 months was 28.6%. At the end of the 12-month period, QNS had been decreased to 4.4% for patients >3 months and to 0% for patients 6 weeks to 3 months.

**Conclusion:** The WMed Health Cystic Fibrosis Program successfully reduced their QNS rate below the CFF-required threshold, which will hopefully result in continued accreditation for the WMed Health Cystic Fibrosis Program pending a CFF review this year. Additional education and optimization of training has also led to improved laboratory processes and renewed confidence in the accuracy of sweat chloride testing performed at BMH.

## ***95: Retained Surgicel Masquerading as Biloma with Retained Gallstones***

Dakota De Cecco BS<sup>1</sup>, Andrew Alfred BS<sup>1</sup>, Saad Shebrain MD<sup>2</sup>

<sup>1</sup>Medical Student, <sup>2</sup>Department of Surgery, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Surgicel™ is a local hemostatic agent used to control bleeding during surgery and is fully absorbable within 7-14 days. Although rare, residual Surgicel™ sheer weave form can calcify and imaging studies can have a pathological appearance, leading to unnecessary operation, which is especially problematic in a compromised patient recovering from surgery.

**Case Presentation:** A 64-year-old man presented to the Emergency Department (ED) with epigastric pain, 16 months post subtotal cholecystectomy for gangrenous cholecystitis. On evaluation, a computed tomography (CT) scan of the abdomen demonstrated mild inflammation with localized hyperdensity within the residual gallbladder suggesting biloma and retained gallstones. A hepatobiliary iminodiacetic acid (HIDA) scan showed non-visualization of the gallbladder and lack of tracer leakage, correlating with the patient's surgical records, clinical presentation, and radiologic evaluation and supporting the diagnosis of calcified sheer woven Surgicel™.



Figure : Acute gangrenous cholecystitis with patchy gallbladder wall necrosis

**Discussion:** Calcification of Surgicel™ sheer weave form is rare and radiographically and can imitate gallstones, abscesses, and tumors. A thorough evaluation of the patient, including previous operative reports, is critical to avoid unnecessary interventions.

## ***96: Street Medicine Kalamazoo: Healthcare Utilization of the Unhoused Across Care Settings***

Rebecca Reardon-Lochbaum<sup>1</sup>, Jessica Zicarello<sup>1</sup>, Nikoli Nickson<sup>1</sup>, Sravani Alluri MD<sup>2</sup>, Nicholas Helmstetter MD<sup>3,4</sup>

<sup>1</sup>Medical student, <sup>2</sup>Department of Family and Community Medicine, <sup>3</sup>Department of Medicine, <sup>4</sup>Department of Pediatric and Adolescent Medicine, Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** One of the many challenges the unhoused population faces is inequitable access to and utilization of the healthcare system. Additionally, poor health can both precipitate and complicate homelessness, placing individuals at high risk of morbidity and mortality. This necessitates specific and targeted interventions to meet the complex needs of the unhoused and ameliorate the pressure placed on emergency departments to act as primary care sites. WMed Street Medicine Kalamazoo (SMKzoo) works to provide mobile outbound care, seeking out unhoused patients and delivering holistic healthcare services directly to them. This provides an important opportunity to gain insight into the most common chief concerns and underlying health problems that affect the unhoused individuals in our community, as well as information on their baseline healthcare utilization prior to introduction of SMKzoo services.

**Methods:** This study is a descriptive, retrospective chart review utilizing patient care information from the health records maintained by SMKzoo as well as those available on the Cerner and Epic EHRs, encompassing the Ascension and Bronson systems, WMed Health, and the Family Health Center.

**Results:** Within the study period of Apr 2021 to Feb 2022, 264 unique individuals were seen by the SMKzoo team across 800 encounters. Encounter reasons spanned from acute processes (e.g., infections, trauma) to chronic disease management (e.g., diabetes, hypertension, viral hepatitis) to primary and preventative care (e.g., immunizations, prenatal care). Most patients were insured. The average number of SMKzoo visits per patient was 3, with a range of 1 to 25. Further results are pending.

**Conclusion/Clinical significance:** Characterizing common concerns and overall health status of our patients, as well as how those facing homelessness utilize healthcare resources in our community, SMKzoo can become better equipped to work in concert with our current healthcare systems to augment health outcomes achieved by our most marginalized. Additionally, this study is unique in its scope and the level to which it describes clinical entities seen by Street Medicine teams. In an effort to codify and advance the discipline of Street Medicine, this will allow other groups to anticipate needs and design programing accordingly.

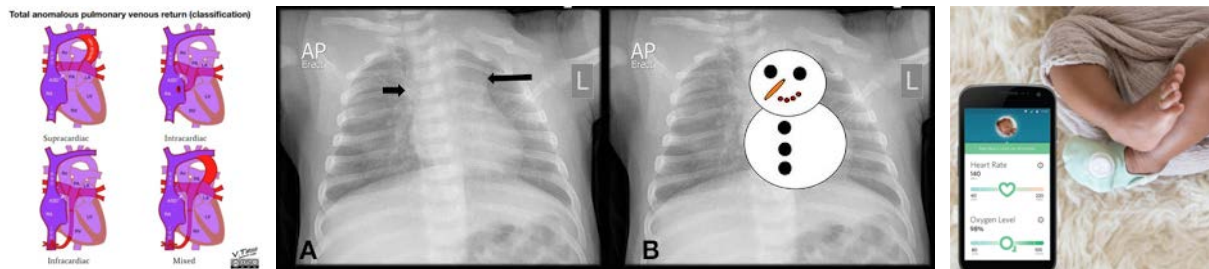
## 98: Owlet Home Baby Monitor Portends Total Anomalous Pulmonary Venous Return

Elizabeth Hoffman MD, Emily Bon DO, John Hoyle MD

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

**Introduction:** Total anomalous pulmonary venous return is a rare congenital heart defect where none of the four pulmonary veins connect to the left atrium creating right-to-left shunting of mixed, partially deoxygenated blood <sup>[1]</sup>. Clinical manifestations vary in severity and timing depending on several factors and prognosis without treatment is poor <sup>[1][2][3]</sup>. In this case diagnosis may have been hastened by a home baby monitor.

**Case Presentation:** The patient is a full term female who briefly required blow by oxygen immediately after birth for mild hypoxia. She was discharged on day 2 of life with oxygen saturation 95%. Parents' home Owlet monitor repeatedly reported oxygen saturations down to 70% prompting three primary care provider visits during the first week of life. She was otherwise well and Owlet readings were deemed inaccurate though pulse oximetry was not confirmed in office. On day 11 of life she appeared cyanotic and lethargic prompting an emergency room presentation. She was unresponsive with acute shock, severe acidosis, hypoxia and respiratory failure. Chest x-ray showed bilateral pulmonary infiltrates. She was emergently intubated and resuscitated. After transfer to pediatric intensive care rapid echocardiogram showed supracardiac total anomalous pulmonary venous return with mild obstruction of the vertical vein and severe pulmonary hypertension. She was transferred to a tertiary facility for emergent surgical repair, requiring extracorporeal membrane oxygenation support for several days and multiple further corrective surgeries.



**Discussion:** Total anomalous pulmonary venous return deformities are often missed on prenatal or postnatal screening prior to discharge from the hospital <sup>[2]</sup>. It is important to keep high clinical suspicion for congenital heart defects especially with concern for possible hypoxia, even with a home baby monitor. Clinicians should always confirm pulse oximetry as some patients may be asymptomatic even with oxygen saturations below 90% <sup>[2]</sup>. Low oxygenation should be further investigated, including echocardiogram. Confirming the defect and performing surgical repair prior to decompensation results in decreased morbidity and mortality <sup>[3][4]</sup>.

**References:** [1] Soriano B. and Fulton D.R. (2015). [2] Strobel A. M. and Lu le N. (2015). [3] Seale A.N. et al. (2010). [4] Lee Y. et al. (2016).



## ***99: Perforated Appendicitis: The Solution to Pollution is Not Dilution***

Joslyn Jose MD<sup>1</sup>, Gordon Liu<sup>2</sup>, Michael Leinwand MD<sup>2,3</sup>

<sup>1</sup>General Surgery Residency, <sup>2</sup>Western Michigan University Homer Stryker M.D. School of Medicine, Kalamazoo, MI. <sup>3</sup>Bronson Methodist Hospital, Kalamazoo, MI

**Introduction:** Surgical dogma is that for perforated appendicitis, the “solution to pollution is dilution.” The authors hypothesized that avoiding irrigation during Single Incision Laparoscopic Appendectomy (SILA) for perforated appendicitis in children would decrease operative time and have no effect on the postoperative abscess rate.

**Methods:** From May 2011 to May 2015, SILAs were performed with irrigation. From June 2015 to August 2021, only suctioning was performed with the operations otherwise performed in the same fashion by a single surgeon. We retrospectively reviewed 55 patients in the Irrigation (I) Group and 82 patients in the No Irrigation (NI) Group.

**Results:** Abscess rate decreased from 16.4% in Group I to 13.4% in Group NI, but this did not reach statistical significance ( $p=0.63$ ). Operative duration decreased from 62.1 to 51.2 minutes ( $p<0.0001$ ). For patients in both groups who developed abscesses, operative duration was longer than in those patients without postoperative abscesses (79.3 v 58.8 minutes,  $p<0.0001$  in Group I; 66.2 v 48.8 minutes,  $p<0.0001$  in Group NI). Of the patients in both groups who developed abscesses, mean weight was higher than in those patients without postoperative abscesses (49.0 v 36.6 kg,  $p=0.046$  in Group I; 44.3 v 36.8 kg,  $p=0.29$  in Group NI), though the difference did not reach statistical significance in Group NI.

**Conclusion:** Irrigation during SILAs for perforated appendicitis did not decrease the occurrence of postoperative abscesses; there was actually a trend toward an increased abscess rate. Avoiding irrigation decreased operative duration, which can help drive down the cost of care.

**IRB Reference Number:** WMed-2021-0840

## 101: Acute Pericarditis Secondary to *Coxiella Burnetii* Infection

Aditya Mehta MD, Melissa Olken MD, PhD

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

**Introduction:** Q (or Query) fever is a zoonotic infection caused by *Coxiella Burnetii* after inhalation of infected aerosols, most commonly from sheep, goats, and cattle. Most commonly it presents with flu-like illness, pneumonia, or hepatitis. Pericarditis is a rare manifestation seen in up to 1% of cases and our patient had risk factors for multiple zoonotic infections but was eventually diagnosed with Q fever.

**Case Presentation:** A 39-year-old man presented with daily fevers up to 102°F, night sweats, fatigue for three weeks. Two weeks prior, he developed a dry cough, generalized weakness, and pleuritic chest pain, which was positional in nature. One week later, he also developed malaise and diffuse body aches which prompted him to come to the hospital. He has extensive occupational history of working as a construction worker and recently had been gutting an early 1990's house that had squirrel infestation. He used to wear an N100 mask most of the time. He lives in a rural area and spends time on his farm as well. He also recalled tick bites a few months ago but never had any rash. He also had cats, dogs, and chickens as his pets. He also butchers hogs and deer. He traveled to New Mexico and Florida in last two months and has a remote history of travel to Kenya 15 years ago. His wife worked at a Primate Institute and reported recent Tuberculosis cases in primates. Given his extensive exposure history, a myriad of infectious lab work was obtained to rule out Lyme, Tuberculosis, Mycosis, Brucella, Q-fever, and other tick-borne illnesses. His presenting EKG was concerning for Acute Pericarditis. CT scan of chest and 2-D echo revealed mild to moderate pericardial effusion with no lymphadenopathy. He also had transaminase elevation with negative hepatitis panel. Q-fever serology revealed 1:128 phase II titers with convalescent sera showing 1:512 Q-fever IgG antibody. He was treated with doxycycline for 2-weeks and repeat titers were 1:64 at 4 months.

Q Fever PHS 1 IgG AB	<1:16	1:32 ↓	1:32 ↓	1:32 ↓
Q Fever PHS 2 IgG AB	<1:16	1:64 ↓	1:512 ↓ <sup>CU</sup>	1:128 ↓
Q Fever PHS 1 IgM AB	<1:16	<1:16	<1:16	<1:16
Q Fever PHS 2 IgM AB	<1:16	<1:16	<1:16	<1:16

**Discussion:** A high index of suspicion should be maintained for zoonotic infections presenting with atypical symptoms, such as pericarditis, in the right clinical context.

## ***102: Plummer-Vinson Syndrome as a Unique Trigger for Disordered Eating***

Jibraan A. Fawad MD, Maria D.I. Cabral MD, Patrick Jones MD

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

**Introduction:** Plummer-Vinson syndrome (PVS) is characterized by the classic triad of iron deficiency anemia (IDA), dysphagia and esophageal webs. PVS is a rare condition particularly in developed countries with low occurrence of severe IDA. Usual presentation is seen in middle-aged White women. We describe a case of an East Asian female adolescent presenting with severe IDA and underweight status later diagnosed with PVS thought to have triggered restrictive eating.

**Case:** A 13-year-old perimenstrual female of East Asian descent was admitted to the pediatric hospital service due to severe anemia (hemoglobin 4 g/dl) during a routine laboratory screening at her wellness visit. Consultation with pediatric hematology was obtained for concerns of microcytic anemia, thrombocytopenia, and leukocytosis of unknown etiology. Bone marrow biopsy was negative for leukemia and patient received blood transfusion. Further history revealed chronic low weight, disordered eating and pill dysphagia. Adolescent medicine consultation conveyed concerns for Anorexia Nervosa versus Avoidant/Restrictive Food Intake Disorder. Patient was placed on the inpatient feeding protocol for closer monitoring of nutritional intake. Per pediatric gastroenterology recommendation, celiac screen, inflammatory markers and fecal occult blood returned negative and noted mildly elevated calprotectin. Patient discharged home hemodynamically stable with planned iron transfusions and esophagogastroduodenoscopy (EGD). A week later, EGD revealed an upper esophageal stricture and biopsies were suggestive of mild reflux. A follow up esophagogram confirmed a diagnosis of an esophageal web. With the classic triad of symptoms, a diagnosis of Plummer-Vinson syndrome was made. The patient underwent multiple balloon dilations leading to improvement of symptoms including weight recovery.

**Conclusion:** This is a unique presentation of Plummer Vinson syndrome in an adolescent female with severe anemia said to be multifactorial and esophageal webs with dysphagia resulting in restrictive/avoidant behavior with disordered eating. Correction of anemia leads to resolution of dysphagia however younger patients tend to require esophageal dilation.

## 106: Covid Toes: A Case Series

Sarah Black MD<sup>1</sup>, Kelsey Sheets MD<sup>1</sup>, Sarah Noffsinger PA-C<sup>2</sup>, Heidi Jerz ATC<sup>2</sup>, James Jastifer MD<sup>2</sup>

<sup>1</sup>Department of Orthopedic Surgery, Western Michigan Homer Stryker M.D. School of Medicine, Kalamazoo, MI. <sup>2</sup>Department of Orthopedics, Ascension Borgess, Kalamazoo, MI

**Introduction:** Three cases of toe vascular changes identified in patients following SARS-CoV2 (Covid 19) infection. d. Complaints of abnormal toe perfusion, and the pathophysiology or prognosis, is not well understood. The purpose of this study is to report a series of patients with abnormal toe perfusion after Covid 19.

**Case Presentations:** Three patients were identified over a 4 month period who were diagnosed with a recent Covid 19 infection and presented for toe perfusion abnormalities. A chart review was performed and patient demographics and clinical course were collected.

One 53 year old male was treated with expectant management, and his toes eventually returned to normal although he still has heat and cold sensitivity. Two other patients eventually required surgical intervention. A 56 year old female who was hospitalized with Covid 19, was diagnosed with toe necrosis 2 weeks later. After wound care, she eventually underwent a transmetatarsal amputation on her left foot and 5th toe amputation on the right foot. A 50 year old male who was hospitalized with Covid 19 developed necrosis of toes 1-4 on the left. After wound care he required a left transmetatarsal amputation.



**Discussion:** This study reports toe necrosis as a complication related to a recent Covid 19 infection. While Covid 19 is a rapidly evolving disease, and complications related to Covid 19 are not well studied. Proposed mechanisms for skin changes and gangrene following Covid 19 include endothelial destruction induced by viral particles. <sup>[1]</sup> Other proposed mechanisms include venous thrombosis leading venous gangrene. <sup>[2]</sup> These cases represent orthopedic manifestations of Covid 19 infection. Further studies should continue to investigate pathophysiology and underlying mechanism of systemic covid-19 related complications.

**References:** [1] Colmenero I, Santonja C, Alonso-Riaño M, et al. SARS-CoV-2 endothelial infection causes COVID-19 chilblains: Histopathological, immunohistochemical and ultrastructural study of seven paediatric cases. *Br J Dermatol.* 2020. [2] Musani MH, Musani MA, Verardi MA. Venous gangrene a rare but dreadful complication of deep venous thrombosis. *Clin Appl Thromb Hemost.* 2011;17(6):E1–3.

## ***107: Sheehan Syndrome-Like Presentation in Male Following Non-Head Traumatic Injury***

Jeffrey Feng M<sup>1</sup>, Chris Sloffer MD, MBA<sup>2,3</sup>

<sup>1</sup>Medical student. <sup>2</sup>Bronson Neuroscience Center, Kalamazoo, MI. <sup>3</sup>Department of Surgery, Western Michigan Homer Stryker M.D. School of Medicine, Kalamazoo, MI

**Introduction:** Sheehan's syndrome classically presents in women who experience infarct of a hypertrophic pituitary from postpartum hemorrhage. This can present with hormonal deficiencies, headache, and cranial nerve deficits. Non-head traumatic injuries with significant blood loss leading to a similar mechanism of injury to the pituitary are exceptionally rare in men.

**Methods:** We report a case of a man who presented with infarct and hemorrhage into a pre-existing occult pituitary tumor in delayed fashion two days following a knife wound that resulted in venous injury and significant blood loss.

**Case Presentation:** A 44 year-old male presented with an acute severe bilateral frontal headache, diplopia, left-sided ophthalmoplegia, and ptosis one day following stable hospital discharge for surgical management of a knife wound that transected his left cephalic vein two days prior. He had no recent head trauma. MRI showed a hemorrhaging pituitary macroadenoma that was previously unknown, and labs showed significant hypopituitarism. Patient underwent emergent endoscopic transnasal transsphenoidal hypophysectomy, during which fibrous and necrotic tumor tissue with dark clots of blood were encountered. Complete resection of tumor tissue was achieved and confirmed with symmetric diaphragma sellae descent and endoscopic visualization. Pathology confirmed non-invasive pituitary adenoma with hemorrhage, infarction, and acute inflammation. Complete resolution of headache, diplopia, ophthalmoplegia, and significant improvement in ptosis was achieved immediately post-op. Resulting symptomatic hypogonadism, hypothyroidism, and hypoadrenalism were managed by endocrinologists with hormone replacement. At 5 years post-op, patient continues to be well-managed on his hormone medications with no additional complications associated with his hypophysectomy.

**Conclusion:** Non-head traumas involving significant loss of blood may precipitate infarct and hemorrhage of a pituitary adenoma in a manner similar to Sheehan's syndrome in postpartum women. Early recognition and evaluation of neurologic and visual deficits at time of any trauma presentation with timely neurosurgical intervention are essential in preventing permanent functional impairment and possible death.

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