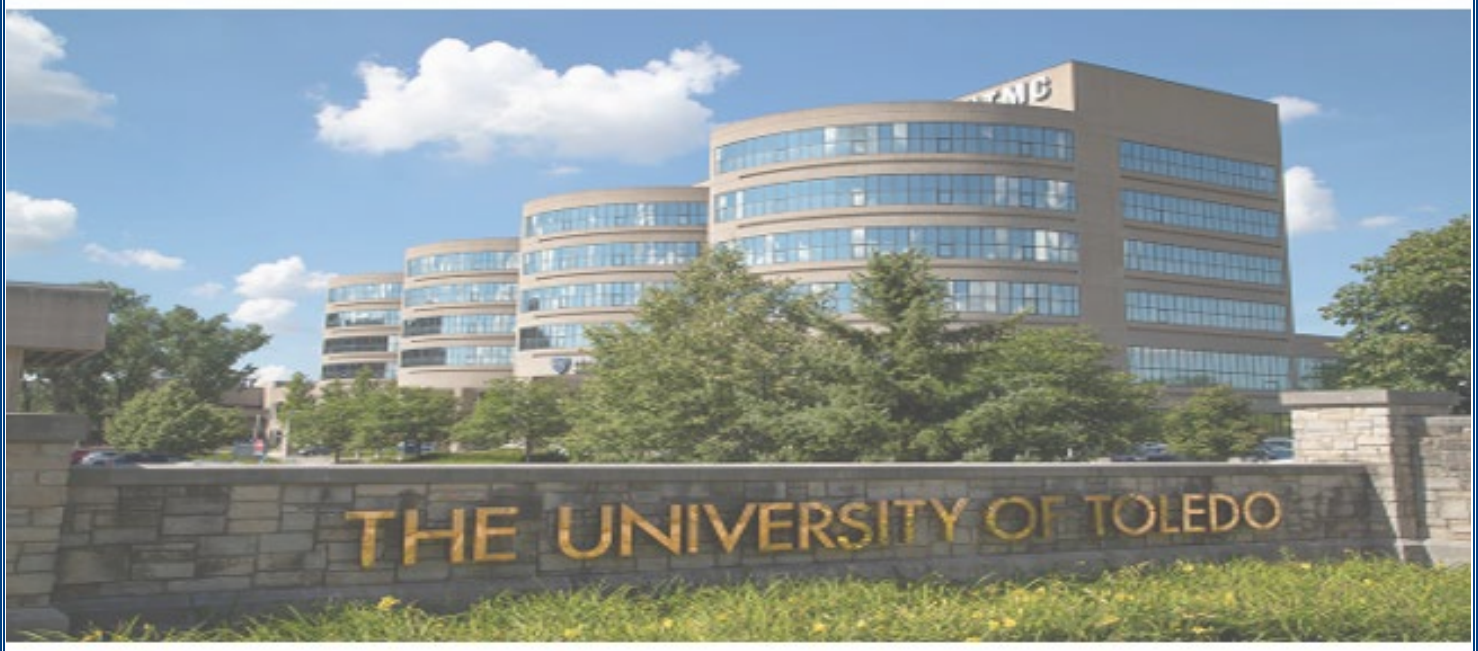
COLLEGE OF MEDICINE AND LIFE SCIENCES
THE UNIVERSITY OF TOLEDO

2024

Dr. Lance D. Dworkin

Department of Medicine
Research Symposium



October 31, 2024
Volume 4

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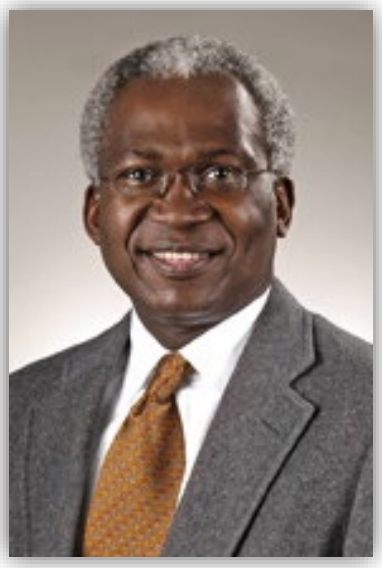
Message from the Chair



It is my pleasure to welcome you to the 4th Annual Department of Medicine Research Symposium, a day dedicated to celebrating innovative and diverse research shaping the future of healthcare. This symposium provides an important platform to highlight the transformative research being conducted by our trainees and faculty, research that is driving advancements in patient care and healthcare outcomes. We are proud to showcase projects from every division within the Department of Medicine, ranging from compelling case reports to cutting-edge clinical and translational research. The symposium reflects our commitment to advancing healthcare through inquiry, collaboration, and excellence in research.

It is fitting to honor the legacy of Dr. Lance D. Dworkin, whose ground-breaking research and exceptional mentorship have left an indelible mark on our field. His dedication to clinical and translational research continues to inspire both the scientific community and our department's ongoing efforts to innovate and improve patient care.

We are honored to have Dr. Matthias Kretzler, Warner-Lambert/Parke-Davis Professor of Internal Medicine-Nephrology and Professor of Computational Medicine & Bioinformatics at the University of Michigan, as our keynote speaker. His expertise will provide invaluable insights into our discussions today and beyond.

We also extend our gratitude to Dr. Imran Ali, Dean of the College of Medicine and Life Sciences, Dr. Rujun Gong, Vice Chair for Research, and Drs. David Kennedy, Steve Haller, and Sadik Khuder for their unwavering support of research. Their contributions, along with the enthusiasm of our faculty and trainees, foster the development and achievement of this symposium.

We are especially proud of all those who contributed to the abstract and manuscript submissions, reflecting the strength of our research community. We also acknowledge the invaluable support of Rick Swaine, CEO; Chris Stesney, COO; and Michael Ellis, CMO of UTMC. The efforts of Dr. Robert Smith and the support provided by Diane McCarthy, Amy Phillips, Margaret Hoogland, Umeeksha Sharma, and Lisa Johnston are deeply appreciated, as their significant contributions ensure the ongoing success of this event.

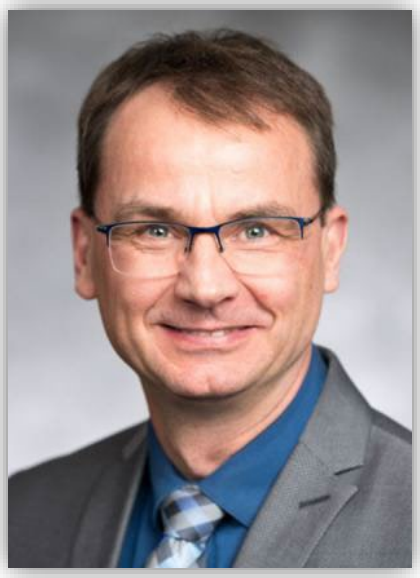
Thank you for joining us in celebrating the spirit of research and discovery. I encourage you to engage with the presentations, explore the abstracts, and take this opportunity to forge new collaborations that will advance our shared mission of improving healthcare.

Basil Akpunonu, MD
Mercy Endowed Professor & Chair
Department of Medicine
Academic Chief of Medicine

Keynote Speaker

Matthias Kretzler, MD

Warner-Lambert/Parke-Davis Professor, Internal Medicine-Nephrology
Professor, Computational Medicine & Bioinformatics
Director, Michigan Kidney Translational Medicine Center
University of Michigan



Dr. Matthias Kretzler, MD, is an internationally recognized leader in nephrology and precision medicine, focusing on the molecular and cellular mechanisms of kidney disease. Currently Warner-Lambert/Parke-Davis Professor of Internal Medicine Professor of Computational Medicine & Bioinformatics at the University of Michigan, Dr. Kretzler has dedicated his career to integrating cutting-edge molecular biology with clinical data to develop innovative treatments for chronic kidney disease. His pioneering work in bioinformatics allows for the identification of molecular signatures that can be used to create targeted therapies, revolutionizing the way kidney diseases are understood and treated.

Dr. Kretzler's leadership has been pivotal in establishing multi-institutional collaborations, both nationally and internationally. He leads the Nephrotic Syndrome Study Network (NEPTUNE) and the Kidney Precision Medicine Project (KPMP), both aimed at transforming the clinical care of patients by enabling personalized, molecularly-guided treatment strategies. His research is not only transformative but highly translational, applying findings from lab-based research directly to patient care, with the goal of improving outcomes for those suffering from chronic kidney conditions.

In addition to his research contributions, Dr. Kretzler has published extensively, with over 300 peer-reviewed papers in high-impact journals and multiple book chapters to his name. His work has garnered widespread recognition, earning him numerous awards and invitations to speak at prestigious conferences worldwide. His dedication to patient care, research, and education ensures that his impact on the field of nephrology will be felt for generations to come.

Schedule of Events

4th Annual Department Of Medicine Research Symposium

Thursday, October 31, 2024

Welcome & Introductions

Collier Building, Room 1000B

12:00 pm	Dr. Basil Akpunonu Chair Department of Medicine
12:05	Dr. Imran Ali Dean, College of Medicine and Life Sciences
12:10	Dr. Rujun Gong Vice Chair, Research Department of Medicine
12:15	Matthias Kretzler, MD Warner-Lambert/Parke-Davis Professor, Internal Medicine-Nephrology Professor, Computational Medicine & Bioinformatics Director, Michigan Kidney Translational Medicine Center University of Michigan

AWARDS

1:00	Awards for Outstanding Abstract Submissions Presented by: Dr. David Kennedy and Dr. Steve Haller Co-Directors, Department of Medicine Medical Student Mentored Research Program

POSTER SESSION

Interprofessional Immersive Simulation Center (IISC)

1:15	Poster presentations and reception

Abstracts

CARDIOLOGY

Brianna N. Bailey, MS

Rare complication of infective endocarditis: A case of septic embolus causing diplopia

Brianna N. Bailey MS, Serena A. Maag MS, Mathieu K. Holt BS, Danyal S. Butt MD, Bibek M. Shrestha MD, Ayman Iqbal MD, Davonte Willis MD, Srini K. Hejeebu DO

Introduction: Infective endocarditis, an infection of the cardiac endothelium, typically affects the heart valves and can lead to serious complications, including bacteremia and the formation of septic emboli. This case report highlights a rare complication of infective endocarditis and emphasizes the importance of early recognition and intervention.
Case Presentation: A 34-year-old male with a history of intravenous drug use was admitted to the intensive care unit (ICU) following an overdose. While intubated, the patient developed bacteremia, with blood cultures revealing methicillin-resistant *Staphylococcus aureus* (MRSA). A transesophageal echocardiogram (TEE) identified a 4 mm vegetation on the anterior leaflet of the mitral valve. Upon extubation, the patient reported abdominal pain and diplopia. A computed tomography (CT) scan of the abdomen revealed bilateral renal artery stenosis, and an ophthalmologic examination showed impaired movement of the left medial rectus muscle. These findings were attributed to septic emboli in the bilateral renal arteries and the inferior ophthalmic artery.
Discussion: This case highlights a rare presentation of infective endocarditis where septic emboli led to diplopia due to embolization to the inferior ophthalmic artery. Although septic emboli are a known risk, their effects can be unpredictable based on their size and location. The patient's diplopia underscores the need for vigilance in identifying septic emboli in new neurological or ophthalmological symptoms and in high-risk patients. Effective management requires a multidisciplinary team and emphasizes early, aggressive treatment of infective endocarditis, including possible surgical intervention. This case illustrates the importance of comprehensive evaluation and timely intervention to prevent severe complications.
Conclusion: Early identification of septic emboli in high-risk patients, such as those with intravenous drug use, is crucial to prevent irreversible organ damage. Clinicians should maintain a high index of suspicion to ensure timely diagnosis and management.

Nahush Bansal, MD

Efficacy of colchicine in improving outcomes in coronary artery disease: A systematic review and meta-analysis

Nahush Bansal, MD, Eunice Kwak, MD, Yusuf Hallak, MD

Background: Inflammation plays a pivotal role in coronary artery disease (CAD), and colchicine has been extensively studied in this context.
Objectives: Colchicine, a potent anti-inflammatory drug, inhibits microtubule growth. This study analyzes its impact and efficacy on outcomes in CAD patients.
Methods**:** We conducted a systematic review and meta-analysis comparing colchicine to standard therapy in CAD. A comprehensive search was performed in PubMed/MEDLINE, Embase, and Cochrane Central Register of Controlled Trials from inception through August 8, 2024. Excluded were animal studies, case reports, reviews, editorials, and letters. The primary outcome was Major Adverse Cardiovascular Events (MACE), defined as a composite of cardiovascular death, acute myocardial infarction (MI), ischemic stroke, and ischemia-driven revascularization. Secondary outcomes included individual components of MACE, acute coronary syndrome (ACS), and all-cause mortality. Risk ratios (RR) and confidence intervals (CI) were

calculated using a random-effects model, with $p < 0.05$ considered statistically significant. Heterogeneity was assessed using the Higgins I^2 index.
Results: Five randomized controlled trials (RCTs) involving 11,843 patients were included. MACE incidence was significantly lower with colchicine versus standard therapy (4.94% vs. 7.32%, RR 0.59, 95% CI 0.43–0.79, $p = 0.0004$, $I^2 = 67\%$). Stroke (0.4% vs. 0.89%, RR 0.46, 95% CI 0.27–0.77, $p = 0.003$, $I^2 = 4\%$) and ACS (1.2% vs. 4.09%, RR 0.30, 95% CI 0.20–0.45, $p < 0.00001$, $I^2 = 27\%$) rates were also lower in the colchicine group. However, no significant differences were observed in MI (3.02% vs. 3.95%, RR 0.72, 95% CI 0.51–1.02, $p = 0.06$, $I^2 = 42\%$), cardiovascular death (0.83% vs. 0.92%, RR 0.90, 95% CI 0.60–1.34, $p = 0.60$, $I^2 = 0\%$), and all-cause mortality (2.26% vs. 1.89%, RR 1.22, 95% CI 0.82–1.82, $p = 0.32$, $I^2 = 35\%$) between groups.
Conclusion: Colchicine, when added to standard therapy, significantly reduces the risk of major cardiovascular events, ACS, and stroke in CAD patients. It did not significantly affect MI, cardiovascular death, or all-cause mortality. Colchicine shows promise as an adjunct therapy in CAD, but further RCTs with larger samples are needed to confirm these findings.

Bella Z. Khatib-Shahidi BS

Oxylipins predict chronic kidney disease severity in heart failure with preserved ejection fraction

Bella Z.Khatib-Shahidi BS, Vaishnavi Aradhyula BS, Anas Fares MD, Prabhatchandra Dube PhD, Steven T. Haller PhD, David J. Kennedy PhD, Rajesh Gupta MD, Samer Khouri MD, MBA

Background: Heart failure with preserved ejection fraction (HFpEF) and chronic kidney disease (CKD) are comorbid conditions that often present as cardiorenal syndrome, which increases morbidity and mortality. The pathogenesis of cardiorenal syndrome is less understood, although an inflammatory paradigm has been proposed. Oxidized lipids, or oxylipins, are critical mediators of inflammation in cardiovascular and renal diseases. The role of oxylipins in predicting CKD severity in the setting of HFpEF is unknown.
Objective: We sought to analyze the role of oxylipins in predicting CKD severity in HFpEF patients.
Methods: Arterial and venous blood samples were collected during right heart catheterization from 87 HFpEF patients. We categorized patients by CKD stages 1-3, or glomerular filtration rate (GFR) greater than 30 (non-severe, n=78) and stages 4,5, or GFR less than 30 (severe, n=9). Oxylipins were quantified using mass spectrometry. Analysis was conducted via student's unpaired T-test and chi-squared analysis.
Results: Patients with severe CKD demonstrated higher venous anti-inflammatory 13,14-dihydro-15-keto prostaglandin E1 (13,14dh-15k-PGE1) (p=0.0023), 19(R)-hydroxy prostaglandin E1 (19(R)-hydroxy PGE1) (p=0.0022), 15-deoxy-Delta-12,14 prostaglandin J3 (15d-D12,14-PGJ3) (p=0.0027), pro-inflammatory tetranor 12-hydroxyeicosatetraenoic acid (tetranor 12-HETE) (p=0.0353), 9,10-dihydroxy-12Z-octadecenoic acid (9,10-DiHOME) (p=0.0071), and pro-resolutory 7(s)-Maresin1 (p=0.0448) and arterial anti-inflammatory prostaglandin E2 (PGE2) (p=0.0117).
Conclusion: This study demonstrates significant differences in venous and arterial oxylipins between severe and non-severe CKD. We identified six venous oxylipins that are more strongly associated with CKD stages 4,5 compared to stages 1-3, indicating their potential as predictors of CKD severity. These findings suggest that these oxylipins could be valuable targets for investigating the role of lipids in CKD progression, particularly in the setting of HFpEF.

Alex J. Kloster MD

Beta Blockers and outcomes in HFpEF

Alex J. Kloster MD, Alborz Sherafati MD, Vaishnavi Aradhyula, Anas Fares MD, Prabhatchandra Dube, Sareeta Manandhar, Bella Khatib-Shahidi, Catalin Dragomirescu, Pamela Brewster BS, Samer J. Khouri MD, David J. Kennedy PhD, Rajesh Gupta MD

Introduction: Beta blockers are some of the most commonly prescribed medications in patients with heart failure (HF), however, their role in the management of heart failure with preserved ejection fraction (HFpEF) remains uncertain.
Objective: To assess the association of beta blocker therapy with outcomes in participants with HFpEF, specifically death and HF hospitalizations.
Methods: Participants with known HFpEF with and without pulmonary hypertension were enrolled in a prospective cohort study from March 2012 and followed through the next 10 years. At the time of enrollment, beta blocker use was ascertained. The primary endpoint was a composite of death or HF hospitalization. Multivariable logistic regression was used to assess the association of beta blocker use with HF hospitalization, death and CAD events, adjusted for age, sex, race, coronary artery disease, and atrial fibrillation.
Results: Among 90 participants in the study (68.8% female; mean [SD] age, 68.44 [10.6]), 60 (66.6%) participants reported beta blocker use. 51 individuals experienced a HF hospitalization or death occurrence. Use of beta blockers was associated with higher odds of a composite of HF hospitalizations or death (Odds ratio 8.04 [95% CI, 2.57-29.34]; p=0.006) and HF hospitalizations (Odds ratio 3.54[95% CI, 1.14-12.72]; p=0.03). Beta blocker use was not significantly associated with death (Odds ratio 3.11[95% CI, 0.93-11.48, p=0.07).
Conclusions: In the cohort of patients with HFpEF, beta blocker use was associated with increased odds of adverse outcomes.

Alex J. Kloster MD

Coronary calcification and HFpEF

Alex J. Kloster MD, Alborz Sherafati MD, Vaishnavi Aradhyula, Anas Fares MD, Prabhatchandra Dube, Sareeta Manandhar, Bella Khatib-Shahidi, Catalin Dragomirescu, Pamela Brewster BS, Samer J. Khouri MD, David J. Kennedy PhD, Rajesh Gupta MD

Introduction: Coronary artery calcifications (CAC) is known to be a significant risk factor myocardial infarction (MI) and heart failure (HF) events. The association of CAC with outcomes in patients with HF with preserved ejection fraction (HFpEF) is not well established.
Objective: To assess for the association between CAC and outcomes in patients with newly diagnosed HFpEF.
Methods: Participants with newly diagnosed HFpEF were enrolled in a prospective cohort study from March 2012 through September 2015. Coronary artery calcifications were assessed on patients with available computed tomography (CT) chest imaging. The degree of CAC was subjectively scored as non-severe (<50%) or severe (>50%). Primary endpoint was the composite of death or HF. A multivariable logistic regression was used to assess the association of severe CAC with primary outcomes, after adjustment for age, sex, race, and atherosclerotic disease risk factors.
Results: Among the 71 patients with CAC scoring, 44 were female (mean age [SD] 68.17 [10.12]). 26 patients had severe CAC. Patients with severe CAC were older (72.1 vs 65.8, p= 0.006), but there were no significant differences in the prevalence of hypertension, diabetes, hyperlipidemia, and smoking status between the two groups. 40 participants experienced either death or a HF hospitalization. Severe CAC was associated with an increased odds of the composite endpoint of death or HF hospitalization (Odds ratio 6.09[95% CI 1.19-40.67]; p=0.03) as compared to participants with non-severe CAC. Severe CAC was not associated with a significantly increased risk for coronary artery events (Odds ratio 2.09 [95% CI 0.55-8.36]; p=0.28).
Conclusions: In patients with newly diagnosed HFpEF, those with severe CAC were at increased odds of death or HF hospitalization. The degree of CAC should be taken into consideration as a variable for risk stratification in patients with HFpEF.

Mario Markho

Identification of novel therapeutic candidates for primary congenital glaucoma targeting CYP1B1 mutations

Mario Markho, Hunter Eby, John Vergis, Jonathan Kopacz, Youngmin Yu, Michael Hershey, Kayla Cartwright, Morgan Markho, Chase Arnold, Connor Knight, Robert McCullumsmith MD PhD

Background: Primary congenital glaucoma (PCG) presents in infancy with enlargement of the corneal and scleral diameters, potentially leading to endothelial tears, corneal clouding, and irreversible vision loss if untreated (1). The CYP1B1 gene is crucial in trabecular meshwork development, and mutations impair aqueous outflow, elevating intraocular pressure and causing optic nerve damage, making it a major genetic cause of PCG (2).
Objective: This in silico study aims to identify novel perturbagens that reverse the gene expression changes from CYP1B1 loss to mitigate PCG complications.
Methods: The Kaleidoscope data exploration tool identified knockdown (KD) iLINCS signatures for CYP1B1. KD signatures were processed through Sig2Lead to find drug candidates with significantly positive or negative concordance. Candidates with the most negative concordance with CYP1B1 KD signatures were further evaluated as potential therapeutic targets for PCG.
Results: Kaleidoscope identified nine CYP1B1 KD signatures. Sig2Lead revealed four top candidates with a concordance score of -0.5 or less: benperidol (-0.517), ecopipam (-0.507), aclidinium bromide (-0.506), and benfluorex (-0.504). The current standard of treatment for PCG includes surgery as first-line, but also includes maintenance therapy with drugs such as timolol (-0.384), latanoprost (-0.31), bimatoprost (-0.469), acetazolamide (-0.330), and pilocarpine (-0.331) (3).
Conclusion: This study supports the efficacy of current PCG maintenance therapy, as each drug was significantly discordant with multiple CYP1B1 KD signatures. Dopamine antagonists benperidol (D2 antagonist) and ecopipam (D1 antagonist) were identified as the two most discordant perturbagens. While the mechanism of action between dopamine antagonism and intraocular pressure reduction is unclear, future studies may investigate this relationship. Aclidinium bromide is an anti-muscarinic typically used to treat COPD, and the relationship between this anti-cholinergic and intraocular pressure warrants further investigation. Finally, while benfluorex seems like a viable candidate, it is no longer widely available due to significant cardiovascular side effects (4).

Yusuf Nawras, BS

Ultrasound assessment of internal carotid stenosis pre- and post-endarterectomy of contralateral near-occluded carotid

Yusuf Nawras BS, Vaishnavi Aradhyula BS, Lauren R. Workman BS, Fedor Lurie MD

Introduction: Internal carotid artery (ICA) stenosis often presents bilaterally and is a major cause of stroke. Carotid duplex ultrasound is used for stenosis estimation via peak systolic velocity (PSV), end diastolic velocity (EDV), and ICA/common carotid artery (CCA) ratio (1,2,3). Carotid endarterectomy (CEA) is a common surgery for ICA stenosis and carries a high risk of stroke and mortality (4,5,6).
Objectives: We hypothesize that estimating velocities of the unoperated ICA pre- and post CEA of the contralateral near-occluded ICA, can lead to the proper development of a new criterion of diagnosis that would provide more accurate estimates of the presence of bilateral ICA stenosis.
Methods: A retrospective study was conducted on 239 patients, >18 years old, who underwent routine carotid duplex ultrasound during 2 years at a single institution. Qualified patients had bilateral carotid stenosis with ICA near occlusive disease on one side and more than 70% stenosis on the other side underwent unilateral CEA on the near occluded side.
Results: Post-CEA of near occluded ICA, the PSV, EDV, and ICA/CCA ratio of contralateral unoperated ICA significantly decreased (PSV pre-CEA=145±80 vs. post-CEA=128±67, $p<0.001$; EDV pre-CEA=42±28 vs. post-CEA=36±230, $p<0.001$; ICA/CCA pre-CEA 1.85±1.2 vs. 1.75±1.2, $p=0.032$). If we classify unoperated ICA stenosis as <50%, there was an 81.6% increase in cases pre- to post-CEA. If we classify stenosis as 50-69%, pre- to post-CEA cases decreased by 72.2%. If we classify stenosis as >70%, pre- to post-CEA cases decreased by 26.7%. Finally, classifying stenosis as 80-99%, pre- to post-CEA cases decreased by 100%.
Conclusions: The contralateral PSV, EDV, and ICA/CCA ratio are elevated in the presence of innate near occlusion, artificially elevating stenosis (Fig. 1). This study provides novel insight into revision of duplex ultrasound criteria for accurate estimation of unoperated ICA stenosis to avoid unnecessary high-risk surgery.

Manthan Patel

A case report of Kratom inducing atrial fibrillation

Manthan Patel, Nahush Bansal, Sunilkumar Rao

Introduction: Kratom or Mitragyna speciosa is tropical tree found in Southeast Asia. In recent years Kratom has gain popularity in United States, upwards of 10 to 16 million people have used it for its analgesic properties without the respiratory depression commonly associated with opioids. However, recent reports have raised concerns about the adverse effects of Kratom. There have been emerging links between Kratom use and multiple organ failure and cardiovascular diseases. This report aims to explore the specific case of Kratom use and atrial fibrillation.
Case presentation: A 66-year-old women with history of hypothyroidism, anxiety, and substance abuse presents to the hospital with chief of complain of worsening, intermitted aphasia for the last couple of days. Patient endorses recent use of Kratom for her chronic pain. She has an extensive history of Xanax and Opioid abuse. Upon examination in the ED, the patient was found to be tachycardic, with heart rate of 169 beats per minute. Electrolytes and other laboratories were within normal limits. EKG showed atrial fibrillation with RVR. Patient was treated with Lopressor and anticoagulation. CT of the head was negative for any bleeding or hematoma. Patient reverted to sinus rhythm spontaneously overnight.
Discussion: The drug's active alkaloids, such as 7-hydroxymitragynine and mitragynine, serve as the active ingredients Kratom that produces the analgesics effects by binding to the u-receptors. Recent studies have demonstrated opioid receptor mediated analgesic effect in mouse model studies. Some of the studies have shown correlation between Kratom use and prolonged QTc interval leading to ventricular arrhythmia and cardiopulmonary arrest. The underlying mechanism by which kratom induces theses cardiovascular effect is unknown. In this case, patient had a history of polysubstance abuse disorder with generalized anxiety disordered and hypothyroidism controlled with medication. This underlines the potential interaction between Kratom and cardiovascular disorder.

Qutaiba Qafisheh MD

Exploring the relationship between vitamin D and cardiovascular health: An American NHANES analysis

Qutaiba Qafisheh MD, Bisher Sawaf MD, Roaa Aljunaidi MD, Nezam Altorok MD

Background: Vitamin D plays a pivotal role in maintaining overall health and affects several physiological processes. We aim to evaluate the relationship between 25-hydroxy vitamin D levels and cardiovascular risk factors.
Methods: A retrospective study used data from the National Health and NHANES conducted between 2001 and 2018. We analyzed a dataset of 43,355 individuals, excluding those under 20 years. Regression and difference tests examined the relationship between vitamin D level and cardiovascular risk factors.
Results: Females showed higher vitamin D levels (63.63 ± 29.17) than males (61.46 ± 24.07) ($p = 0.002$). Patients with borderline diabetes exhibited lower levels of vitamin D (65.57 ± 26.42) ($p = 0.002$). BMI equal to or greater than 30 was associated with decreased vitamin D levels (57.82 ± 25.49) ($p = 0.000$), while BMI less than 18.5 was associated with higher levels (67.15 ± 27.91) ($p = 0.000$). Patients with high blood pressure (systolic ≥ 140/ diastolic ≥ 90), high fasting blood glucose (>126), high body mass index (>30), high triglyceride (>150), and high cholesterol (>150) had lower odds of having high-level 25-hydroxy vitamin D (>70.60) than the other reference subgroups (AOR=0.68, 95%CI:0.63-0.74, AOR:0.62, 95%CI:0.57-0.68, AOR:0.62, 95%CI:0.51-0.76, AOR:0.83, 95%CI:0.78-0.88, AOR:0.89, 95%CI:0.83-0.96, respectively)(P-value<0.05).
Conclusion: Our research confirmed a significant negative correlation between 25-hydroxy vitamin D levels and blood pressure, fasting blood glucose, body mass index, triglycerides, and cholesterol. Large multicenter clinical trials are needed to validate our findings

Vincent M Smith MS

Sex-specific differences in oxylipin profiles in heart failure with preserved ejection fraction

Vincent M Smith MS, Vaishnavi Aradhyula, Bella Z Khatib-Shahidi, Pamela Brewster, Sareeta Manandhar PhD, Alborz Sherafati MD, Alex J Kloster MD, Prabhatchandra R Dube PhD, Anas Fares MD, Rajesh Gupta MD, Samer J Khouri MD, David J Kennedy PhD

Introduction: Heart Failure with preserved ejection fraction (HFpEF) is more common in postmenopausal women, although they have better survival rates compared to men. Elevated levels of polyunsaturated fatty acid (PUFA) oxylipins are associated with increased cardiovascular risk in this population. Oxylipins are bioactive molecules that play a key role in immune function and signaling. Estrogen, which declines post-menopause, is linked to the production of cardioprotective oxylipins like epoxyeicosatrienoic acids (EETs). In other settings, namely post-pubertal/pre-menopausal females, oxylipins have been found in higher concentrations. This study aimed to investigate sex-based differences in oxylipin concentrations among HFpEF patients, which may improve prediction and management of the disease.
Objective: To assess sex-specific variations in the levels of pro-inflammatory, pro-resolutory, and anti-inflammatory oxylipins in HFpEF patients.
Methods: Ninety HFpEF patients (62 females, 28 males) were enrolled over 8 months at a single institution. Venous oxylipin samples were obtained during right heart catheterization and analyzed using an unpaired T-test to compare lipid concentrations between the sexes.
Results: Female patients had a higher average body mass index (BMI) than males (37.1 vs. 31.4, p=0.0089), while no significant differences in age were observed. Analysis of the venous oxylipin profile revealed significantly higher levels of pro-inflammatory 12,13-DiHOME (0.933 vs. 0.610, p=0.0319) and 12(13)-EpOME (6.977 vs. 0.220, p=0.0252) in females compared to males.
Conclusion: The findings demonstrate notable sex-specific differences in risk factors and lipid profiles among HFpEF patients. Specifically, postmenopausal women exhibited elevated levels of two key pro-inflammatory oxylipins (12,13-DiHOME and 12(13)-EpOME). These results suggest that these lipids may contribute to the higher incidence of HFpEF in women, despite their improved survival rates. The study underscores the importance of sex-specific strategies for the prevention and management of HFpEF, given the distinct lipid profiles and risk factors between men and women.

Feehaan H. Sultan MD

Impact of HIV infection on outcomes in patients admitted with complete heart block: A Nationwide study

Feehaan H. Sultan MD, Nahush R. Bansal MD, Eunice Kwak MD

Background: Immune dysregulation and social stigma associated with HIV infection have been linked to poor outcomes in hospitalized patients. This study aims to compare in-hospital outcomes in patients admitted with complete heart block (CHB) with and without HIV.
Methods: The National Inpatient Sample (NIS) 2020 Database was analyzed for adult patients with complete heart block as the primary discharge diagnosis and HIV infection as a secondary discharge diagnosis, identified using ICD-10 codes. The primary outcome measured was inpatient mortality, with secondary outcomes including length of stay (LOS), hospitalization charges, cardiogenic shock, cardiac arrest, acute respiratory failure, and pacemaker intervention rates and timing. Multivariate logistic and linear regression analyses were employed to adjust for confounders. Statistical analyses were conducted using STATA software.
Results: Out of 37,480 patients admitted with complete heart block, 112 (0.30%) were identified as having HIV. The adjusted odds ratio (aOR) for inpatient mortality in CHB patients with HIV, compared to those without HIV, was 1.72 (95% CI 0.19-4.99, p=0.621). HIV status did not significantly influence the rates (aOR 1.04, 95% CI 0.32-3.36, p=0.94) or timing (p=0.28) of permanent pacemaker intervention.
Conclusions: HIV infection did not significantly impact mortality, health, or procedural outcomes in patients admitted with complete heart block. These findings support the notion of equitable care in complete heart block patients, regardless of HIV status.

Kevin J. Wunderly MD
Coronary involvement in MoyaMoya disease
Kevin J. Wunderly MD, Shuhao Qiu MD PhD

Introduction: Moyamoya disease is a rare, chronic vascular condition characterized by progressive narrowing of the internal carotid arteries and the circle of Willis (1). While most research focuses on cerebral vessel involvement, less is known about its potential effects on coronary arteries. A few case reports have documented coronary artery stenosis and vasospasm in Moyamoya disease, indicating this is a rare presentation (2,3).
Case: A 26-year-old woman with a history of Moyamoya disease complicated by recurrent strokes presented with chest pain and syncope. She reported experiencing chest pain for several months, typically relieved by nitroglycerin. However, following her most recent dose, she experienced syncope. The chest pain was primarily exertional but sometimes occurred at rest. An echocardiogram performed at an outside facility one month ago showed no abnormalities. A Coronary CTA also performed at that time demonstrated mild stenosis in the proximal RCA and the LAD. During hospitalization, nitroglycerin was discontinued, resulting in no further syncopal events.
Conclusion: The relationship between Moyamoya disease and coronary artery involvement remains under-researched. In this case, although coronary CTA angiography showed no significant stenosis, the possibility of vasospasm or subtle ischemic changes could not be excluded. A full ischemic workup, including echocardiography and left heart catheterization, is crucial for Moyamoya patients presenting with chest pain. Although involvement of both carotid and coronary arteries is rare, ischemic heart disease should be considered in these patients, even at a young age. Additionally, nitroglycerin's role in managing chest pain in Moyamoya patients requires further study, especially given its potential to exacerbate syncope.

DERMATOLOGY

Shivani S. Ambardekar BS
Management of Kyrle's disease in a patient with diabetes mellitus and chronic kidney disease
Shivani S. Ambardekar BS, Nancy A. Parquet MD

Introduction: Kyrle's disease (KD) is a rare skin disorder characterized by elimination of abnormal keratin through the epidermis. It is a subtype of the acquired perforating dermatosis (APD) and occurs more commonly in patients with diabetes mellitus and renal disease. Clinically, KD presents as multiple discrete eruptive papules with central keratin plugging accompanied by intense pruritus.
Case Presentation: A 45-year-old female with type II diabetes mellitus and stage V chronic kidney disease on hemodialysis presented to the outpatient dermatology clinic for management of known KD and hidradenitis suppurativa (HS). She complained of pruritic lesions on the distal lower extremities and extensor elbow region. Previous treatment with ammonium lactate 12% cream, a first-line keratolytic treatment for KD, had failed to provide adequate relief. Narrowband ultraviolet B (NBUVB) phototherapy was initiated 2-3 times weekly, starting at 330 millijoules (mJ) and increasing by 15% each session for a maximum dose of 4000 mJ. The patient reported decreased pruritus after the first phototherapy session, with complete resolution of the pruritus following the third session. She then completed 25 sessions of phototherapy over two months, resulting in sustained improvement of the skin lesions. She continues to receive phototherapy at the time of this report with no adverse effects.
Conclusion: KD is a rare disorder that typically arises in adults with underlying systemic disease and significantly impacts quality of life. While management of the underlying systemic condition leads to improvement in KD, effective treatment of the skin condition remains challenging and lacks evaluation in randomized trials. In addition to topical and systemic therapies, phototherapy should be considered as a valuable approach in the management of KD.

Andrew Fickert

The Efficacy and Safety of red light therapy

Andrew Fickert, Sahil Kapur, Mario Markho, Mark Houdi, Craig G. Burkhart, MD

Background: Red Light Therapy (RLT) is a popular non-invasive treatment for skin rejuvenation, targeting wrinkles and loss of elasticity by stimulating collagen production and enhancing skin texture. Studies have shown significant improvements in skin appearance, yet comprehensive research on RLT's long-term safety and efficacy is limited. (1)
Objective: Explore the research of RLT and its safety and efficacy of treating age related stress lines and wrinkles.
Methods: This project conducted a review of articles in the fields of dermatology and anti-aging studies using PubMed as the database. Search criteria included: "Red Light therapy" WITH "Skin Treatment" from material published in 2020 and onward. Using this search logic, 20 articles were amassed for this literature review.
Results: Recent studies on Red Light Therapy (RLT) have demonstrated promising results in skin rejuvenation and anti-aging. Some studies show significant reductions in visible signs of aging, such as wrinkles and fine lines, following RLT treatment, with patients experiencing noticeable skin improvements. (1) Similarly, another such study found a 30% reduction in periocular wrinkle volume in their randomized controlled trial, indicating the effectiveness of RLT in targeted facial areas. (2) Evaluation of the safety and efficacy of a home-use LED device, noting high user satisfaction and improvements in skin texture. (3) However, despite these positive outcomes, the limited number of recent studies emphasizes the need for further research to solidify RLT's long-term safety and efficacy, ensuring its continued viability as an anti-aging treatment.
Conclusion: Despite promising short-term results, the rapid commercialization of RLT products, driven by consumer demand, may outpace scientific validation. Recent studies highlight user satisfaction but stress the need for more rigorous long-term trials. (2,3) While RLT shows potential as an anti-aging therapy, providers should guide patients in making informed decisions, emphasizing the importance of evidence-based practice to ensure both efficacy and safety.

Benjamin W French

Microcystin-LR disrupts skin integrity: Mechanistic insights from in vitro and in vivo dermal exposure models

Benjamin W French, Caitlin M Murphy, Shereen G Yassine, Evan M Benson, Bivek Timalsina,
Nancy A Parquet MD, David J Kennedy PhD, Steven T Haller PhD

Background: Harmful algal blooms (HABs) are on the rise globally, including locally in Lake Erie. HABs produce cyanotoxins, with microcystin-LR (MC-LR) being one of most prevalent among over 300 congeners. Diseases such as atopic dermatitis (AD) can disrupt the skin barrier, potentially increasing susceptibility to MC-LR. Dermal contact represents one of the most common exposure routes to HAB cyanotoxins and dermatologic symptoms represent one of the most common complaints after exposure. Objectives: We sought to evaluate the impact of Microcystin-LR on the skin barrier using in vivo and in vitro models.
Methods: In vitro studies used primary adult keratinocytes or dermal fibroblasts exposed to 1, 0.1, or 0.01 µM MC-LR or saline for 6, 12, or 24 hours. RT-PCR was used to examine expression of structural proteins loricrin (LOR), filaggrin (FLG), involucrin (IVL), collagen1a1 (COL1a1) and 3a1 (COL3a1). In vivo studies utilized SKH1 mice (hairless), dermally exposed to 10 µM MC-LR or vehicle for 6 hours/day, 5 days/week, for 3 consecutive weeks.
Results: In vitro: Keratinocytes had significantly elevated expression of IVL ($p=0.0308$), LOR ($p=0.0276$), and FLG ($p<0.0001$), and dermal fibroblasts showed significantly increased expression of COL1a1 ($p=0.0012$) and COL3a1 ($p=0.0230$) after exposure to 1 µM MC-LR for 24 hours. In vivo: SKH1 mice exposed to MC-LR demonstrated hyperplasia or thickening of total epidermis ($p<0.0001$) and stratum corneum ($p<0.0001$), vs. vehicle exposure. SKH1 skin exposed to MC-LR showed a decrease in FLG ($p=0.0034$) and LOR ($p<0.0001$) expression. Histological changes in MC-LR exposed skin also showed signs consistent with chronic dermatitis

including variable inflammatory infiltrate (both epidermal and dermal), intercellular edema between epidermal cells (spongiosis), and disruption of the stratum corneum (hyperkeratosis).
Conclusion: Microcystin-LR (MC-LR) significantly disrupts skin barrier function, as demonstrated by both in vivo and in vitro models. Exposure to MC-LR led to increased expression of skin barrier proteins (in vitro) and structural thickening in the skin (in vivo). Chronic skin exposure induced histologic changes consistent with dermatitis, including hyperplasia, inflammatory infiltration, and spongiosis. These results suggest that MC-LR may exacerbate skin barrier dysfunction, particularly in individuals with pre-existing skin conditions such as atopic dermatitis, highlighting the potential health risks associated with dermal contact in regions affected by harmful algal blooms.

Caitlin M Murphy

In vitro exposure to microcystin-LR increases inflammatory markers and decreases cell growth

Caitlin M Murphy, Benjamin W French, Shereen G Yassine, Evan M Benson, Bivek Timalsina, Nancy A Parquet MD, David J Kennedy PhD, Steven T Haller PhD

Background: Cyanobacteria Harmful Algal Blooms (cyanoHABs) produce several families of toxins, including microcystins. Microcystin-LR is one of the most prevalent and potent congeners and operates as a potent protein phosphatase 2A inhibitor. Most research has investigated the oral route of exposure, with some attention now shifting to inhalation. There is very limited research on dermal contact, despite the skin being one of the most common means of contact and dermatological complications being a common complaint of patients coded for HAB toxin exposure.
Objectives: Our study evaluates the inflammatory effects of microcystin-LR on the skin barrier using in-vitro models.
Methods: Studies were conducted using primary adult keratinocytes or dermal fibroblasts. Adult keratinocytes were exposed to 10 or 1 µM MC-LR or saline for 6, 12, or 24 hours. Dermal fibroblasts were exposed to 10, 1, or 0.1 µM MC-LR or saline for 2 or 24 hours. Cells were then subject to RT-PCR, examining expression of pro-inflammatory markers IL-IP, TNF-a, TGF-P, IL-4 and IL-13. Keratinocytes were also assessed for cell growth post-exposure via confluency. Results: Keratinocytes had elevated expression ofTNF- a ($p=0.072$) at 1 µM after 24 hours but decreased expression ofTNF- a ($p<0.01$) at 10 µM after 24 hours. Additionally, keratinocytes showed elevated IL-1 P ($p<0.001$). Keratinocyte confluency was significantly decreased after 24 hours of exposure ($p<0.0001$) and did not recover by 24 hours ($p=0.0018$). Dermal fibroblasts showed decreased expression of IL-13 ($p<0.0$ 1) after 2-hour exposure but demonstrated increased IL-13 expression ($p<0.05$) after 24-hour exposure.
Conclusion: Our findings indicate that microcystin-LR induces inflammatory responses in skin cells, with increased expression of pro-inflammatory markers like TNF-a and IL-IP in keratinocytes, as well as disrupted cell growth. The dermal fibroblasts showed variable responses in IL-13 expression depending on exposure duration. These results underscore the potential for microcystin-LR to disrupt the skin barrier and contribute to dermatological inflammation, highlighting the need for further research on dermal exposure to this toxin, particularly in communities affected by HABs.

Kolby Quillin BA

Management of wrestling team with cutaneous MRSA infection: A case series

Kolby Quillin BA, Brian Buck ME, Craig Burkhart MD, MPH

In the Winter months of 2023, four wrestlers from the same Ohio high school team were referred to the dermatologist by their coach because of infection. Through culture and sensitivity testing and a proper history, it was concluded that their infections were all from the same strain of methicillin resistant Staphylococcus aureus (MRSA). Because of this, all the wrestlers were treated with the same oral antibiotics of Bactrim and doxycycline successfully. The dermatologist soon after made an announcement to the state's dermatological association and high school athletic association, describing the infections so that dermatologists, coaches, and

referees could monitor for other cases in the community. This case series outlines the prevalence of MRSA in the wrestling community and provides recommendations for the management of wrestlers by dermatologists. Additionally, the importance of the dermatologist-coach-wrestler relationship is highlighted as an important method to limit the spread of wrestling acquired infections.

Yongqing Wang

Potential role for CD40L/CD40 interactions in scleroderma vasculopathy

Yongqing Wang, Bashar Kahaleh

Background: Increased expression of CD40 in Scleroderma Microvascular Endothelial Cells (SSc-MVECs) was noted in a gene expression array and increased concentrations of soluble CD40 ligand (sCD40L) in SSc are reported.
Objectives: In this study, we investigated the effect of CD40 ligation on endothelial apoptosis, activation, and function.
Methods: MVECs were isolated from the skin of the involved SSc and matched healthy subjects. MVECs apoptosis was assessed by cell viability and caspases3/7 activity. MVECs gene expression was determined by RT- PCR and results were confirmed by western blot analysis. Endothelial permeability was measured using the FITC-Dextran permeability assay.
Results: A significant increase in CD40 expression was noted in SSc-MVECs (2.8 folds ± 0.3 in SSc vs. control MVECs). The addition of CD40 ligand to MVECs resulted in the following observations:
1. Reduction in NOS3, and prostacyclin synthase (PTGS1) expression, and increase in endothelin 1 expression.
2. Increased EC permeability.
3. Enhanced MVECs' apoptosis. Increased caspase activity, expression levels of proapoptotic genes, and reduced expression of antiapoptotic genes were noted.
4. Increase in expression of the chemokines including CXCL1,3, 4, and 5, IL1B, IL6, IL8, HGF, SELE, and ICAM1. Downregulation of FGIF (VEGF-D), EGF, IGF1, and FGF were noted.
Conclusion: The study demonstrates increased expression of CD40 in SSc MVECs. CD40 ligation led to reduced expression of vasodilatory genes and increased expression of vasoconstrictive genes. Moreover, the addition of CD40L increased endothelial permeability and the acquisition of an activated/ dysfunctional phenotype in association with increased MVEC apoptosis. In all instances, SSc MVECs were more susceptible to CD40 signaling effects than control MVECs. The results suggest that the blockade of CD40/CD40 ligand interaction could be an effective therapeutic strategy in SSc.

GASTROENTEROLOGY

Hasan Al-Obaidi MD

Comparative efficacy of endoscopic ultrasound (EUS)-Guided coiling vs. cyanoacrylate injection (CYA) for gastric varices an updated systematic review and meta-analysis

Hasan Al-Obaidi MD, Nooraldin Merza MD, Yusuf Nawras MS, Rockwell Kristen Elizabeth MD, Emily Moore MD, Abdallah Kobeissy MD

Gastric varices (GV) are enlarged veins in the esophagus and stomach caused by portal hypertension and are a major cause of upper gastrointestinal bleeding. GV is common among patients with liver cirrhosis, affecting approximately 20% of cirrhotic patients. The incidence of bleeding has been reported in approximately 25% of GV patients. The re-bleeding rates have been recorded as high as 40%, with mortality rate estimates of up to 50%. Endoscopic ultrasound interventions are the superior choice for treating bleeding GV in emergencies. EUS-guided coil application is a promising but costly method for improving outcomes.
Methods: A systematic search was conducted in electronic databases (PubMed/Medline, Cochrane Library, and Google Scholar) from their inception to February 16, 2024. All statistical analyses were conducted in Review

Manager 5.4.1. Studies meeting inclusion criteria were selected. A random-effect model was used when heterogeneity was seen to pool the studies, and the result was reported in Odds ratio (OR) with their respective 95% confidence intervals (Cl). Qualitative analysis was also carried out for those factors that did not provide sufficient data to carry out quantitative analysis.
Results: Six observational studies were used to conduct our study. Analysis revealed a significantly higher risk of subsequent bleeding episodes in the CYA injection group compared to the EUS-guided coiling group (OR= 0.28 (0.15, 0.53); p < 0.0001; 12 = 0%). Although an insignificant difference was observed rate of mortality between the two groups of patients (OR = 0.93 (0.21, 4.06); p = 0.92; 12 = 0%). The overall odds of cumulative adverse effects were significantly higher in the CYA injection group compared to the coiling group (OR= 0.43 (0.24, 0.75); p = 0.003; 12 = 11%). Other factors like cost, length of stay, etc were also discussed using a qualitative approach.
Conclusion: Our study showed that wholistically EUS-guided coil provided better results for the patients and acted as a more superior intervention as compared to CYA injections in treating GV, even though coiling cost more than CYA injections.

Hasan Al-Obaidi MD

Evaluating mortality rate patterns related to gastric varices in the United States: An analysis of death certificates 2009-2021

Hasan Al-Obaidi MD, Nooraldin Merza MD, Yusuf Nawras MD, Michaelangelo Raphael Zullo MD, Abdallah Kobeissy MD

Introduction: Gastric varices (GV), which are dilated submucosal collateral veins arising from portal hypertension, are a significant cause of upper gastrointestinal bleeding. Affecting about 20% of patients with liver cirrhosis, GV poses a severe risk due to its high mortality rate, surpassing that of esophageal variceal bleeding. This study delves into the mortality rates associated with gastric varices in the United States over the past twenty years. By analyzing extensive data from American death certificates, the research sheds light on the prevalence of the disease, notable demographic differences, and evolving trends over time.
Methods: This study leveraged the CDC WONDER database to analyze mortality rate trends from 1999 to 2021, with a particular focus on deaths caused by gastric varices. The abstract examined all recorded fatalities linked to gastric varices in the United States during this timeframe. R software version 4.2.2 was used for data analysis and visualization, utilizing the ggplot2 package to generate all graphical representations.
Results: From 1999 to 2022, the mortality rate of gastric varices per 100,000 showed no significant change, with both the starting and ending mortality rate at 0.010. When categorized by state, mortality rates were slightly higher in states with major cities, and states with higher populations had a greater number of deaths. Stratification by gender revealed a small but consistent increase in gastric variceal mortality among males compared to females throughout the study period. Data for individuals under 55 years old was sparse and inconsistent across the analyzed time period due to limited data points. The age range of 65-74 showed a slightly higher mortality rate in 2018 and 2022 compared to the age range of 55-64.
Discussion: Our research reveals that over the past 23 years, higher mortality rates from gastric varices were consistently observed in males compared to females and in patients over 65 years old compared to younger patients. Due to the low number of recorded deaths secondary to gastric varices, no conclusion could be made when stratifying mortality by race. Significantly, there has been no improvement in mortality rates since 1999, despite considerable advancements in medical treatments. This study highlights areas for potential advancements in research, policy implementation, and focused interventions to reduce mortality secondary to gastric varices.

Hasan Al-Obaidi MD

Factors predicting ineffective biliary drainage among patients with hepatocellular carcinoma; A systematic review and meta-analysis

Hasan Al-Obaidi MD, Nooraldin Merza MD, Yusuf Nawras MS, Reem Z Sharaiha MD

Introduction: Obstructive jaundice associated with hepatocellular carcinoma (HCC) is uncommon. Endoscopic biliary drainage (EBO) and percutaneous transhepatic biliary drainage (PTBD) are effective interventions for patients with obstructive jaundice. However, these techniques carry potential complications and inconveniences associated with long-term drainage. This systematic review and meta-analysis were conducted to retrieve the patients-related, tumor-related, and management-related factors of ineffective biliary drainage among patients with HCC and obstructive jaundice.
Methods: Reviewing the literature through five databases was performed on 20 March 2024. All clinical studies comparing the patients-related, tumor-related, obstruction-related, or procedure-related factors among patients with ineffective and effective biliary drainage and obstructive jaundice caused by HCC were included.
Results: This study included ten retrospective studies, encompassing 620 patients. Of them, 374 developed effective biliary drainage, and 246 had ineffective biliary drainage. The overall risk of ineffective biliary drainage was 37.7%, with a higher risk among patients treated with ERBD. A higher risk of ineffective drainage was revealed among male patients (1.15), patients with HCV infection (1.93), and patients with Child-Pugh class C (2.36). Patients with tumor extent >50% and patients with prolonged duration to procedures were associated with ineffective drainage. Patients with ineffective biliary drainage had a 2.25 times higher risk of mortality.
Conclusions: A considerable risk of ineffective biliary drainage was revealed among patients with HCC. Male patients, patients with HCV infection, and patients with advanced hepatic pathology and extensive infiltration were at higher risk of ineffective biliary drainage.

Hasan Al-Obaidi MD

Trends and disparities in autoimmune hepatitis-related mortality in the United States: A population-based study from 2003-2022

Hasan Al-Obaidi MD, Nooraldin Merza MD, Hussein Harb MD, Mustafa Al-Obaidi MD, Yusuf Nawras MS, Iya Agha MS, Abdallah Kobeissy MD

Introduction: Autoimmune hepatitis is a chronic, progressive liver inflammation with an unclear etiology. If left untreated, severe cases result in a mortality rate of 40% to 50% within six months to five years. This study focuses on the mortality rates tied to autoimmune hepatitis in the U.S. from 2003 to 2022. The abstract endeavors to provide critical insights into the prevalence of this disease, demographic disparities, and shifting patterns over time.
Methods: This study employed the CDC WONDER database to examine mortality rate trends from 2009 to 2021, with a particular focus on deaths attributed to autoimmune hepatitis. The analysis covered all recorded fatalities related to autoimmune hepatitis in the United States during this period. Data analysis and visualization were carried out using R version 4.2.2, with all graphical illustrations created using the ggplot2 package.
Results: From 2003 to 2022, the overall mortality rate per 100,000 people for autoimmune hepatitis increased from 0.117 to 0.138, with higher rates observed in the northwestern states, Oklahoma, and New Mexico. Between 2021 and 2022, New Mexico and Idaho consistently showed elevated mortality rates. Gender analysis revealed that females consistently had higher mortality rates than males throughout the study period. Stratification by race indicated that White individuals had higher mortality rates for most of the study period compared to African Americans, followed by Asian or Pacific Islanders and American Indians. Age-specific data showed the highest mortality rates in the 75-84 age group for almost the entire study period, with rates for the 65-74 age group and those older than 84 being similar until 2020, when rates for those over 84 increased. Individuals younger than 65 had lower mortality rates, which decreased progressively with younger age (Table 1).
Discussion: This study highlights an overall increase in mortality rates per 100,000 individuals for autoimmune hepatitis in the United States from 2003 to 2022. States with initially higher rates, such as those in the northwest, Oklahoma, and New Mexico, saw the most significant rises. Elderly individuals, particularly those aged 75-84, females, and White individuals exhibited the highest mortality rates. This research provides

valuable insights into the impact of autoimmune hepatitis on vulnerable populations, guiding resource allocation, policy formulation, and targeted actions to enhance healthcare outcomes.

Keith M. Burns MD

From abscess to adenocarcinoma: A case of perforated cecal adenocarcinoma

Keith M. Burns MD, Eun Seo Kwak MD, and Yaseen S. Y. Alastal MD

Introduction: Colonic perforations are rare and often secondary to iatrogenic, inflammatory, or infectious causes. Complications of perforations can include peritonitis, abscess formation, sepsis or death and require urgent medical attention. Perforation secondary to colon cancer is a rare entity but should be considered during diagnostic evaluation.
Case Description: A 77-year-old male with a history of partial colectomy secondary to prior complicated diverticulitis presented to his primary care physician with a 5-week history of progressive right lower quadrant abdominal pain. A CT Abdomen and pelvis with IV contrast demonstrated a right lower quadrant abscess measuring up to 10.9 cm involving the abdominal wall and cecum with adjacent enlarged mesenteric lymph nodes measuring up to 1.6 cm. The patient underwent ultrasound-guided percutaneous drainage of the abscess, with fluid cultures isolating polymicrobial gram negative bacteria. The patient had previously undergone a colonoscopy for colorectal cancer (CRC) screening 10 years prior which was notable for diverticulosis but otherwise was normal. Given suspicion for possible underlying malignancy, colonoscopy was completed demonstrating a 5 cm ulcerated and friable lesion in the cecum with biopsies confirming invasive adenocarcinoma. Subsequently, exploratory laparotomy with colectomy, ileostomy, and debridement of abdominal wall was completed with surgical pathology demonstrating localized metastasis to the abdominal wall. The patient had further complications including recurrent intrabdominal fluid collections, pneumonia, and decompensated heart failure and ultimately transitioned to inpatient hospice care.
Discussion: Colonic adenocarcinomas can present in numerous clinical contexts that range from mild, non-specific symptoms, to complications requiring urgent or emergent surgical intervention. Peri-colonic abscess may be secondary to other underlying conditions such as fistulizing Crohn's disease or complicated diverticulitis, however it is important to also consider underlying colorectal cancer as the primary cause.

Dharmindra Dulal

COVID-19 and gastroparesis: Exploring the post-viral increase in incidence of gastroparesis

Dharmindra Dulal, Deepanshu Singh, Sadik A. Khuder, DDS, MPH, PhD, Benjamin Hart, MD, PhD

Objectives: Gastroparesis, characterized by delayed gastric emptying due to weak or abnormal stomach contractions, leads to symptoms such as nausea, vomiting, bloating, early satiety, and abdominal pain. It is commonly linked to diabetes, gastrointestinal surgeries, GLP-1 agonists, and opioid use. While post-viral gastroparesis has been previously studied, the effect of COVID-19 on gastroparesis incidence remains unclear. This study aims to evaluate the relationship between COVID-19 and the incidence of gastroparesis.
Methods: Using the TriNetX database, we analyzed data from 89,435,828 patients (2016–2023) to determine the baseline incidence for gastroparesis. To specifically assess the impact of COVID-19, we created a secondary cohort of 60,885,976 patients from the same period by excluding individuals with common risk factors such as Type 1 or Type 2 diabetes mellitus, previous gastrointestinal surgeries, and medications affecting gastrointestinal motility (e.g., GLP-1 agonists or opioids). R programming was employed for time series analysis, and t-tests compared gastroparesis incidence rates pre- and post-COVID, with July 1, 2020, as the cutoff.
Results: In the baseline cohort, t-tests revealed a significant increase in both the incidence rate ($t = -6.96$, $p<0.001$) and incident cases ($t = -3.20$, $p<0.001$) of gastroparesis post-COVID-19. Similarly, in the secondary cohort excluding common risk factors, both incidence cases ($t = -4.68$, $p<0.001$) and incidence rate ($t = -7.29$, $p<0.001$) showed significant rises. Both cohorts confirm a clear increase in gastroparesis incidence after COVID-19.

Conclusion: Our study highlights a significant rise in the incidence of gastroparesis after the onset of COVID-19, even in patients without traditional risk factors. This suggests a potential association between COVID-19 and gastroparesis development. Further research is needed to understand the mechanisms of post-viral gastroparesis and its long-term impact on gastrointestinal health, particularly in relation to COVID-19, to inform future patient management strategies.

Sami Ghazaleh MD

Bilateral vs. unilateral endoscopic stenting for unresectable malignant hilar biliary obstruction - A systematic review and meta-analysis

Sami Ghazaleh MD, Megan Karrick DO, Zohaib Ahmed MD, Keith Burns MD, Wasef Sayeh MD, Nooraldin Merza MD, Yaseen Alastal MD

Background: Several malignancies can cause a hilar biliary obstruction, including cholangiocarcinoma, gallbladder cancer, hepatocellular carcinoma, and metastasis. Endoscopic biliary stenting plays an important role in the palliative management of unresectable hilar biliary obstruction. A few studies have compared the success rates and complications of bilateral and unilateral stents, but whether bilateral or unilateral stenting should be used remains unclear because of paucity of studies.
Patients and Methods: We conducted a systematic review and meta-analysis of studies that compared bilateral and unilateral stenting for unresectable malignant hilar biliary obstruction. We performed a comprehensive search in the databases of PubMed and Embase from inception through August 16, 2024. The random-effects model was used to calculate the odds ratios (OR) and confidence intervals (CI). A p value <0.05 was considered statistically significant. Heterogeneity was assessed using the Higgins I2 index.
Results: Ten studies involving 1529 patients were included. Technical success rate was significantly lower in bilateral stenting (OR 0.56, 95% CI 0.33 – 0.96, p = 0.04, I2 = 0%). Clinical success rate was significantly higher in bilateral stenting (OR 1.61, 95% CI 1.12 – 2.33, p = 0.01, I2 = 0%). Bilateral and unilateral stenting were similar in early complication rate (OR 1.12, 95% CI 0.58 – 2.19, p = 0.73, I2 = 67%), late complication rate (OR 0.98, 95% CI 0.65 – 1.48, p = 0.92, I2 = 0%) and stent malfunction rate (OR 0.74, 95% CI 0.49 – 1.11, p = 0.15, I2 = 47%).
Conclusion: Our meta-analysis demonstrated that bilateral stenting has a lower technical success rate and a higher clinical success rate than unilateral stenting for unresectable malignant hilar biliary obstruction. Early and late complication rates and stent malfunction rates were similar between bilateral and unilateral stenting. Further randomized controlled trials with large sample sizes are needed to confirm our findings.

Sami Ghazaleh MD

Endoscopic ultrasound-guided transmural gallbladder drainage (EUS-GBD) versus percutaneous transhepatic gallbladder drainage (PT-GBD) in high-risk patients with acute cholecystitis - A systematic review and meta-analysis

Sami Ghazaleh MD, Megan Karrick DO, Keith Burns MD, Zohaib Ahmed MD, Nooraldin Merza MD, Wasef Sayeh MD, Ali Nawras MD

Background: Cholecystectomy is the gold-standard treatment for patients with acute calculous cholecystitis. Gallbladder drainage or cholecystostomy is an option for high-risk surgical patients who are critically ill or fail to improve with antibiotics. Percutaneous transhepatic gallbladder drainage (PT-GBD) is generally preferred due to its ease and safety. Recent studies have investigated the role of endoscopic ultrasound-guided transmural gallbladder drainage (EUS-GBD) as an alternative treatment.
Patients and methods: We conducted a systematic review and meta-analysis of studies that compared EUS-GBD and PT-GBD in high-risk surgical patients with acute cholecystitis. We performed a comprehensive search in the databases of PubMed and Embase from inception through August 25, 2024. The random-effects model was used to calculate the risk ratios (RR) and confidence intervals (CI). A p value <0.05 was considered statistically significant. Heterogeneity was assessed using the Higgins I2 index.

Results: Eight studies were included in the meta-analysis. EUS-GBD and PT-GBD were similar in technical success (RR 0.98, 95% CI 0.95 – 1.00, p = 0.06, I2 = 0%) and clinical success (RR 0.99, 95% CI 0.94 – 1.05, p = 0.81, I2 = 42%). EUS-GBD was superior in adverse events (RR 0.50, 95% CI 0.37 – 0.69, p < 0.0001, I2 = 32%), reintervention rate (RR 0.16, 95% CI 0.04 – 0.71, p = 0.02, I2 = 89%) and unplanned readmission rate (RR 0.34, 95% CI 0.18 – 0.63, p = 0.0006, I2 = 67%). Mortality rate was similar between EUS-GBD and PT-GBD (RR 0.87, 95% CI 0.27 – 2.80, p = 0.82, I2 = 23%).
Conclusions: Our meta-analysis demonstrated that EUS-GBD was as effective as PT-GBD in high-risk patients with acute cholecystitis. Both procedures had comparable technical success, clinical success, and mortality. EUS-GBD was superior to PT-GBD in adverse events, need for reintervention, and unplanned readmissions. Further randomized controlled trials are needed to confirm our findings.

Jacob Itkin BS

Assessing GLP-1 RAs in diabetic gastroparesis: A literature review

Jacob Itkin BS, Sudheer Dhoop MD, Thomas C. Sodeman MD

Introduction: Diabetic gastroparesis (DG) is a complication of diabetes mellitus (DM) characterized by impaired motility of the upper gastrointestinal tract and delayed gastric emptying (DGE) without mechanical obstruction. DG may cause nausea, vomiting, abdominal pain, and early satiety. Glucagon-like peptide-1 receptor agonists (GLP-1 RAs) are widely used in type 2 DM management to improve glycemic control by stimulating insulin release and slowing gastric emptying. However, their use in patients with DG has been controversial due to concerns about exacerbating pre-existing gastric motility issues.
Objectives: This paper evaluates the impact of GLP-1 RAs on gastric motility in DG and assesses their safety and efficacy in this population.
Methods: A comprehensive search was conducted in Embase, MEDLINE (OVID), Cochrane Central, Web of Science Core Collection, Korean Citation Index, SciELO, and Global Index Medicus. Data from randomized controlled trials, observational studies, and case reports were analyzed to assess the effects of GLP-1 RAs on gastric emptying in non-gastroparetic and gastroparetic populations. Additional ad hoc searches were conducted in PubMed and Embase.
Results: The review revealed that while GLP-1 RAs are associated with DGE, this effect is dose- and formulation-dependent (long vs. short-acting) and diminishes over time due to significant tachyphylaxis. Importantly, in DG patients, vagus nerve dysfunction appears to attenuate the gastrointestinal effects of GLP-1 RAs, reducing the risk of further motility impairment, especially with long-acting formulations. With GLP-1 RA use, no significant exacerbation of DG symptoms occurred, suggesting these medications may be safer in this population than previously thought.
Conclusion: The findings suggest that DG should not be considered an absolute contraindication for GLP-1 RA therapy. Emerging data support revising clinical guidelines to direct GLP-1 RA use in DG. Given their efficacy and potential to reduce cardiovascular and renal complications, GLP-1 RAs should be considered in DG patients with personalized therapeutic strategies.

Eun Seo Kwak MD

A case of hepatic portal venous gas associated with ischemia related large necrotic gastric ulcer

Eun Seo Kwak MD, Zohaib Ahmed MD, Nahush Bansal MD, Tony Dong, Emily Moore, Yaseen S. Y. Alastal MD, Kurt Bernsdorff MD

Introduction: Hepatic portal venous gas (HPVG) is a rare radiological sign that typically indicates an acute intra-abdominal process. Although the presence of HPVG is often viewed as a potentially life-threatening condition requiring immediate management, modern use of abdominal computed tomography (CT) imaging has led to detection of HPVG in more benign conditions. Therefore, HPVG rather serves as a diagnostic clue in patients with underlying acute abdominal pathology. Previous cases have found successful outcomes with conservative treatments depending on the associated abdominal pathology. Similarly, we present a case of

patient with necrotic gastric ulcer associated HPVG who was successfully treated with conservative management.
Case: A 44-year-old male with history significant for ischemic cardiomyopathy and atrial fibrillation was admitted for tachycardia. On the fourth day of hospitalization, he reported mid-abdominal pain accompanied by nausea and vomiting. He was also noted to be hypotensive, with laboratory tests revealing leukocytosis and transaminitis. Abdominal CT scan showed intrahepatic portal venous gas, with gas present in the superior mesenteric vein, gastroepiploic veins, and mild colic veins, along with cholelithiasis and extensive gastric mural thickening. Endoscopy identified a large ulcer with black eschar on the anterior wall of the stomach body, extending into the antrum. Biopsies of the necrotic tissue were negative for malignancy. The gastric ulcer was suspected to result from poor perfusion due to ischemic cardiomyopathy.
Given the resolution of symptoms, he did not undergo surgical intervention and was managed with antibiotics and pantoprazole, with plans for outpatient repeat endoscopy. He showed clinical improvement and was discharged in stable condition.
Conclusion: Our case contributes to existing literature that suggest prognosis is more closely related to the primary pathology rather than the presence of HPVG itself. This underscores the importance of considering a conservative approach to managing HPVG, based on the specific underlying abdominal pathology.

Nooraldin Merza MD

Evaluating primary EUS-guided biliary drainage versus ERCP drainage in malignant biliary obstruction a systematic review and meta-analysis

Nooraldin Merza MD, Hasan Al-Obaidi MD, Yusuf Nawras MS, Zullo Michaelangelo Raphael MD, Odoeke Moses MD, Abdallah Kobeissy MD

Aim: We aim to compare the effects of endoscopic ultrasound (EUS) guided coiling with cyanoacrylate (CYA) injection in treating gastric varices (GV).
Methods: A systemic search was conducted from electronic databases (PubMed/Medline, Cochrane Library, and Google Scholar) from inception to 16th February 2024. All statistical analyses were conducted in Review Manager 5.4.1. Studies meeting inclusion criteria were selected. A random-effect model was used when heterogeneity was seen to pool the studies, and the result was reported in Odds ratio (OR) with their respective 95% confidence intervals (CI). Qualitative analysis was also carried out for those factors that did not provide sufficient data to carry out quantitative analysis.
Results: Six observational studies were used to conduct our study. Analysis revealed a significantly higher risk of subsequent bleeding episodes in the CYA injection group compared to the EUS-guided coiling group (OR = 0.28 (0.15, 0.53); $p < 0.0001$; $I2 = 0\%$). Although an insignificant difference was observed rate of mortality between the two groups of patients (OR = 0.93 (0.21, 4.06); $p = 0.92$; $I2 = 0\%$). The overall odds of cumulative adverse effects were significantly higher in the CYA injection group compared to the coiling group (OR = 0.43 (0.24, 0.75); $p = 0.003$; $I2 = 11\%$). Other factors like cost, length of stay, etc. were also discussed using a qualitative approach.
Conclusion: Our study showed that wholistically EUS-guided coil provided better results for the patients and acted as a more superior intervention as compared to CYA injections in treating GV, even though coiling cost more than CYA injections.

Nooraldin Merza MD

The association between primary sclerosing cholangitis (PSC) and microscopic colitis (MC): A systematic review

Nooraldin Merza MD, Hasan Al-Obaidi MD, Yusuf Nawras MS, Zullo Michaelangelo Raphael MD, Odoeke Moses MD, Abdallah Kobeissy MD

Introduction: Primary sclerosing cholangitis (PSC) is a chronic, progressive cholestatic liver disease marked by inflammation and fibrosis of the intrahepatic and extrahepatic bile ducts. PSC is frequently associated with

inflammatory bowel disease (IBD) including ulcerative colitis (UC), with up to 80% of PSC patients having concurrent IBD. The association between primary sclerosing cholangitis (PSC) and microscopic colitis (MC) is unclear, with limited evidence suggesting a potential correlation.
Methods: A systematic review was undertaken to look at the relationship between PSC and MC. Relevant studies were identified using searches in PubMed, Embase, and the Cochrane Library. Data was collected and evaluated using descriptive analysis and qualitative synthesis.
Results: Two studies were included in the systematic review, one case report and a retrospective case series {n= 13). The case series revealed a higher prevalence of MC diagnosis following PSC (75%), with a sizable number of individuals asymptomatic. The case report corroborated this link by describing a patient with collagenous colitis who later acquired PSC.
Discussion: The findings underscore the importance of raising awareness of MC in the PSC population, especially considering the high prevalence of asymptomatic patients. Early diagnosis and treatment of MC may enhance patient outcomes and quality of life. However, more research, particularly large-scale prospective studies, is needed to validate this connection, understand the underlying mechanisms, and assess the efficacy of MC screening and treatment regimens in the setting of PSC.

Nooraldin Merza MD

The risk of developing periampullary tumors after cholecystectomy: A systematic review and meta-analysis

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Background: The link between cholecystectomy and the risk of periampullary tumors (PTs) is uncertain. These malignancies develop in the periampullary region, which is where the pancreatic and common bile ducts meet the duodenum. This region includes the distal common bile duct, the pancreatic head, the periampullary portion of the duodenum, and the ampulla of Vater. These cancers are typically aggressive, with a poor prognosis due to late presentation and restricted therapy choices. The purpose of this systematic review and meta-analysis was to examine the available evidence on this association.
Methods: A systematic literature search was carried out in PubMed, Embase, and Web of science for relevant studies published between 1996 and 2024. We considered studies that reported relative risks (RRs) for PTs after cholecystectomy. The Newcastle-Ottawa Scale was used to assess the risk of bias.
Results: The analysis includes five trials (n = 107,476). A forest plot of individual study RRs and 95% confidence intervals (Cls) demonstrated significant variation in the outcomes. The pooled relative risk was 1.516 (95% CI 0.90-3.59), indicating an elevated risk of PTs linked with cholecystectomy, but the confidence interval did not pass the line of null effect. However, the separate research yielded varying results, with some reporting substantial connections and others not.
Conclusions: The existing evidence on the link between cholecystectomy and PTs risk is equivocal, however a pooled study implies an elevated risk. More research, particularly large-scale prospective studies with established methodology, is required to better understand this link and inform therapeutic decision-making.

Alicia M. Nahhas BS

A delayed presentation of immune checkpoint inhibitor colitis

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Introduction: Immune checkpoint inhibitors (ICIs) have emerged as a revolutionary option for cancer immunotherapy, becoming increasingly more common as a treatment choice for various malignancies. With this, it is important for providers and patients to be aware of common side effects, especially gastrointestinal adverse events which occur in 35-50% of patients[1]. ICI colitis is one such reported adverse event that can occur within weeks to months after starting ICIs and can quickly progress to severe colitis.
Case Presentation: An 80-year-old male with a past medical history of urothelial carcinoma presented with severe watery diarrhea for four months. The patient had been started on enfortumab vedotin and pembrolizumab

two months prior to onset of diarrhea. C. difficile PCR was positive, but he did not respond to oral vancomycin or fidaxomicin. This suggested that he was colonized rather than infected with C. difficile. Flexible sigmoidoscopy showed diffuse mild inflammation in the sigmoid colon and rectum with erythema, edema, and erosions. Colon biopsies revealed active colitis with focal crypt distortion and increased apoptosis which favors immune checkpoint inhibitor colitis. The patient was then started on prednisone which significantly improved his symptoms.
Conclusion: Regardless of duration, patients receiving ICI therapy presenting with diarrhea should be evaluated for ICI colitis. If labs are positive for an infectious cause, it is crucial to monitor patients closely for recovery after appropriate treatment and to keep clinical suspicion for underlying ICI colitis high if non-therapeutic. A colonoscopy with tissue biopsies should be performed early to confirm the diagnosis, assess severity, and guide treatment. Given that the majority of ICI colitis cases affect the left colon, flexible sigmoidoscopy is sufficient in most cases[2]. Treatment includes holding immunotherapy and initiating systemic glucocorticoids. Biological agents, such as Infliximab, may be necessary in refractory cases or patients requiring rapid treatment response[3].

Yusuf Nawras BS

Effect of pemafibrate, a selective peroxisome proliferator-activated receptor? Modulator (SPPARM?), on the lipid profile, liver function, and liver fibrosis among patients with non-alcoholic fatty liver disease: A systematic review and meta-analysis

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Background: Metabolic dysfunction associated steatotic liver disease (MASLD) and Metabolic dysfunction associated steatohepatitis (MASH) are prevalent conditions linked to obesity and metabolic disturbances, with potential complications such as cirrhosis and cardiovascular risks (1). This systematic review and meta-analysis aimed to evaluate the efficacy of Pemafibrate, a drug targeting fat and sugar metabolism genes, in treating patients with MASLD/MASH.
Methods: Databases such as MEDLINE, Web of Science, Cochrane Library, and Scopus were searched until September 2023 to identify relevant studies. Selected studies underwent a thorough quality assessment using tools like ROB-2 and the NIH Quality Assessment Tools. Comprehensive Meta-analysis software was used for statistical evaluations, with a focus on lipid profiles, liver function tests, and fibrosis measurements.
Results: A total of 13 studies were included; 10 of them were included in the quantitative analysis. Our findings showed that pemafibrate significantly decreased LDL-C (ES= -9.61 mg/dL, 95% CI: -14.15 to -5.08), increased HDL-C (ES= 3.15 mg/dL, 95% CI: 1.53 to 4.78) (2,3-13), and reduced triglycerides (TG) (ES= -85.98 mg/dL, 95% CI: -96.61 to -75.36). Additionally, pemafibrate showed a marked reduction in liver enzyme levels, including AST, ALT, GGT, and ALP, with significant effect sizes and p-values. For liver stiffness outcomes, pemafibrate decreased APRI (ES= -0.180, 95% CI: -0.221 to -0.138).
Conclusion: Pemafibrate, with its enhanced selectivity and safety profile, presents as a pivotal agent in MASLD/MASH treatment. Its lipid-regulating properties, coupled with its beneficial effects on liver inflammation markers, position it as a potentially invaluable therapeutic option.

Yusuf Nawras BS

Submucosal tunneling endoscopic resection for submucosal tumors of less than 35 mm in the upper and lower gastrointestinal tract: A systematic review and meta-analysis

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Objectives: We conducted a systematic review and meta-analysis to synthesize the current evidence on the efficacy and safety of submucosal tunneling endoscopic resection (STER) for submucosal tumors (SMTs) of the gastrointestinal (GI) tract (3,4).
Methods: This study adhered to PRISMA guidelines and included observational studies on patients with upper or lower GI tract SMTs who underwent STER (5, 6). Data were extracted from these studies and analyzed using Open Meta[Analyst] and Jamovi software, with outcomes including resection rates, recurrence, and complications. Quality assessment and risk of bias were evaluated using the Newcastle-Ottawa Scale and NIH Quality Assessment Tool, and publication bias was evaluated via funnel plots and regression tests.
Results: This meta-analysis of 27 studies indicated high complete and En-bloc resection rates of 96.1% (95% CI: 94.1% to 98.0%) and 90.3% (95% CI: 85.6% to 94.9%), respectively (1,2,3,7–30). The studies exhibited a low recurrence rate of 2.0% (95% CI: 1.2% to 3.4%) and moderate incidence of complications such as subcutaneous emphysema and pneumomediastinum (10.0%, 95% CI: 5.5% to 17.6%) and pneumothorax (6.6%, 95% CI: 3.9% to 11.0%). Other adverse events like perforation and bleeding were rare, occurring at rates of 2.3% (95% CI: 1.1% to 4.7%) and 2.5% (95% CI: 1.2% to 5.2%), respectively. Furthermore, the average operative time was 59.28 min (95% CI: 53.83 to 64.73), with an average hospital stay of 4.77 days (95% CI: 3.91 to 5.63).
Conclusion: STER demonstrates high resection rates and low recurrence in the treatment of gastrointestinal SMTs. While complications like subcutaneous emphysema, pneumomediastinum, and pneumothorax do occur, they remain low in incidence. Rarer complications, such as perforation and bleeding, underscore the overall safety of the procedure.

Yusuf Nawras BS

Temporal trends in racial and gender disparities of early onset colorectal cancer in the United States: An Analysis of the CDC WONDER database

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Background: The mortality rates of early-onset colorectal cancer (EOCRC) have surged globally over the past two decades (1). While the underlying reasons remain largely unknown, understanding its epidemiology is crucial to address this escalating trend. This study aimed to identify disparities potentially influencing these rates, enhancing risk assessment tools, and highlighting areas necessitating further research.
Methods: Using the CDC Wide-Ranging Online Data for Epidemiologic Research (WONDER) database, this study assessed EOCRC mortality data from 2012 to 2020. Individuals under 50 years who succumbed to EOCRC were identified through the International Classification of Diseases, Tenth Revision (ICD-10) codes (2,3). Data interpretation and representation were performed using R 4.2.2 software.
Results: Between 2012 and 2020, EOCRC mortality rates fluctuated marginally between 1.7 and 1.8 per 100,000. Male mortality rates increased from 1.9 to 2.0 per 100,000, while female rates varied between 1.5 and 1.6 per 100,000. Significant variations were observed across age groups, with the 40-49 years category experiencing an increase from 6.34 (2012) to 6.94 (2020) per 100,000. Racial category-based data revealed the highest mortality rates among African Americans. Geographically, Mississippi and Alabama exhibited elevated mortality rates. Age-Adjusted Mortality Rate (AAMR) assessments indicated a marked decline for both genders from 2012 to 2020, with consistently higher rates for men.
Conclusion: The findings highlight the evolving landscape of EOCRC mortality, revealing significant gender, age, and racial disparities. These results underscore the urgent need for tailored health strategies and intensified research efforts targeting these disparities.

Yusuf Nawras BS

Unmasking granulomatosis with polyangiitis: A diagnostic odyssey in a patient initially diagnosed with giant cell arteritis

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Introduction: Systemic vasculitis poses a diagnostic challenge due to its diverse manifestations across multiple organ systems. Anchoring bias can limit a comprehensive understanding, especially when encountering cases resembling common conditions like Giant Cell Arteritis (GCA). GCA and Antineutrophil cytoplasmic antibodies (ANCAs) vasculitides, such as Granulomatosis with Polyangiitis (GPA), represent distinct entities. However, their concurrent occurrence underscores the importance of adopting a nuanced diagnostic approach. In this context, we explore a unique case of ANCA vasculitis initially presenting as GCA.
Case Presentation: A 66-year-old Middle Eastern male with essential hypertension and type 2 diabetes mellitus presented with sinus congestion, severe headache, visual disturbances, jaw pain, and muscle stiffness for 2-3 weeks. Further investigation revealed CT imaging of chronic sinusitis, an abnormal urinalysis (proteinuria and hematuria), and positive C-ANCA and PR3 antibodies. He was diagnosed with GCA based on clinical presentation, supported by elevated inflammatory markers. Bilateral temporal artery biopsies, which resulted after the patient was discharged on steroids, did not show evidence of GCA. A delayed kidney biopsy confirmed pauci-immune focal segmental crescentic glomerulonephritis, leading to a revised diagnosis of granulomatosis with polyangiitis.
Conclusion: GCA and GPA exhibit distinct profiles. While GCA involves large vessels, GPA, an ANCA-associated vasculitis, affects small to medium vessels. Like ANCA-associated vasculitides, GCA is often diagnosed through elevated C-reactive protein and erythrocyte sedimentation rates. Temporal artery biopsy should be done to confirm diagnosis, although studies have suggested the modality may not be highly sensitive [1]. GCA's pathogenesis primarily involves cell-mediated mechanisms, with lymphocytes, macrophages, and multinucleated Langerhans cells comprising the inflammatory infiltrate [2,3]. Distinguishing between GCA and other systemic vasculitides is crucial due to GCA's association with rapid visual loss and cerebrovascular accidents [4]. This case underscores the need for an open-minded diagnostic approach, avoiding anchoring bias and considering the dynamic nature of systemic vasculitis presentations.

Reem Sharaiha MD

The efficacy of Antireflux Mucosectomy (ARMS) and Antireflux Mucosal Ablation (ARMA) for Gastroesophageal Reflux Disease (GERO) by 24-Hour pH monitoring: Systematic review and meta-analysis

Reem Sharaiha MD, Hasan Al-Obaidi MD, Nooraldin Merza MD, Yusuf Nawras MS, Zullo Michaelangelo Raphael MD, Odoeke Moses MD, Abdallah Kobeissy MD

Background: Gastroesophageal Reflux Disease (GERO) is a prevalent and chronic disorder impacting a significant proportion of the global population of almost 15%. Most of GERO patients show improvement with medical treatment, which includes proton pump inhibitors (PPis), around forty percent of them continue to experience symptoms even with ongoing PPI use. Antireflux mucosa! ablation (ARMA) and antireflux mucosa! resection (ARMS) are minimally invasive endoscopic procedures for treating Gastroesophageal Reflux Disease (GERO).
Objective: This meta-analysis aimed to evaluate their efficacy of ARMA and ARMS through DeMeester score, acid exposure time (AET), and clinical success rate.
Methods: Studies reporting pre- and post-procedure esophageal 24-hr pH monitoring following ARMA and ARMS were included. Pooled data analysis assessed changes in DeMeester score and AET. Clinical success rate, defined as significant symptom improvement or reduced reliance on proton pump inhibitors, was also analyzed.
Results: Pooled data from three ARMA studies showed a significant post-procedure decrease in medianAET (19.61 [14.10, 25.13], $p<0.0001$). Similarly, six ARMS studies demonstrated a significant reduction in

DeMeester score (2.69 [1.52, 3.85], p<0.0001). The overall clinical success rate for ARMS was 85.8% (moderate heterogeneity, 12=59%) and 88.3% for ARMA (moderate heterogeneity, 12=51 %).
Conclusions: Both ARMA and ARMS displayed promising efficacy in improving GERO-related outcomes, based on reductions in AET and DeMeester score, and achieving high clinical success rates. However, moderate heterogeneity observed suggests further research is needed to identify patient-specific factors influencing treatment response.

Deepanshu Singh BS
Impact of early vitamin D Deficiency on long-term outcomes in patients with primary biliary cirrhosis: A 10-year retrospective study
Deepanshu Singh BS, Dharmindra Dulal BS, Mona Hassan MD

Objectives: Primary biliary cirrhosis (PBC) is a chronic, immune-mediated destruction of bile ducts, leading to liver damage. Vitamin D (VD) deficiency is frequently observed in PBC. This study aims to investigate the correlation of vitamin D deficiency during the early stages of PBC with long-term clinical complications. Additionally, we aim to determine if VD status can be a prognostic marker in PBC.
Method: A ten-year retrospective cohort study was conducted on PBC patients using TriNetX database. VD deficiency was defined as ≤29 ng/dL. Patients with unspecified kidney failure, end-stage renal disease, chronic kidney disease, or age<18 years were excluded. To reduce confounding, propensity score matching was performed based on baseline characteristics including age, alcoholic liver disease, portal hypertension, esophageal varices, alanine aminotransferase, aspartate aminotransferase, total bilirubin, albumin, and INR. Statistical analyses compared key outcomes, including mortality, cirrhosis, esophageal varices, portal hypertension, hepatic encephalopathy, synthetic liver function, hepatocellular carcinoma, and liver transplantation of two groups of 746 patients.
Results: Patients with VD ≤29 ng/dL had higher rates of mortality (13.0% vs. 9.5%, p<0.05), hepatocellular carcinoma (5.1% vs. 2.8%, p<0.05), esophageal varices (19.8% vs. 14.1%, p<0.01), portal hypertension (23.3% vs. 16.8%, p<0.01), hepatic encephalopathy (8.3% vs. 4.6%, p<0.01), and worse liver function, indicated by higher bilirubin, INR, and lower albumin (p<0.001). No significant differences were seen in cirrhosis, hospital admissions, or liver transplantation rates.
Conclusion: Early VD deficiency is associated with long-term complications in PBC, including higher risks of mortality, hepatocellular carcinoma, and liver function decline. It can potentially be used as a prognostic marker in predicting adverse PBC outcomes. Regular monitoring and correction of VD deficiency might also improve outcomes for patients.

GENERAL INTERNAL MEDICINE

Anwer Aldhaheri
Cardiovascular diseases among patients with systemic lupus erythematosus 3
Anwer Aldhaheri, Nezam Altorok, Sadik A. Khuder

Background: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by widespread inflammation affecting multiple organ systems. Patients with SLE are at an increased risk of developing cardiovascular diseases (CVDs), which are now recognized as a leading cause of death in this population. The relationship between SLE and CVD is complex, involving a combination of traditional risk factors, such as hypertension and dyslipidemia, and SLE-specific factors like chronic inflammation and autoantibody production.
Objectives: To evaluate the effect of SLE on the risk of CVDs.
Methods: All hospitalization of patients with Lupus from ages ≥ 18 were extracted from the National Inpatient Sample Database, 2021. Cardiovascular diseases (Atherosclerosis, Cardiomyopathy, and Heat Failure) were

identified using the International Classification of Disease (ICD)-10. Weighted logistic regression analyses were conducted to summarize associations adjusted for age and gender. Results: Among 6,666,752 hospitalizations, 29,304 were for Lupus. Lupus was significantly associated with increased odds of Atherosclerosis (OR = 1.40; 95% CI:1.26,1.55), Cardiomyopathy (OR = 1.97; 95% CI:1.87,2.07), and Congestive Heart Failure (CHF) (OR = 2.02; 95% CI:1.92,2.14). Older age and male gender were associated with significantly higher OR for the three cardiovascular diseases.
Conclusions: This study underscores the strong association between Systemic Lupus Erythematosus (SLE) and increased risk of CVDs, including atherosclerosis, cardiomyopathy, and heart failure. Analysis of data from the National Inpatient Sample Database, 2021, revealed significantly higher odds of these CVDs in SLE patients, particularly among older adults and men. The interplay of chronic inflammation, autoantibody production, and traditional risk factors exacerbates cardiovascular risk in this population. These findings emphasize the critical need for proactive cardiovascular monitoring and targeted interventions to improve outcomes and reduce CVD-related morbidity and mortality in SLE patients.

Anwer Aldhaheri

Investigating the common genes involved in development of Sjogren's syndrome and cardiomyopathy

Anwer Aldhaheri, Nezam Altorok, Sadik A. Khuder

Background: Recent research has identified an association between SS and cardiomyopathy (CMP). However, the underlying mechanisms and shared genetic factors contributing to the coexistence of SS and CMP remain unclear.
Objectives: To identify common genes involved in the development of both SS and CMP.
Methods: Gene expression data for SS and CMP, including RNA sequencing (include the GSE number of each RNA-seq) and microarray (include the GSE number of each microarray dataset) datasets, were obtained from the Gene Expression Omnibus (GEO) database. GEO2R was used to identify the top 1,000 differentially expressed genes for each disease. The WGCNA package was used to identify co-expression modules significantly associated with each disease state. The DAVID database was used for Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis. Hub genes were identified, and their associated pathways were examined.
Results: WGCNA revealed ten significant modules related to SS and CMP. Thirteen genes were selected based on the DAVID analysis results, with criteria including their known roles in disease development, shared pathways, and evidence from the literature. These genes—IFNLR1, IRF5, MDK, IL1RN, SOD2, PIAS4, SSPN, ELAVL1, TRAF3, TRAF6, CTNNB1, HIF1A, and JAK1—were differentially expressed and linked to both SS and CMP. IL1RN, for example, is protective against inflammation, but its polymorphisms are associated with various inflammatory, cancerous, and autoimmune conditions. INF genes overexpression is known to recruit T cell for its inflammatory response. T cell activity in both SS and CMP drives tissue damage and inflammation, worsening disease progression.
Conclusion: This study identified 13 genes implicated in the shared development pathways of both SS and CMP. These findings provide new insights into the concurrent development of these diseases and offer potential targets for therapeutic intervention.

Mohammad AlSakka

Trends in stroke prevalence among the USA population: American analysis report

Mohammad AlSakka, MD, Bisher Sawaf, MD, Yusuf Hallak, MD, Nezam Altorok, MD, MPH

Background: Analyzing stroke prevalence can guide interventions to ease the burden of stroke, improve patient outcomes, and reduce financial strain in the region. This study aimed to investigate the prevalence of stroke among the American population from 1996 to 2022 and explore multiple factors and their associations with stroke occurrence during this period.

Methods: This investigation employed data obtained from the Behavioral Risk Factor Surveillance System (BRFSS), focusing on individuals aged 18 years and above who participated in surveys administered by the BRFSS between 1996 and 2022 and were diagnosed with stroke. Univariate and multivariate logistic regression analyses were used to examine the factors influencing the prevalence of stroke.
Results: The study examined a cohort comprising 313,463 individuals, revealing a stroke prevalence of 3.73% within the United States population from 1996 to 2022. The prevalence of stroke has increased from 2.7% to 4.4% between 1996 and 2019, followed by a decrease of 4.1% from 2020 to 2022. The identified stroke risk factors included age > 65 years (odds ratio [OR]: 8.16-10.29), Black and non-Hispanic ethnicity (OR: 1.25-1.78), retirement (OR: 2.1-16.84), smoking (OR: 1.4-2.25), and diabetes mellitus (OR: 1.67-3.84) ($p < 0.05$).
Conclusion: Our study demonstrates a significant increase in stroke prevalence in the US population from 1996 to 2022. Longitudinal studies are essential to inform evidence-based policies and clinical practices for effective stroke prevention and management.

Vaishnavi Aradhyula

Impact of smoking and nicotine exposure on Vitamin D Status: Associations with age, body weight and supplementation in a U.S. population

Vaishnavi Aradhyula, Mani Khorsand Askari MD, Anand Mutgi MD, Sadik Khuder PhD, Basil Akpunonu MD, Hoda Shabpiray MD, Douglas Federman MD

Introduction: Previous studies have demonstrated that smokers are more likely to have lower circulating vitamin D levels, with recent research highlighting that nicotine and other compounds in tobacco smoke significantly increase vitamin D metabolism. Given vitamin D's important role in cell proliferation and immune response, deficiency is associated with chronic obstructive pulmonary disease exacerbations, mycobacterium infections, and chronic inflammatory pulmonary changes. A 2024 study using NHANES data identified a negative association between tobacco smoke exposure and serum vitamin D levels, underscoring smoking as a modifiable risk factor for deficiency.
Methods: This study analyzed data from the NHANES 2017-2018 database. Smoking status was assessed via cotinine levels, a biomarker for nicotine exposure, while vitamin D levels were measured using 25OHD2+25OHD3 (nmol/L). Weighted linear regression examined the association between vitamin D and cotinine levels, and a weighted logistic regression predicted vitamin D status, adjusting for age, body weight, and vitamin D supplementation.
Results: A significant negative association between cotinine levels and vitamin D was observed ($p=0.009$), indicating that higher nicotine exposure leads to a 37% reduction in vitamin D levels. Individuals over 60 had 1.83 times higher odds of lower vitamin D levels, and those with higher body weight had significantly lower vitamin D levels (OR = 0.68, 95% CI 0.51-0.92). Lack of vitamin D supplementation was strongly associated with lower vitamin D levels ($p<0.0001$).
Conclusion: Our study confirms a negative association between smoking and vitamin D levels, even after adjusting for age, body weight, and vitamin D supplementation. Monitoring vitamin D status in smokers and considering supplementation are crucial for mitigating health risks.

Vaishnavi Aradhyula

The critical role of accurate ICD-10 coding in hospital discharge diagnoses and impact on healthcare management

Vaishnavi Aradhyula, Mani Khorsand Askari MD, Anand Mutgi MD, Sadik Khuder PhD, Basil Akpunonu MD, Lisa Heyman, Hoda Shabpiray MD, Douglas Federman MD

Introduction: Accurate coding using the ICD-10 is critical for reliable diagnoses, healthcare reimbursement, and thorough patient care; however, the transition to this new coding system is a challenge for many institutions, leading to significant healthcare burden. This study evaluates the frequency of usage of specific versus nonspecific ICD-10 coding in hospital discharge diagnoses, focusing on four common disorders,

including diabetes mellitus, heart failure, chronic obstructive pulmonary disease (COPD), and pneumonia. The impact of race, gender, age, and length of stay (LOS) on the use of nonspecific ICD codes was also analyzed.
Methods: A retrospective cross-sectional analysis was conducted using the 2021-2022 National Hospital Discharge Data from the Healthcare Cost and Utilization Project. Patients with primary or secondary diagnoses of diabetes mellitus, heart failure, COPD, and pneumonia were included. Descriptive statistics and logistic regression models assessed the use of specific versus nonspecific ICD-10 codes and the influence of demographic factors.
Results: Among 6,666,752 discharges in 2021, the rates of specified coding by disease were: Diabetes (97.86%), Heart Failure (94.01%), Pneumonia (91.42%), and COPD (77.13%). Age and race were significant predictors of unspecified diagnosis for all four diseases. Older patients and those with extended LOS were also associated with higher nonspecific coding rates ($p<0.0001$). Gender was significant predictors for COPD and Pneumonia. Females were more likely to receive nonspecific codes, particularly in COPD.
Conclusion: Nonspecific ICD-10 coding is common and more frequent in COPD and is influenced by demographic factors and LOS. Nonspecific coding can lead to inaccurate diagnoses, and subsequent delayed and inaccurate reimbursement. This impacts healthcare statistics and budget planning by insurance companies. Targeted efforts to standardize coding practices and enhance the specificity of ICD-10 codes are necessary to improve data quality, patient care, and financial outcomes.

Chase M Arnold

Evaluating the impact of cadaver-based microsurgery training on resident physicians' surgical skill development

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Background: Surgical proficiency is essential in residency training to prepare physicians for independent practice. Didactic surgical simulations have been shown to be effective in enhancing surgical skills (I). Given a lack of "gold standard" in the literature, there is need to develop a curriculum for resident education.
Objective: The goal of this study was to develop a didactic surgical simulation curriculum to assess learner knowledge and confidence in performing microsurgery before vs. after completing a novel surgical curriculum.
Methods: Participants were Urology residents (n= 8 Junior residents: PGY 1-3, n= 4 Senior residents, PGY4-5). The curriculum was a single two-hour session held in a surgical simulation lab, with a didactic overview and hands-on skill session. A pre/post-test survey was administered following this session to measure gains in content knowledge and satisfaction.
Results: Residents rated their skills pre- vs. post-pa1ticipation in this skills lab. Residents reported a 23% gain in content knowledge (Junior: 23.8%, Senior: 20.8%, >0.05), with greatest gains coming from hands-on skill training as compared to the didactic overview (e.g., review of anatomy, $p<0.05$). The curriculum was rated highly (Mean= 4.92/5, $p<0.05$). Trainees said it improved their knowledge, prepared them for national exams, allowed them to practice skills taught in the course, and that they would recommend it to their peers ($p<0.05$). Residents believe this curriculum would be most beneficial to Junior Residents (Mean= 83.3), Senior Residents (100%), and Chief Residents (66.6%), as compared to Fellows (58.3%), or Medical Students (33.3%)
Conclusions: This study suggests that this novel microsurgery model for hands-on simulation training in urologic surgery is efficacious. Learners found this novel microsurgery curriculum beneficial for understanding and perfom1ing associated procedures. Participants highlighted the impo1tance of hands-on cadaver training under instructor supervision with 'live' feedback. This may provide a model for similar future education, given the affordability and ease of this lab. 1. Shetty, S., Zevin, B., Grantcharov, T. P., Roberts, K. E., & Duffy, A. J. (2014). Perceptions, training experiences, and preferences of surgical residents toward laparoscopic simulation training: a resident survey. Journal of surgical education, 71(5), 727-733.
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Michael K. Besly BA

Effective management of refractory restless leg syndrome in an anemic elderly patient using intravenous iron therapy: A case report

Michael K. Besly BA, Ayda Fatholla Pour MD, Elizabeth Schumacher MBA, Nora Abdul-Aziz BA, Mani Askari MD, Hoda Shabpiray MD

Background: Restless leg syndrome (RLS), also known as Willis-Ekbom disease, is a common neurological disorder characterized by an uncontrollable urge to move the legs, often accompanied by uncomfortable sensations such as creeping or tingling. These symptoms typically worsen during periods of inactivity and are temporarily relieved by movement. The prevalence of RLS is estimated to be 5-10% of the population, with higher rates observed in women and older adults. The pathophysiology of RLS is linked to brain iron deficiency and dysfunction in dopaminergic neurotransmission. Iron supplementation, and potentially intravenous (IV) iron, is an essential treatment, particularly for patients with iron deficiency.
Case Presentation: An 83-year-old female with a history of non-ischemic dilated cardiomyopathy, type 2 diabetes mellitus, chronic obstructive pulmonary disease (COPD), and RLS presented with worsening leg cramps and shortness of breath. She was found to be acutely anemic (hemoglobin 6.6 g/dL) due to a suspected upper gastrointestinal bleed. Initial treatment with oral iron was inadequate, leading to persistent severe leg cramps. Subsequently, the patient received IV iron therapy, resulting in significant symptom relief and resolution of her leg cramps. The patient's hemoglobin level stabilized, and she was discharged with continued oral iron supplementation and follow-up care.
Conclusion: This case highlights the effectiveness of IV iron therapy in rapidly alleviating RLS symptoms in a patient with severe anemia. The transition from oral to IV iron therapy was crucial in achieving symptom resolution, suggesting that IV iron should be considered in patients with refractory RLS symptoms, particularly those with significant anemia. The improvement observed in this case underscores the importance of addressing underlying iron deficiency in the management of RLS. Further research is necessary to establish clear guidelines for the use of IV iron in clinical practice.

Danyal Butt MD

Are you waiting for me to explode?! A case of an unresolving, deadly headache

Danyal Butt MD, Halah Alfatlawi MD, Anan Bseiso MD, Rawish Fatima MD, Nezam Altorok MD

Introduction: Giant cell arteritis (GCA), or temporal arteritis, is a common vasculitis primarily affecting older adults and characterized by inflammation of medium to large arteries. It frequently presents with temporal headaches and elevated inflammatory markers, with temporal artery biopsy typically revealing transmural inflammation and giant cell infiltration. However, GCA's clinical presentation can overlap with other conditions, including malignancies. This case highlights an unusual presentation of squamous cell carcinoma (SCC) of the scalp mimicking GCA.
Patient Case: A 68-year-old man with a complex medical history, including a prior squamous cell carcinoma of the scalp, presented with a 3-month history of left temporal headache and jaw pain. Initial laboratory tests indicated elevated erythrocyte sedimentation rate (31 mm/h), but other inflammatory markers were normal. Despite the suspicion of GCA, high-dose corticosteroids were initiated. Temporal artery Doppler ultrasound revealed bilateral halo signs, and biopsies were performed. The left temporal artery biopsy surprisingly showed invasive SCC with perineural invasion, while the right biopsy was unremarkable. Further imaging and PET scans confirmed local SCC extension but no metastatic disease.
Discussion: GCA typically presents with non-specific symptoms such as headaches, and timely glucocorticoid therapy is crucial to prevent complications like blindness and stroke. However, alternative diagnoses must be considered if steroid treatment fails, or biopsy results are negative. This case underscores the importance of differential diagnosis in elderly patients presenting with symptoms suggestive of GCA. SCC, though rare, can present with similar symptoms and should be considered, particularly in patients with a history of skin

malignancies. This case contributes to the understanding of GCA mimics and emphasizes the need for comprehensive evaluation when initial treatments do not yield expected results.

Nathaniel B. Dusseau II MS

Financial analysis of a large-scale student-run free clinic: A model for cost optimization and sustainability

Nathaniel B. Dusseau II MS, Zaina Kret BS, Samuel Steffen BS, Katherine Esser BS, Coral Matus MD, Richard Paat MD

Introduction: Student-run free clinics play a crucial role in advancing health equity by offering accessible healthcare services to the underinsured. Staffed by volunteer medical students and professionals, these clinics provide a broad spectrum of care, including primary, preventive, and specialized services. However, delivering such comprehensive care incurs significant financial costs. Understanding these expenditures is essential for ensuring the sustainability of free clinics and optimizing their budgetary strategies to continue providing high-quality care to underserved populations.
Methods: Accounting data from the 2023 fiscal year were analyzed. All incurred costs were categorized as either direct patient care costs or non-direct patient care costs. Two price-per-visit metrics were calculated: one based solely on direct patient care costs, and another that also included non-direct patient care costs, such as administrative expenses.
Results: In the 2023 fiscal year, the clinic cared for a total of 876 unique patients and staffed 1,675 patient encounters. On average, the price-per-visit in the 2023 fiscal year was $22.96. When including non-direct patient costs, price-per-visit was $36.06 . Patient care represented the majority of total operating costs (64%), with the remaining 36% of costs attributed to non-direct patient care costs. The average price-per-visit for general clinic supplies was $8.00. For pharmacy expenditures, the average price-per-visit was $7.25. These purchases accounted for approximately 42% of all spending.
Conclusions: This financial analysis underscores the considerable resources required to operate a large-scale free clinic, emphasizing the importance of efficient budget allocation. By breaking down expenditures into direct and non-direct patient care costs, this study provides a framework for understanding the financial demands of such clinics. The findings highlight the potential for optimizing resource use. This model serves as a valuable tool for other free clinics aiming to enhance cost-effectiveness while maintaining high-quality patient care.

Katherine L Esser

The demographic gap: A comparative analysis of the demographics of free clinic patients with the city served

Katherine L Esser, Johnny McKeown, Tatiana White, Steuart Besly, Addison Sparks, Sydney Hatch, Coral Matus, MD, Richard Paat, MD

Background: The United States comprises approximately 1,400 free clinics that served over 5.8 million patients collectively in 2022. With reports between 2022 and 2023 showing that 27.6 million (8.4%) of Americans of all ages did not have health insurance, these free clinics often serve as public safety nets. The demographics of patients that receive care at these clinics has been reported, however, there is a paucity of data regarding how these patients compare to their communities at large. An intake survey was implemented at a free clinic in 2022 to record the health needs and demographics of patients served at each clinic site in an effort to identify opportunities for improved care. As free clinics continue to expand, it is necessary for its services to reflect the current social determinants of health and health disparities the patient population encounters.
Objectives: A student-run free clinic compared patient demographics to the city's census data to analyze health needs, barriers to care, and characteristics of the underserved population.
Methods: A retrospective survey reviewed 1,338 visits from February 2023 to February 2024. Parameters included race, education, sex, health insurance status, and primary language. Comparative analysis used 2020 Census data for Toledo, OH.

Results: Significant demographic differences were found. The clinic served 22.63% fewer White patients, 17.27% more Hispanic/Latino patients, and 5.62% fewer African American patients. Among patients under 65 years, 61.91% were uninsured compared to 8.3% in Toledo. Fewer English speakers (66.60% vs. 93.2%) and more Spanish speakers (21.72% vs. 3.2%) were treated.
Conclusions: The study highlights demographic differences between CCC patients and the city, aiding in identifying those benefiting from these services. Policymakers and public health agencies should consider these inconsistencies in patient demographics across free clinics in the United States.

Tahrima Ferdous

A Subtle case of Myxedema coma or decompensated hypothyroidism

Tahrima Ferdous, Halah Alfatlawi

Introduction: Decompensated hypothyroidism, formerly known as myxedema coma, is an endocrine emergency associated with profound thyroid dysfunction [1]. The term "myxedema coma" is misnomer believing that they must either have edema or appear comatose to have this condition [2]. It should be considered in patients who have altered mental status may include confusion, lethargy, stupor, or coma and may progress over weeks to months with bradycardia, hypotension, and/or hypothermia. The most common precipitating factor is infection such as pneumonia, urinary tract infections, and septicemia [3,4]
Case Presentation: A 53-year-old African American female with PMH of HTN, HLD, obesity, H/O total thyroidectomy with benign pathology who presented with history of dizziness, lethargy, generalized weakness, body aches, shortness of breath, chills, nausea, upper abdominal pain, and urinary frequency.
Initial workup significant for Cr 1.37 (baseline 0.7), eGFR 46 (baseline >90), TSH 80, free T4 <0.25, CK 1091, total cholesterol 412, LDL 292, UA positive for moderate LE. According to diagnostic scoring of myxedema coma (Adapted from Popoveniuc G, ChaNdra T, Sud A, et al. Endocr Pract 2014; 11:1-36.) a score greater than 60 is highly suggestive of myxedema coma. Patient scored 75. These include abdominal pain, precipitating factor UTI, bradycardia HR of 52, EKG changes, hypotension and decrease in GFR.
She received a single dose of IV hydrocortisone 100 mg for episodes of hypotension. A dose of 400 mcg IV levothyroxine followed by 100 mcg/day. She had significant clinical and biochemical improvement within 3 days of treatment. She completed keflex for UTI. Probable causes of hypothyroidism such as medication noncompliance, incorrect pill technique, drug interactions and malabsorption were ruled out. Generic Levothyroxine was switched to Tirosint, free of any additives that interfere with absorption. She was discharged on 150 mcg of oral Tirosint daily.
Conclusion: Decompensated hypothyroidism is a dangerous condition with the potential for significant morbidity and mortality. Due to its similarities with other common conditions and subtle clinical manifestations severe hypothyroidism can be difficult to detect. If myxedema coma is suspected, treatments should be given with adrenal and thyroid hormone supplementation and treatment of the inciting event without delays.

Dena Hasan

Trauma-induced pituitary macroadenoma presenting as hypothyroidism and adrenal insufficiency post-MVA: a case report

Dena Hasan, Chelsie Baylor, Brady Williams, MD, Mani K. Askari, MD, FACP, FACMQ, CPHQ

Introduction: Pituitary adenomas constitute 10-15% of all intracranial neoplasms, often presenting with mass-effect symptoms and anterior hypopituitarism[1,2,3]. While genetic syndromes are recognized risk factors, other potential risk factors are less understood[3]. Post-traumatic hypopituitarism (PTHP), with an incidence of 15-68% in traumatic brain injury (TBI) patients, is a notable condition[4]. This case explores a pituitary macroadenoma presenting as hypothyroidism and sudden syncope due to central adrenal insufficiency following a motor vehicle accident (MVA).
Case Presentation: A 56-year-old South Asian male with type II diabetes mellitus, hypertension, and depression (managed with paroxetine, duloxetine, and clonazepam) presented to the emergency department (ED) after a

syncopal episode with loss of consciousness. Initial examination revealed facial laceration, periorbital edema, and absence of visual field defects. The patient reported fatigue, headaches, cold intolerance, dizziness, and severe constipation over recent months. A head CT scan revealed a soft mass in the sella turcica extending into the suprasellar cistern. An MRI confirmed a 1.5 cm enhancing lesion with a mass effect on the optic chiasm. Neurosurgical consultation is advised against surgery. Laboratory tests indicated severe hypothyroidism (Free T4 <0.5 mcg/dL) and central adrenal insufficiency (8 AM cortisol <2 mcg/dL) despite normal ACTH levels, leading to treatment with levothyroxine and hydrocortisone. Iron deficiency anemia was also identified and managed with intravenous Venofer. The patient's depressive symptoms were likely exacerbated by hypothyroidism secondary to the macroadenoma.
Conclusion: This case illustrates an atypical presentation of a pituitary macroadenoma, manifesting as secondary hypothyroidism and syncope linked to central adrenal insufficiency. The patient's prior unremarkable head CT following an MVA and the subsequent development of a macroadenoma suggest a possible association between TBI and pituitary neoplasms. Further investigation into TBI as a risk factor for pituitary adenomas is warranted.

Mona Khalafi MS

Trends in mortality rates due to complications of medical and surgical care in the United States (1999-2020)

Mona Khalafi MS, Taryn Hibshman BS, Oscar Salichs BS, Sishir Doddi BS, Mani Khorsand Askari MD

Background**:** Complications of care in healthcare, encompassing surgical errors, healthcare-associated infections, medication-related issues, and other iatrogenic injuries, pose a significant threat to patient well-being and increase mortality rates.
Objectives**:** This study aims to analyze trends related to complications of care from 1999-2020, supporting healthcare providers, policymakers, and researchers in their efforts to optimize patient safety and healthcare delivery.
Methods**:** CDC WONDER public database was accessed to retrieve age-adjusted mortality data (AAMR) from 1999 to 2020 using ICD-10 Codes: Y40-Y84 classified as "Complications of medical and surgical care". Annual percentage changes (APC) were examined using the Joinpoint Regression Program. Subgroups were categorized by sex, race, and ethnicity.
Results**:** *Sex*: Women and men experienced a decline in AAMR from 1999 to 2015, followed by an increase until 2020 (women APC, 13.7% [95% CI, 9.9% to 17.6%]; p<0.01; men APC, 16.6% [95% CI, 13.1% to 20.2%]; p<0.01). *Race*: Black/African American showed the highest mortality rates throughout the study; all races showed a decrease in AAMR from 1999 to 2015 and an increase until 2020. *Ethnicity*: Hispanic/Latinx experienced a downtrend in AAMR from 1999 to 2015 followed by a significant uptrend from 2015 to 2020 (APC, 21.5% [95% CI, 15.4% to 28%]; p<0.01).
Conclusion: All subgroups observed a similar trend with an AAMR decline from 1999 to 2015 due to advancements in minimally invasive surgeries, anesthesia, and antimicrobial protocols. Black/African American consistently had the highest mortality due to greater baseline disease burdens, socioeconomic challenges in access, and systemic healthcare disparities. The rise after 2015 reflects a rise in the aging population with higher surgical risks, a shift to value-based care with increased transparency and documentation, and specifically for 2020: the strain of COVID-19 on healthcare delivery. These results emphasize the need for targeted interventions to address the AAMR inequities.

Zaina Kret

Integrating comprehensive diabetic care in student-run free clinics: A model for addressing healthcare disparities

Zaina Kret, Kaylee Scarnati, Aya Dakroub, Katherine Esser, Coral Matus, MD, Richard Paat, MD

Student-run free clinics (SRFCs) play a pivotal role in delivering healthcare services to uninsured and underinsured populations, who experience higher rates of diabetes compared to the general population.

Addressing this disparity requires the integration of comprehensive diabetic care within SRFCs to ensure evidence-based interventions that can improve outcomes for these underserved communities. This paper outlines a strategic framework for integrating diabetic services at one of the nation's largest SRFCs. Our approach includes a thorough assessment of patient needs, the development of an efficient clinical workflow, and the implementation of targeted diabetic interventions, all within the financial constraints typical of free clinics. By providing a detailed model for enhancing diabetic care, this paper aims to guide other SRFCs not only in reducing the long-term health impacts of unmanaged diabetes in vulnerable populations but also in selecting cost-effective interventions that maximize the use of limited resources.

Serena A. Maag MS

Septic shock of unknown etiology

Serena A. Maag MS, Brianna N. Bailey MS, Mathieu K. Holt BS, Danyal S. Butt MD, Bibek M. Shrestha MD, Ayman Iqbal MD, Davontae Willis MD, Srini K. Hejeebu DO

Introduction: Septic shock, marked by hypotension, tachycardia, multi-organ failure, and altered mental status (AMS), presents significant diagnostic challenges. Conditions such as untreated liver cirrhosis, acute kidney injury (AKI), and rabies can mimic sepsis. This case report discusses the complexities of diagnosing the cause of septic shock in an Amish woman with limited healthcare access, emphasizing the need for a broad differential diagnosis in such populations.
Case Presentation: An 81-year-old woman with a history of hypertension presented with fever, hypotension, new-onset atrial fibrillation. She was admitted to the ICU for pressor support as labs revealed leukocytosis and elevated inflammatory markers. Urinalysis, blood cultures, ammonia levels, and Hepatitis B and C tests were negative. Despite various antibiotic trials and consultations, no definitive diagnosis was made. She continued to deteriorate, and family decided to withdraw support. Infectious Disease considered Histoplasma, Aspergillus, West Nile virus, and rabies. Due to lack of a lumbar puncture (LP) during a week-long admission at an outside hospital, Internal Medicine recommended an LP. Neurology deemed the patient too unstable for the procedure and suggested an MRI. The patient was discharged to home hospice before MRI was performed.
Discussion: The cause of septic shock and potential encephalopathy of unknown origin can be particularly challenging to diagnose, especially in populations with limited access to healthcare. This case underscores the importance of early lumbar puncture in refining the differential diagnosis and emphasizes the need to consider both common and rare causes of sepsis and AMS to avoid diagnostic anchoring and improve patient outcomes.
Conclusion: For patients with sepsis and AMS, especially those from backgrounds with limited healthcare access, considering rare causes alongside common ones is crucial to avoid diagnostic biases and ensure effective management.

Rida Z. Naqvi BS

The necrotic mystery of dapagliflozin

Rida Z. Naqvi BS, Anu Garg MD, Kiya Safavi MD

Background: Pancreatitis is clinically diagnosed by the presence of two or more of the following: epigastric pain which usually radiates to the back, elevated serum lipase or amylase, and consistent imaging findings. Complications may include insulin-dependent diabetes mellitus, failure to thrive, pancreatic pseudocysts, as well as necrotizing pancreatitis. Dapagliflozin, an SGLT-2 inhibitor commonly used in the management of type 2 diabetes mellitus, also reduces mortality in chronic kidney disease and heart failure. While dehydration and UTIs are common complications, acute pancreatitis may rarely occur. There are no reported cases of necrotizing pancreatitis, a life-threatening complication, caused solely by SGLT-2 inhibitors. We present the case of a 72-year-old female with necrotizing pancreatitis secondary to Dapagliflozin.
Case Presentation: A 72-year-old female with insulin-dependent type 2 diabetes managed with Dapagliflozin, coronary artery disease, and nonalcoholic steatohepatitis presented with dark brown emesis. Initial workup revealed anion gap metabolic acidosis, lipase of 16,000, and lactate of 2.7. CT and MRI demonstrated

edematous pancreatitis with necrotic tissue. The patient denied any history of alcohol or tobacco use, gallstones, previous bouts of pancreatitis, and recent abdominal trauma. The home medications including insulin, allopurinol, clopidogrel, aspirin, and carvedilol were not associated with pancreatitis. After treatment with IV antibiotics, she was discharged but then returned with worsening symptoms. CT demonstrated progressive necrosis. She was treated with additional IV antibiotics, ERCP with sphincterotomy, endoscopic cystogastrostomy, and necrosectomy before discharge. She was again admitted with chest pain and hypotension. A CTA chest revealed bilateral pleural effusions and a gas-containing fluid collection. She received further IV antibiotics and necrosectomy before her final discharge.
Discussion: While studies suggest that SGLT-2 inhibitors are not associated with pancreatitis, the rising number of cases highlights the importance of reassessing their association (1). This potential for severe adverse effects emphasizes the need for careful monitoring and further research.

Antara Nigam MS

Clinical Case Review of Bilateral Retinal Metastisis

Antara Nigam MS, Kashvi Patel MD/MBA , Shivani Rana MS, Anu Garg MD

Bilateral retinal metastasis is a rare disease that represents less than 1% of ocular metastases. Additionally, the prevalence of ocular metastases overall is only 5-10%. It is uncommonly found due to the absence of a lymphatic system in the eye. Ocular metastasis is spread hematogenously, and the retina only receives 5% of blood flow, contributing to the rarity of this condition. Retinal metastasis has been reported to mimic symptoms of retinitis which include watery eye discharge, conjunctival injection and pain with ocular movement which leads to a harder diagnosis. Treatment options for retinal metastasis include systemic chemotherapy, intravitreal chemotherapy, plaque radiotherapy. However, despite treatment, retinal metastasis often has a poor prognosis. This is a case of a 65-year-old woman with a history of breast carcinoma status post mastectomy who initially presented with metastatic infiltration of the lung and liver. However, she later developed an interesting case of retinal metastasis which presented as symptoms of retinitis and indicated widespread dissemination of an unknown primary neoplasm.

Manthanbhai S. Patel MD

The hidden burden: How malnutrition worsens outcomes in pulmonary hypertension patients

Manthanbhai S. Patel MD, Nahush R. Bansal MD

Background: Pulmonary hypertension is a serious condition with high morbidity and mortality. While much is known about its inherent risks, there is limited data on how modifiable factors like malnutrition impact outcomes in these patients. Malnutrition has been linked to worse outcomes in various cardiac conditions. This study aims to explore the influence of malnutrition on in-hospital outcomes for patients with pulmonary hypertension, with attention to the severity of malnutrition.
Methods: We conducted a retrospective cohort study using the National Inpatient Sample database, including adult patients with a primary diagnosis of pulmonary hypertension. Outcomes were compared between those with and without malnutrition, identified via ICD-10 codes. Multivariate logistic and linear regression analyses adjusted for confounders, and statistical analysis was conducted using STATA software.
Results: Out of 11,930 patients with pulmonary hypertension, 509 (4.27%) were identified as having concomitant malnutrition. These patients faced significantly worse outcomes compared to their well-nourished counterparts. Specifically, malnourished patients had a nearly fourfold increase in mortality rates (aOR 3.91; 95%CI 2.20-6.97), prolonged hospital stays (average increase of 11.37 days; P<0.001), and substantially higher hospital charges (average increase of $348,234; P<0.001). Additionally, these patients experienced higher incidences of cardiogenic shock (aOR 2.57; 95% CI 1.53-4.33; P<0.001), acute respiratory failure (aOR 1.77; 95%CI 1.15-2.74; P=0.01), and acute kidney injury (aOR 2.07; 95%CI 1.32-3.28; P=0.01). Outcomes worsened in proportion to the severity of malnutrition, with those suffering from severe malnutrition faring the worst.

Conclusions: Malnutrition in patients with pulmonary hypertension significantly exacerbates their risk of mortality, extends their hospital stay, inflates hospitalization costs, and increases the likelihood of severe complications such as cardiogenic shock, acute respiratory failure, and acute kidney injury. These adverse effects are directly correlated with the degree of malnutrition, underscoring the critical need for timely and tailored nutritional interventions to improve patient outcomes.

Ayda Fathollah Pour

Atypical hemolytic uremic syndrome in a postoperative patient: Diagnostic challenges and therapeutic strategies

Ayda Fathollah Pour, Alborz Sherafati, Mani Askari, Hoda Shabpiray, Sherwin Steven Foster, Shaun Kumar Joshi

Introduction: Atypical Hemolytic Uremic Syndrome (aHUS) is a rare, life-threatening condition characterized by microangiopathic hemolytic anemia, thrombocytopenia, and acute renal failure. This case report highlights a rare instance of aHUS triggered by a recent surgery.
Case Presentation: A 67-year-old female with history of chronic kidney disease (CKD) and recent total knee replacement surgery presented to the hospital with poor appetite, cough, fever, chills, and malaise. Her white blood cell count (WBC) was elevated, and her chest X-ray showed consolidation of the left lower lobe. She was initially diagnosed with sepsis secondary to pneumonia. Laboratory results also revealed a creatinine level of 5.70 mg/dL, compatible with acute kidney injury (AKI) on CKD. Despite broad-spectrum antibiotic therapy, the patient's condition deteriorated with worsening renal function. Additional tests showed elevated lactate dehydrogenase (LDH) and a significant drop in hemoglobin and platelet counts. Coagulation factors and fibrinogen levels were within normal limits. The patient's blood cultures remained negative and her procalcitonin levels were not significantly elevated, making sepsis unlikely. The patient underwent a renal biopsy to investigate the cause of AKI, which confirmed the presence of thrombotic microangiopathy (TMA) consistent with a diagnosis of aHUS. The patient did not have any diarrhea or abdominal pain, making Shiga toxin-associated HUS unlikely. Her negative blood cultures and low procalcitonin level were also against an infectious etiology. However, the onset of the patient's symptoms shortly after her total knee replacement surgery strongly pointed to the surgery as the most likely trigger for aHUS. The patient was treated with eculizumab, a monoclonal antibody targeting complement protein C5. Her condition started to improve after receiving eculizumab, supporting the complement dysregulation as the primary driver of her condition.
Conclusion: aHUS can be triggered by surgery in elderly patients. Prompt diagnosis and early intervention with complement inhibitors like eculizumab could be lifesaving.

Nahshon A. Puente

MTERF2, RPS6KA5, and SYNE2 define the link between systemic lupus erythematosus and breast cancer

Nahshon A. Puente, Mahasin Osman, MSc, PhD, Sadik A. Khuder, DDS, MPH, PhD

Background: Systemic lupus erythematosus (SLE) is a complex heterogenous systemic autoimmune disease. Previous studies have shown that SLE may be related to breast cancer (BC), but the mechanism underlying their relationship is still unclear.
Objectives: To explore the genetic molecular mechanisms common to and core genes shared by BC and SLE.
Methods: SLE (GSEl 75839) and BC (GSEl 83635) RNA-seq data were downloaded from the National Center for Biotechnology Information (NCBI) GEO database. GEO2R was used to identify the top 1000 differentially expressed genes for each disease. Weighted gene co-expression network analysis (WGCNA) was used to identify co-expression modules that were significantly correlated with each disease state. Three core shared genes were screened out and validated using GEO2R differential expression analysis results.
Results: Using GEO2R, 44 genes were identified as shared by BC and SLE. Using WGCNA, two modules were identified as significantly correlated to SLE and BC, from which three core shared genes-MTERF2, RPS6KA5,

and SYNE2-were screened out and validated by the GEO2R results. All three genes were significantly downregulated in both diseases.
Conclusion: The present study identified three core genes shared by SLE and BC that may be involved in the relationship between the two diseases.

Nahshon A. Puente

RNA-seq data analysis uncovers a link between systemic lupus erythematosus and glioblastoma

Nahshon A. Puente, Mahasin Osman, MSc, PhD, Sadik A. Khuder, DDS, MPH, PhD

Background: Systemic lupus erythematosus (SLE) is a complex heterogenous systemic autoimmune disease. Our previous study using US Healthcare Cost and Utilization Project (HCUP) 2020 National Inpatient Sample (NIS) data showed that SLE may reduce the risk of glioblastoma (GB), but the mechanism underlying this reduction is still unclear.
Objectives: To explore the genetic molecular mechanisms and core genes underlying GB risk reduction in SLE.
Methods: SLE and GB RNA-seq data were downloaded from the National Center for Biotechnology Information (NCBI) Gene Expression Omnibus (GEO) database. GEO2R was used to identify the top 1000 differentially expressed genes for each disease. Weighted gene co-expression network analysis (WGCNA) was used to identify co-expression modules that were significantly correlated with each disease state. Six core shared genes were screened out and validated using GEO2R differential expression analysis results.
Results: Using WGCNA, three modules were identified as significantly correlated to SLE and GB. Six core shared genes–CEMIP, GIMAP6, NCAM1, RPS6KA5, SBSPON, and UHRF1–were screened out. Of these genes, CEMIP, GIMAP, RPS6KA5, and SBSPON were significantly downregulated in both diseases. Interestingly, NCAM1, and UHRF1 showed differences in their expression between SLE and GB and may contribute to the reduction in GB risk observed previously.
Conclusion: The present study identified six core genes shared by SLE and GB, of which two–NCAM1, and UHRF1–may be involved in GB risk reduction.

Elizabeth A. Schumacher MBA

Evaluating attitudes and educational gaps in transgender healthcare among healthcare professionals at a university medical center

Elizabeth A. Schumacher MBA, Sara J. Zandvakili, Hoda Shabpiray MD, Lori M DeShetler PhD, Sadik Khuder PhD, Basil Akpunonu MD, Anand Mutgi MD, Mani K. Askari MD

Introduction: Of the estimated 1.6 million transgender individuals (TI) in the USA (1), many do not seek regular medical care due to fear and stigma (2). Studies demonstrate healthcare providers struggle to provide appropriate gender-affirming care to this group. This deficit is often linked to inadequate knowledge and training (3-4). Educating providers about the needs of TI is the most effective way to improve healthcare for this population (3, 5, 6). Our study assesses healthcare professionals' attitude, comfort, and prior education of TI's care.
Methods: A survey was delivered to the target group across different specialties. The data are multi-institutional, with preliminary data collected from students and physicians working in a tertiary university-based medical center. Survey participation was voluntary with no reward or penalty tied to submission, and no identifying data was collected. The 25-question, Likert scale rating, survey assesses attitudes regarding transgender care. The survey received IRB approval for distribution and use of human subject data. Written informed consent was collected.
Results: Demographic analysis showed 51% of the respondents were female at birth, 45% male at birth, and 4% did not disclose. Eighty-four percent of the respondents were <40 years old. Female respondents showed more positive attitudes toward transgenders than males ($P<0.0001$). Males were more likely to believe they received appropriate education to medically manage TI than females (P 0.002). Medical students' interest in more education on healthcare needs of TI was statistically significantly higher than of faculty (P 0.038).

Elizabeth Schumacher, MBA

Hyponatremia in Parkinson's Disease: The impact of carbidopa-levodopa therapy

Elizabeth Schumacher, MBA, Nora Abdul-Aziz, MS, Hoda Shabpiray MD, Amin Sanei Moghaddam, MD, Mani Khorsand Askari, MD

Parkinson's Disease is a progressive neurodegenerative disorder marked by the loss of dopamine-producing neurons in the substantia nigra, a key area of the brain involved in movement regulation. Managing patients with Parkinson's disease (PD) involves varied treatments, although the progressive nature of PD and the side effects associated with long-term use of these medications present ongoing challenges. Treatment of PD primarily involves the restoration of dopamine function in the brain. Carbidopa-levodopa, which increases brain dopamine levels, remains the most effective method for managing motor symptoms but often leads to complications like effectiveness fluctuations and dyskinesias development over time. The adverse effects most commonly reported from carbidopa-levodopa are dyskinesias, nausea, vomiting, insomnia, impulse control disorders, and orthostatic hypotension [4]. Few cases from the literature have demonstrated an association between Levodopa and hyponatremia. This case study involves a 69-year-old male with PD who developed gradual asymptomatic hyponatremia after starting Carbidopa-levodopa. His sodium levels, initially stable, declined significantly over several months. His sodium levels improved to pre-treatment levels with fluid restriction and increased protein intake without interruption in Carbidopa-levodopa therapy. This case highlights the need for regular monitoring of sodium levels in PD patients on dopaminergic medications with timely and multidisciplinary strategies to prevent potentially serious complications.

Rachel Senchenkova

Medical management of a severe case of anorexia nervosa

Rachel Senchenkova, Sabrina Khuder MD, Hoda Shabpiray MD

Introduction: Anorexia nervosa (AN) is a psychiatric disorder characterized by severe food restriction and an intense fear of weight gain. Refeeding edema is common during the refeeding process in anorexia nervosa. This case demonstrates a severe presentation of refeeding edema in a patient with a BMI of 10 as a result of nutritional rehabilitation which caused significant pain and distress.
Case Presentation: A 38-year-old Caucasian female was admitted to the hospital with abdominal pain and fecal incontinence. Past medical history was significant for AN, bipolar disorder, and generalized anxiety disorder. Laboratory results showed hypokalemia (potassium at 2.7 mEq/L), hypoalbuminemia (albumin at 3.0 g/dL) and total protein at 4.3 g/dL. Treatment was started for electrolyte imbalance and a gradual increase in caloric intake. Refeeding led to the development of bilateral lower extremity pitting edema, edema in the abdomen, significant weight gain, severe leg pain rated 10 out of 10 and distress due to weight gain. Initial management including monitoring fluid intake, low-salt diet, leg elevation and compression stockings were ineffective. An echocardiogram was performed to rule out heart failure which can occur in refeeding syndrome which showed a normal ejection fraction. Spironolactone, and eventually Furosemide, were started for short term management which resolved edema.
Discussion: Refeeding edema is common during the refeeding process in anorexia nervosa and likely results from the increased release of insulin associated with increased caloric intake which leads to sodium retention through increased reabsorption of sodium in the renal distal tubules. Additionally, hypoalbuminemia can contribute to the development of peripheral edema during the early refeeding phase. While the clinical significance of refeeding edema is usually minor; it can occasionally cause discomfort. Peripheral edema, often mistaken for weight gain, can lead to unnecessary psychiatric distress in an already vulnerable group of patients. Although diuretics are typically not used, they can be considered for short-term management if edema becomes severe, causing tissue breakdown or significant pain. Clinicians should explain to the patient that nutritional rehabilitation must continue for edema to stabilize and resolve.

Alyssa Siano MS

A case of drug-induced liver injury secondary to ceftriaxone

Alyssa Siano MS, Rupesh Ramtel MD, Mani Askari MD

Ceftriaxone continues to be one of the most prescribed antibiotics and has a relatively low incidence of liver injury. We present this case to raise awareness to this rare side effect associated with a commonly prescribed antibiotic used to treat a wide range of conditions.

We present a case of drug-induced liver injury in an 81-year-old male with no prior history of liver-related health issues. Following the diagnosis of E. coli bacteremia the patient was started on ceftriaxone and was later found to have elevated liver enzymes. It was originally believed that the elevated liver enzymes were secondary to hepatic congestion and the patient was started back on his home diuretics to target this issue. However, his liver enzymes remained elevated. abdominal ultrasound showed gallbladder wall thickening, likely due to passive congestion, but no evidence of gallstones. It also showed a liver with a homogenous pattern, no focal mass, no ascites, and a patent portal vein. Laboratory analysis revealed a negative viral hepatitis panel. Ceftriaxone was then discontinued and switched to Unasyn. The patient's liver enzymes then began to downtrend and the diagnosis of drug-induced liver injury was made.

This case report adds to the growing body of evidence that, although rare, ceftriaxone can cause significant liver injury. The case highlights the importance of close monitoring of liver function in patients receiving ceftriaxone, particularly those with underlying health conditions that may predispose them to drug-induced hepatotoxicity. Early identification and discontinuation of the offending agent are essential to preventing further liver damage and ensuring patient safety.

Juliana Simon

Multisystem organ dysfunction in plasma cell dyscrasias: A case of MGUS and ATTR cardiac amyloidosis

Juliana Simon, Gabriella-Marie Dela Cruz-Smilo, Robert Jame MD, Divya Vijendra MD

Introduction: Amyloidosis is a heterogenous, multisystem disease caused by deposition of amyloid proteins in various organ systems. Differentiating immunoglobulin light chain (AL) from transthyretin (ATTR) amyloidosis is critical in guiding management and should be thoroughly investigated in patients with plasma cell dyscrasia and signs concerning for multisystemic organ dysfunction.
Case Presentation: A 73-year-old male was being followed by the Hematology/Oncology clinic for management of light chain monoclonal gammopathy of unknown significance (MGUS). Patient was diagnosed in 2022, after bone marrow biopsy revealed 5% plasma cells and no evidence of amyloidosis. Immunofixation electrophoresis of urine was positive for elevated light chains. In October 2023, the patient began experiencing dyspnea on exertion. Transthoracic echocardiogram and pyrophosphate amyloid imaging demonstrated evidence of ATTR cardiac amyloidosis. One month later, he underwent abdominal ultrasound for further evaluation of abdominal pain and elevated alkaline phosphatase. Perihepatic ascites and diffuse hepatocellular disease were visualized, suggestive of cirrhosis, despite negative history of alcohol use or hepatitis infection. Given the patient's multi-organ dysfunction secondary to MGUS, assessment of AL amyloidosis was extensively pursued with biopsy Congo red staining of abdominal fat pad, liver, and bone marrow biopsy samples displayed no evidence of amyloidosis. These findings led to the diagnosis of concurrent ATTR cardiac amyloidosis and MGUS. Cardiology initiated aggressive diuresis alongside tafamidis to stabilize transthyretin protein and reduce amyloid deposition in myocardial tissue.
Conclusion: This case demonstrates the importance of thoroughly evaluating for amyloidosis in patients with plasma cell dyscrasias, as treatment of AL amyloidosis differs from ATTR and necessitates chemotherapy initiation. Although this patient was found to have ATTR amyloidosis and findings suggestive of cardiac cirrhosis, it is necessary to determine that multisystemic symptoms are not attributable to AL. Physicians should

conduct a comprehensive clinical evaluation and detailed history when assessing patients with MGUS and multisystemic organ dysfunction.

Hannah M. Starbuck

Straight to the dome - Cefepime induced neurotoxicity

Hannah M. Starbuck, Zachary T. Holtzapple MD, Muhammad Usman Ali MD

Introduction: The commonly used cephalosporin, Cefepime, has been reported to cause encephalopathy at an incidence rate of up to 14.3%. This neurotoxicity is highly dependent on route of administration, continuous versus intermittent dosing, renal function, and patient population. (1-2)
Case Presentation: An 80-year-old male with no history of kidney disease presented to the emergency department as a stroke alert. The patient had a history of chronic back pain requiring multiple surgeries complicated by cerebral spinal fluid cultures growing Pseudomonas Aeruginosa. The patient was started on intravenous Cefepime one month prior to admission. Magnetic resonance imaging of the brain revealed no intracranial abnormalities nor signs of cerebral vascular accident. The patient was hemodynamically stable and noted to have stage 3 acute kidney injury. Electroencephalogram (EEG) revealed myoclonic seizure activity. The diagnosis of Cefepime induced neurotoxicity was made as the patient was on the standard dose of Cefepime in the setting of worsening renal function. The patient was transferred to the intensive care unit for emergent dialysis followed by continuous renal replacement therapy (CRRT). Subsequently, mental status continued to improve with resolution of seizure activity on EEG.
Discussion: Cefepime induced neurotoxicity (CIN) should be considered a diagnosis of exclusion requiring high clinical suspicion and pertinent history. EEG findings are typically characterized by generalized periodic discharges with triphasic wave or nonconvulsive status epilepticus. (3) Patients with impaired renal function are at an increased risk of CIN due to reduced clearance. Hemodialysis effectively removes Cefepime due to its pharmacologic properties including low protein binding and low molecular weight. The symptoms of CIN can last up to 2-3 days in patients with severe kidney injury without dialysis. (4)

HEMATOLOGY/ONCOLOGY

Nora Abdul-Aziz MS

Unmasking hepatocellular carcinoma in a non-cirrhotic liver: A case report of an advanced tumor in the absence of traditional risk factors

Nora Abdul-Aziz MS, Omar Abdul-Aziz MS, Elizabeth Schumacher MBA, Noor Abdulhameed BS, Divya Vijendra MD, Ellen Hagopian MD

Introduction: Hepatocellular carcinoma (HCC) arises from chronic liver damage leading to dysregulated hepatocyte proliferation and tumor formation. HCC is predominantly associated with cirrhosis and traditional risk factors such as chronic hepatitis B and C, alcohol use, and non-alcoholic steatohepatitis. Long-standing diabetes can lead to steatosis and increase the risk of developing HCC, yet current screening guidelines do not include the diabetic population. This case emphasizes the importance of developing screening guidelines for HCC in diabetics as exemplified by this patient's presentation.
Case Presentation: A 73-year-old native Nigerian male with type 2 diabetes mellitus presented to the emergency department in March 2024 for evaluation of abdominal pain. He denied history of alcohol abuse, hepatitis B or C. A CT abdomen demonstrated a large left liver tumor. Further work-up demonstrated an elevated AFP at 131,025. CT abdomen in April 2024 demonstrated a large heterogeneously enhancing mass in the left hepatic lobe, measuring 13.8 x 10.1 x 10.5 cm. US elastography demonstrated moderate fibrosis of the liver. Portal hepatic venous duplex US demonstrated patent portal vein with normal directional flow. In May 2024, the patient underwent left hepatic artery chemoembolization. In July 2024, he underwent surgery at which time, a larger tumor encompassing the entire left liver and involving the middle and left hepatic veins was found. A left

hepatectomy was performed. Pathology demonstrated a moderately to poorly differentiated HCC measuring 18.0 cm with focal treatment-associated necrosis (10%). The background liver did not demonstrate cirrhosis.
Conclusion: Hepatocellular carcinoma is a malignancy typically associated with chronic liver disease, such as cirrhosis, and traditional risk factors like hepatitis B and C, alcohol use, or non-alcoholic steatohepatitis. Chronic diabetes can result in steatosis and elevate the risk of HCC; however, existing screening guidelines do not encompass the diabetic population. HCC in a non-cirrhotic liver is a complex condition characterized by distinct risk factors, pathogenesis, clinical features, management, and prognosis compared to its cirrhotic counterpart. This case highlights the need for broader studies to include the incidence of HCC in diabetic populations to develop screening recommendations.

Omar Abdul-Aziz MS

Achenbach Syndrome: A diagnostic dilemma

Omar Abdul-Aziz MS, Nora Abdul-Aziz MS, Elizabeth Schumacher MBA, Noor Abdulhameed BS, Divya Vijendra, MD

Introduction: Achenbach syndrome is a poorly understood condition involving paroxysmal hematomas of the distal upper extremity digits. Achenbach is unique in which this condition is not associated with more serious underlying autoimmune etiologies and is a diagnosis of exclusion. Due to Achenbach syndrome's rarity, it can pose a diagnostic challenge to clinicians who may suspect a more serious underlying condition.
Case Presentation: A 44-year-old female with a past medical history significant for Raynaud's disease presented to the Hematology/Oncology clinic complaining of easy bruising and bleeding of her fingers. A nurse in the operating room, she reported a 2-3-year history of digital splitting that bled easily, often resolving within a day. The patient denied digital ulcers or gangrene. Her family medical history is significant for similar symptoms in both her father and sister. Initial workup, including coagulation studies, platelet aggregation, Von Willebrand screen, and Complete Blood Count with differential, were unremarkable. However, an abnormally elevated ANA titer of 1:160 prompted referral to rheumatology. Further testing for autoimmune diseases, including lupus anticoagulant, cardiolipin antibody, anti-double-stranded DNA antibodies, anti-scleroderma antibodies, complement levels, anti-centromere antibodies, Anti-Rho (SS-A), and Anti-La (SS-B), was negative. Physical examination revealed elongated capillaries with microhemorrhage in the right index finger but no sclerodactyly. Based on these findings, a diagnosis of Achenbach syndrome was made. Given the absence of significant underlying pathology and the characteristic clinical presentation, no further testing or investigation was deemed necessary.
Conclusion: Achenbach syndrome, a rare condition characterized by paroxysmal hematomas in the distal upper extremity digits, presents a diagnostic challenge due to its atypical presentation and potential for misdiagnosis. While many autoimmune diseases can exhibit similar clinical features, Achenbach syndrome is distinct in its lack of association with more serious underlying conditions. Recognizing Achenbach syndrome as a diagnosis of exclusion is crucial to avoid unnecessary investigations and interventions.

Noor Abdulhameed, B.S.

Recurrent solitary fibrous tumor with severe hypoglycemia: A case of tumor-induced metabolic disturbances

Noor Abdulhameed, B.S., Elizabeth Schumacher MBA, Omar Abdul-Aziz M.S., Nora Abdul-Aziz M.S., Divya Vijendra, MD, Ellen Hagopian, MD

Introduction: Solitary fibrous tumors (SFTs) are rare mesenchymal neoplasms originating in the pleura but also appear in extrapleural sites such as the abdomen. Although often benign, they can exhibit malignant behavior, particularly upon recurrence. This case highlights the diagnostic and management challenges of SFTs, particularly when complicated by metabolic disturbances like hypoglycemia.
Case Presentation: In 2010, the patient presented with a large abdominal mass which was resected. Pathology identified it as a nonmalignant "fibrous" tumor with negative margins. The patient has radiation exposure history from Chernobyl during military service in Germany. In September 2023, the patient returned with

abdominal distention and altered mental status secondary to severe hypoglycemia. Laboratory tests revealed a serum glucose of 34 mg/dL, low insulin, and low insulin-like growth factor-2 (IGF-2). The hemoglobin A1c was 4.9%, suggesting the hypoglycemia was an acute issue and not poor glycemic control. CT revealed a large, heterogeneous mesenteric mass adjacent the small bowel and left colon, indicating tumor recurrence (Fig. 1). In October 2023, en bloc resection of the mass and small bowel was performed with placement of bilateral ureteral stents (Fig. 2). Pathology confirmed recurrent SFT (Fig. 3A-C). Hypoglycemia resolved post-surgery. Surveillance was advised after multidisciplinary discussion. At follow-up July 2024, CT scans showed no tumor recurrence.
Conclusion: SFTs, while generally benign, can exhibit malignant behavior, especially when recurrent, large, or with atypical histology. This patient's recurrence, coupled with hypoglycemia, suggests an aggressive tumor phenotype. This patient's hypoglycemia can be attributed to ectopic IGF-2 produced by the SFT. Low IGF-2 and insulin levels with the large mass indicate the tumor's role in mediating episodic hypoglycemia. Recurrent SFTs underscore the complex interplay between tumor biology and metabolic disturbances. Continuous surveillance and prompt intervention is crucial, given recurrence risk and complications. Further research of molecular mechanisms driving the hypoglycemia in SFTs may enhance management strategies.

Umeer Ashraf MD, MSHA

Effective management of carfilzomib-induced thrombotic microangiopathy in multiple myeloma using eculizumab

Umeer Ashraf MD, MSHA, Jennifer Kim BS, Danae M. Hamouda MD

Introduction: Carfilzomib, a proteasome inhibitor, is used to treat refractory multiple myeloma (MM). Although rare, there have been reports of carfilzomib-induced thrombotic microangiopathy (TMA), a serious condition characterized by thrombocytopenia, hemolytic anemia, and acute kidney injury. Early detection and appropriate management of TMA are crucial due to its high risk of mortality and morbidity. Currently, there are no established guidelines for managing carfilzomib-induced TMA. Here, we present a case of a 71-year-old woman with refractory MM who developed TMA following carfilzomib treatment and was successfully treated with eculizumab.
Case Presentation: The patient, with a history of relapsed IgG-kappa MM, presented with fatigue and shortness of breath. She had received her first dose of carfilzomib three weeks prior. Initial tests revealed acute kidney injury, anemia, and severe thrombocytopenia. Coagulation studies were unremarkable. Haptoglobin was undetectable, while D-dimer and lactate dehydrogenase were elevated. Peripheral blood smear showed schistocytes, supporting a diagnosis of microangiopathic hemolytic anemia. Imaging studies revealed right pneumonic infiltrate and bilateral pleural effusions but no intra-abdominal pathology.
Plasmapheresis was initiated, and ADAMTS-13 activity, coming back at 91%, ruled out thrombotic thrombocytopenic purpura (TTP). Hemolytic uremic syndrome (HUS) and atypical HUS (aHUS) were also excluded through negative stool shiga-toxin and normal complement levels, respectively. Eculizumab was then administered, dramatically improving platelet count and hemolytic parameters within 24 hours. The patient was discharged and continues on weekly eculizumab treatment.
Conclusion: Diagnosing drug-induced TMA is challenging as it requires ruling out conditions like DIC, TTP, HUS, and aHUS. Plasmapheresis, while commonly used, often has limited impact due to TMA's heterogeneous nature. Identifying the underlying cause and appropriate management are essential. This case highlights the potential of eculizumab in treating carfilzomib-induced TMA and may inform future treatment protocols and understanding of the disease.

Umeer Ashraf MD, MSHA

Investigate the familial clustering of antiphospholipid syndrome with venous thromboembolism

Umeer Ashraf MD, MSHA, Jennifer Kim BS, Divya Vijendra MD, Mary R. Smith MD

Introduction: Antiphospholipid syndrome (APS) is characterized by vascular thrombosis, recurring obstetric complications, and the persistent presence of antiphospholipid antibodies (aPL). Despite extensive research, the precise cause of APS remains elusive. However, studies have identified a correlation between aPL and specific genes/alleles within the major histocompatibility complex, offering valuable insights into understanding APS. We present the case of a 68-year-old man with a diagnosis of thromboembolism and a notable family history of APS.
Case Presentation: A 68-year-old man with ulcerative colitis and a recent prostate cancer diagnosis experienced vein thrombosis in his left lower extremity and pulmonary embolism following radical prostatectomy. Upon discharge, he was initiated on apixaban. During a follow-up visit, the patient recounted the significant history of thromboembolism in both his parents, along with three of his siblings being diagnosed with APS-related deep vein thrombosis. These cases included a brother with lung cancer, a sister with lupus, and another sister with breast cancer. His mother passed away from a stroke at age 39, and his father died from a pulmonary embolism. Owing to the extensive family history, a thrombophilia workup was conducted, revealing evidence of triple positive APS. Consequently, the patient was switched to lifelong anticoagulation with warfarin.
Discussion: Although the underlying mechanisms of APS continue to elude clear understanding, genetic factors play a pivotal role in some instances. Research indicates a familial clustering of aPL antibodies, often with a single index case, and a high prevalence of underlying autoimmune conditions. To the best of our knowledge, this represents the first documented case of multiple family members with APS and verified aPL presence, signifying related thromboembolic events. This case underscores the broader implications of the intricate nature of APS and prompts consideration for genetic testing to explore its genetic underpinnings further.

Brianna N. Bailey MS
Medical management of pigmented villonodular synovitis of the right ankle and foot
Brianna N. Bailey MS, Anan Bseiso MD, Divya G. Vijendra MD

Introduction: Pigmented Villonodular Synovitis (PVNS) is a rare, benign condition involving the overgrowth of synovial tissue, typically affecting the knee but also other joints like the hip and ankle. It causes joint pain, swelling, and reduced mobility, and can be either localized or diffuse. While the exact cause is unclear, it may involve inflammatory or neoplastic processes. Diagnosis relies on clinical symptoms, imaging (MRI), and histology. Though non-malignant, PVNS can be aggressive and cause joint damage if untreated. Treatment usually involves surgical resection or synovectomy, sometimes with radiotherapy to prevent recurrence.
Case Presentation: A 66-year-old female with fibromyalgia and osteoporosis presented with right ankle pain and swelling. Radiographs in September 2023 showed severe degenerative changes in the tibiotalar and first MTP joints, with joint effusion and varus alignment. MRI in October 2023 confirmed advanced osteoarthritis and synovial thickening. After temporary relief from a cortisone injection, a core biopsy in July 2024 revealed Pigmented Villonodular Synovitis (PVNS). With no bacterial growth, the patient declined surgery and was referred to hematology/oncology for treatment with pexidartinib, a CSF-1 inhibitor.
Discussion: The management of Pigmented Villonodular Synovitis (PVNS) has evolved from relying solely on surgery to incorporating therapies that reduce recurrence and manage challenging cases. While surgical resection, either via arthroscopy or open synovectomy, remains the primary treatment, diffuse PVNS poses a higher risk of recurrence and joint damage. Recent advancements have introduced CSF1R inhibitors like pexidartinib, which target the disease's molecular drivers, offering a non-surgical option for diffuse or refractory cases. Other therapies, such as radiation synovectomy, have also shown promise but carry potential risks. Ultimately, treatment should be individualized based on disease severity and patient health.

Yoon-Jung Chang
Diagnosis and management of retroperitoneal leiomyoma: A case report
Yoon-Jung Chang, Juliana Simon, Divya Vijendra MD, Ellen Hagopian MD

Introduction: Leiomyomas are benign tumors of smooth muscle cells. If benign, they can be further categorized into two subtypes: leiomyomas of somatic soft tissue and retroperitoneal-abdominal leiomyomas. While uterine leiomyomas are encountered frequently, retroperitoneal/abdominal leiomyomas are exceedingly rare, especially among male patients.
Case Presentation: Patient is a 69-year-old male who initially presented for evaluation of bilateral lower quadrant pain, described as sharp and "belt-like" in distribution. Patient also experienced a sensation to void and defecate, but the inability to do so. He was diagnosed with diverticulitis and initially treated with oral antibiotics. Subsequent imaging showed a large soft tissue mass in the retroperitoneal cavity, measuring approximately 20 cm, with superior extension into the left upper quadrant and possible involvement of the iliac vessels and bladder. A PET-CT did not demonstrate significant activity. Core needle biopsy demonstrated features typical of benign leiomyomas, with no evidence of cytologic atypia or areas of necrosis. The patient's symptoms and tumor size were concerning for leiomyosarcoma, and surgical resection was recommended. At the time of retroperitoneal mass excision, the tumor was found to not involve surrounding structures. Pathology demonstrated spindle cells resembling normal smooth muscle cells, as well as evidence of increased mitotic activity. Immunohistochemistry was positive for desmin and focally reactive to estrogen receptor. Significant findings microscopically include small Mullerian remnants staining positive for estrogen receptor and PAX8, suggesting similarities to gynecologic leiomyoma. Final pathology diagnosis was a smooth muscle tumor of uncertain malignant potential and surveillance was recommended. At 6-month follow-up, patient was doing well without evidence of recurrence.
Conclusion: Retroperitoneal/abdominal leiomyomas in male patients are rare and diagnostically challenging. While histologically similar to benign gynecologic leiomyomas, these tumors require further evaluation for malignant potential, including resection and follow up management. Differentiation from leiomyosarcomas through radiologic and histologic findings should be further studied.

Cassidy E. Eby MD
Ulcerative colitis: Therapy or disease association with cancer development
Cassidy E. Eby MD, Hunter M. Eby MS, Mani K. Askari MD

Ulcerative colitis is an immune-mediated disease, a dysregulation of the immune-response that results in inflammation and triggers an inflammatory reaction in the colonic mucosa [1]. In ulcerative colitis, there are three circumstances in which cancer can arise. The first circumstance is related to the disease, the chronic inflammation of UC puts individuals with UC at 5.7 times higher risk of developing colorectal cancer then the general population [2,3]. The second circumstance is due to treatments related to the UC causing cancer, this is what this manuscript covers. Finally, the third circumstance is cancer not related to UC or the treatment of UC [3] Since the mechanism of ulcerative colitis leading to colorectal cancer is not known. It is important to mitigate the risk of cancer if possible and try to avoid treatments that increase an individual's risk of cancer. This review covers the different treatments plans used based on the severity of the disease and their malignancy risk.

Matthew D Geiger MD
A rare case of classical multiple myeloma presenting as cavernous sinus syndrome
Matthew D Geiger MD, Yusuf O. Hallak MD, Nahush Bansal MD, Bisher Sawaf MD, Abdallatif Dawoud MD, Michael Besly, Mani Askari MD

Background: Multiple Myeloma (MM) is a hematologic malignancy arising from a single plasma cell clone. It usually presents as constitutional symptoms related to hypercalcemia or hyperviscosity, pathologic fractures or bone pains, or incidentally through routine blood screening for other conditions. However, intracranial multiple myeloma is uncommon and rarely associated with concomitant cavernous sinus syndrome (CSS). CSS relates to any disease process affecting the cavernous sinus, it typically presents as proptosis, chemosis, ophthalmoplegia,

Horner's syndrome or trigeminal sensory loss on the ipsilateral side. Most commonly, it occurs in the setting of neoplasms, infections, inflammation, vascular or traumatic processes.
Case Presentation: In this report, we present the case of a 68-year-old male with subacute complaints of constipation, fatigue, nausea and vomiting on a background of a two-month history of worsening double vision, eye drooping, vertigo, and headaches who was found to have a cavernous sinus mass on imaging and classical findings of multiple myeloma (Anemia, Hypercalcemia, Kidney injury, and bone lytic lesions in the scalp) on further workup.
Conclusion: Although intracranial multiple myeloma is a rare phenomenon, it is advisable to maintain a high index of clinical suspicion and obtain further imaging to rule out cavernous syndrome when stumbling upon ocular symptoms in the setting of classical laboratory findings of multiple myeloma.

Ashaq Hussain
Loss of IQGAP1 lends advantage to female mice against predisposition to Type 2 diabetes
Ashaq Hussain, Rawan Moussa, Mahasin Osman

Type 2 Diabetes (T2D) is a chronic metabolic disorder characterized by hyperglycemia and elevated insulin resistance accompanied by low levels of insulin production in pancreatic β cells. Although sex differences in T2D manifestation have been recognized in human and animal models the molecular underpinning remains unclear. The scaffold signaling protein IQGAP1 has been implicated in insulin signaling and recycling and its mRNA is down regulated in humans with T2D. Here we report a female-specific protective role of IQGAP1 in mice against predisposition to developing T2D. Our results show significant metabolic differences in male and female mice lacking *iqgap1* gene (*iqgap1*$^{-/-}$). We find that the loss of *iqgap1* lends protection against obesity in male mice only under high fat diet (HFD) conditions. Compared to *iqgap1*$^{-/-}$ male mice, *iqgap1*$^{-/-}$ females exhibit significantly reduced body weight under both normal and HFD conditions. Measurements of physiological parameters revealed that *iqgap1*$^{-/-}$ females have increased insulin sensitivity and better plasma glucose clearance rate than their male counterparts. Analyses of the involved IQGAP1 pathway and organ site of action suggest involvement of ERα-IQGAP1-AMPKα signaling node in the pancreas. Further studies are underway to define how IQGAP1 executes his roles in this process differentially.

Alice Lu
Identification of a novel signaling platform as a cisplatin target in kidney injury
Alice Lu, Shahd S. Soutari, Mahasin A. Osman PhD

Cisplatin is an effective standard of care chemotherapeutic agent used in the clinic for treating a wide range of human tumors. However, kidney injury is an adverse side effect of cisplatin therapy for which treatment is unavailable due to lack of mechanistic understanding of cisplatin action. While cisplatin interferes with DNA replication in highly proliferation tumor cells, it is unknown how it affects normal kidney cells. Our cell biological analyses in cultured cells and animal models largely supported our novel hypothesis that cisplatin targets adhesion proteins in kidney epithelia, disrupts cell-cell contacts and ultimately leads to kidney damage. Here, we provide further supportive evidence from bioinformatics analyses, using the Nephroseq platform. Our RNAseq data analyses identified a distinct signal transduction and structural pathway composed of a receptor tyrosine kinase, a scaffold signal modulator and a group of cell adhesion proteins. Together, these proteins form a signaling platform that regulate secretion and ion transport across kidney tubules. These findings pave the way for devising targeted therapies for cisplatin-induced kidney damage while preserving its efficacy in oncology.

Wei-Shin Lu BS
Capecitabine, tucatinib, and trastuzumab chemotherapy-associated diabetic ketoacidosis: A case report
Wei-Shin Lu BS, Vaishnavi Aradhyula BS, Logan Shirk BSPS, Cheyenne Santos PharmD, Reilly Miles BSPS, Omar Horani MD, Hani Saad MD, Sarmed Mansur MD

Capecitabine is an antineoplastic drug which acts by inhibiting DNA synthesis. Tucatinib is a tyrosine kinase inhibitor that is selective for HER2 which inhibits cell proliferation. Trastuzumab is an anti-HER2 receptor monoclonal antibody. The combination of these three medications is used as chemotherapy for HER2-positive metastatic breast cancer due to increased antitumor activity. There are some reports of chemotherapy medications leading to type 1 diabetes; however, there is scarce literature documenting chemotherapy-induced diabetic ketoacidosis (DKA), and no literature that demonstrates development of DKA in association with these three medications. We present a case of a 54-year-old man with no prior history of diabetes mellitus who was admitted for DKA following chemotherapy with capecitabine, tucatinib, and trastuzumab to treat metastatic triple-positive breast cancer. The patient was also treated with radiosurgery and took dexamethasone for one month before the DKA episode. In the present visit, he was found to have new-onset diabetes with a1c of 12.2%; however, the panel of antibodies for type 1 diabetes screening, including GADA, IAA, IA2, and ZnT8, was negative. The patient subsequently recovered and was discharged on insulin therapy. Chemotherapy-associated DKA is a critical condition that needs appropriate assessment. We seek to highlight the importance of monitoring patients who begin chemotherapy with these agents to safeguard against this potentially life-threatening complication in the future.

Mario Markho

Identification of potential therapeutic perturbagens for CNS-metastatic retinoblastoma using in silico analysis of RB1 gene signatures

Mario Markho, Hunter Eby, John Vergis, Jonathan Kopacz, Youngmin Yu, Michael Hershey, Kayla Cartwright, Morgan Markho, Chase Arnold, Connor Knight, Robert McCullumsmith MD PhD

Background: Germline retinoblastoma is a malignant retinal tumor, classically presenting bilaterally in infants with leukocoria, strabismus, and visual impairment due to an autosomal dominant RB1 mutation. Despite advances in intraocular treatments, effective drugs treating retinoblastoma metastasized to the central nervous system (CNS) remain limited. (1).
Objective: This in silico study aims to identify novel retinoblastoma perturbagens that may reverse the molecular effects of germline retinoblastoma with metastasis to the CNS.
Methods: The Kaleidoscope data exploration tool identified knockdown (KD) and overexpression (OE) iLINCS signatures for the RB1 gene. KD signatures were processed through Sig2Lead to find drug candidates with significantly positive or negative concordance. Candidates with the most negative concordance with RB1 KD signatures were further evaluated for their ability to penetrate the blood-brain barrier (BBB).
Results: Kaleidoscope identified 12 RB1 KD iLINCS signatures and one OE signature. Sig2Lead revealed three top candidates that consistently reversed all 12 KD signatures: galantamine (concordance = -0.355), AZD-1775 (-0.343), and amuvatinib (-0.337). While carboplatin, vincristine, and etoposide are standard treatments, only vincristine (-0.333) and etoposide (-0.306) showed effectiveness in reversing KD signatures, with vincristine reversing four and etoposide reversing seven signatures.
Conclusion: Carboplatin does cross the BBB, but it was not found to reverse any RB1 KD signatures (3). Meanwhile, vincristine and etoposide were effective in reversing KD signatures, but both have limited BBB permeability (4). The acetylcholine esterase inhibitor galantamine does cross the BBB and is currently being investigated as a treatment of visual deficits in neurotrauma, making it a strong candidate for treatment of retinoblastoma with CNS involvement (5). Additionally, AZD-1775 can penetrate the CNS and is being studied as a treatment of p53-deficient tumors when combined with carboplatin (6)(7). Future studies should investigate the efficacy of galantamine and AZD-1775 paired with carboplatin as potential therapeutic agents for CNS-metastatic retinoblastoma.

Mahmood Meqdad

Haloperidol modulates IQGAP1 signaling and inhibits proliferation in triple-negative breast cancer cell lines

Mahmood Meqdad, Varun J. Iyer, Mahasin Osman

Background: The triple-negative breast cancer (TNBC) is a heterogenous disease lacking hormonal and growth factor receptors, and therapeutic targets. IQGAP1 is a regulatory signaling scaffold identified as an oncoprotein and biomarker in TNBC.
Objective: Was to define the mechanism of haloperidol (Haldol) inhibition of IQGAP1 signaling pathway in TNBC
Methods: Cell proliferation assays and a drug screen in several TNBC cell lines identified the antipsychotic Haldol as a potential inhibitor (IC_{50} 10-20 mM) of IQGAP1. Mass spectrometry was applied on IQGAP1 immunoprecipitates isolated from Haldol-treated and vehicle control MDA-MB-231 and MDA-MB-468 TNBC cell lines to define potential differences in signaling partners.
Results: Haloperidol inhibited cell proliferation in multiple TNBC cell lines and altered IQGAP1 signaling by modulating its interaction partners differentially in MDA-MB-231 and MDA-MB-468 cells. Untreated cells showed distinct IQGAP1 associations with proteins involved in transcription and protein trafficking, whereas Haldol treatment promoted interactions linked to transcriptional regulation and apoptosis. Additionally, Haldol significantly reduced the overall protein mass in TNBC cells, consistent with its inhibitory effects on cell proliferation.
Conclusion: We identified novel IQGAP1 partners suggesting that Haldol specifically modulate IQGAP1 signaling in cell proliferation and can potentially be re-purposed for personalized treatment of TNBC and other cancers.

Swamroop V. Nandwani BS
Multiple myeloma mortality trends in older adults between 1999-2020
Swamroop V. Nandwani BS, Alexander J. Didier BS, Lucas Unver BS, Alan Fahoury BS, Mona Khalafi BS, Divya Vijendra MD

Introduction/Objective: Multiple Myeloma (MM) is the second most common hematologic malignancy in adults over the age of 65. Our aim was to analyze demographic differences and trends in MM mortality within the U.S. between 1999 to 2020.
Methods: The CDC WONDER database was used to determine mortality statistics from Multiple Myeloma between 1999 and 2020. Age-adjusted mortality rates (AAMR) were calculated, and Joinpoint regression software was used to identify temporal trends.
Results: Between 1999 and 2020, MM accounted for 193,691 deaths in adults 65+ with an AAMR decreased by 13%. During this period, a significant increase in mortality was seen between 2009-2012. In 1999, the AAMR for males was nearly 36% higher at 28.5 compared to the females. By 2020, this difference had increased to 45%. The APC for females during this period was higher at –1.3% *. NH Black individuals had the highest AAMR at 42, and NH AAPI were lowest at 12.9. All groups except NH AAPI experienced a significant drop in APC with NH White experiencing the highest decrease at -.9%. When assessed by census region, the South had the highest AAMR at 23.7 compared to the Northeast at 22. The APC for all census groups dropped significantly with the Northeast having the largest drop in APC at –1.5%. Suburban populations had the lowest AAMR of 22.7 with Rural populations experiencing the highest at 23.7. The APC for all population densities significantly dropped with rural populations having the largest drop to –1.1%.
Conclusions: Although mortality due to MM has been decreasing, the burden of mortality is disproportionate. Male, NH Black, Rural, and individuals living in the South experienced a higher mortality rate from MM. Understanding these patient demographic backgrounds may help to identify potential patients at risk for developing higher mortality rates due to MM.

Swamroop V. Nandwani BS
Non-Hodgkin lymphoma mortality in elderly adults between 1999 and 2020
Swamroop V. Nandwani BS, Alexander J. Didier BS, Lucas Unver BS, Alan Fahoury BS, Mona Khalafi BS, Divya Vijendra MD

Introduction/Objective: Non-Hodgkin Lymphoma (NHL) has the highest incidence of all hematologic malignancies in those 65 years of age or older. Our aim was to evaluate for trends in NHL mortality within the United States between 1999-2020 for those who are 65 years or older.
Methods: The CDC WONDER database was used to determine mortality statistics for patients with an underlying cause of death from NHL between 1999 and 2020. Age-adjusted mortality rates (AAMR) were calculated, and Joinpoint regression software was used to identify temporal trends.
Results: Between 1999 and 2020, NHL accounted for 348,047 deaths in individuals 65 years of age or older. Over this period, the AAMR decreased by 35%. In 1999, males had an AAMR of 59.3 which was 34% higher than the female AAMR. By 2020, this difference had increased to 53% with males having an AAMR of 40.7 . By race, NH White individuals had the highest AAMR recorded at 51.2 but also had the largest decrease in AAMR dropping nearly 38%. NH White individuals had the largest drop in APC at –2.0.
By population density, those in suburban populations had the highest AAMR of 48.8, and urban had the lowest AAMR of 46.5. By census region, it was found that the Midwest had the largest AAMR in 1999 at 52.8 and continued to hold the highest AAMR till 2020 at 34.7. The West had the lowest AAMR in 1999 at 45.4, but the South had the lowest AAMR in 2020 at 29.7
Conclusion: Since 1999 there has been an overall decrease in mortality from NHL; however, the burden of mortality is disproportionate amongst various demographic groups. Those that were male, NH White, from suburban or rural populations, and the Midwest were found to have experienced the highest mortality rate from NHL relative to their counterparts.

Yusuf Nawras BS

Gender-based differences in pancreatic cancer outcomes and hospital mortality rates: A ten-year review using the us nationwide inpatient sample database

Yusuf Nawras BS, Nooraldin Merza MD, Halah Alfatlawi MD, Jerome Hosny MD, Tony Varughese MD, Mona Hassan MD, Abdallah Kobeissy MD

Background: Pancreatic cancer is a highly lethal gastrointestinal cancer with a low 5-year survival rate and difficulty in early detection (1, 2, 3). A comprehensive understanding of gender-based epidemiology, comorbidities, clinical presentations, and risk factors for pancreatic cancer are of great significance for possible effective prevention and helping target future therapies (4, 5).
Methods: We identified patients with a discharge diagnosis of pancreatic cancer in the National Inpatient Sample from 2004 to 2014 using the International Classification of Diseases Clinical Modification, 9th revision (ICD-9-CM) codes. We looked at gender-based primary epidemiology, the yearly trend in hospitalizations with pancreatic cancer, and outcomes, which included length of stay (LOS), hospital charges, and in-hospital mortality. We also performed multivariate analysis to look for the predictors of mortality.
Results: We identified 177,763 patients with a discharge diagnosis of pancreatic cancer. There was a significant increase in hospitalizations with pancreatic cancer in 2014 compared to 2004. Most of the patients were White (74.4%), had Medicare as primary insurance (58.1%), were from the Southern region (36.5%), and had a higher Charlson Comorbidity Index (CCI) (42.7% with CCI > = 3). Trends of the mortality rate for hospitalized individuals with pancreatic cancer in the male gender decreased from 12.2% (2004) to the lowest mortality rate of 8.09% in (2014). Interestingly, based on gender stratification, mortality rates were consistently higher in the male gender than 7.03% in females.
Conclusions: Our study showed overall downward trends for in-hospital mortality despite increasing hospitalizations with pancreatic cancer. Based on gender stratification, mortality rates were consistently higher in males.

Anuj Ojha

Gap-App: A sex-distinct AI-based predictor for pancreatic ductal adenocarcinoma survival as a web application open to patients and physicians

Anuj Ojha, Shu-Jun Zhao, Basil Akpunonu MD, Jian-Ting Zhang PhD, Kerri A. Simo MD, JingYuan Liu PhD

In this study, using RNA-Seq gene expression data and advanced machine learning techniques, we identified distinct gene expression profiles between male and female pancreatic ductal adenocarcinoma (PDAC) patients. Building upon this insight, we developed sex-specific 3-year survival predictive models along with a single comprehensive model. These sex-specific models outperformed the single general model despite the smaller sample sizes. We further refined our models by using the most important features extracted from these initial models. The refined sex-specific predictive models achieved improved accuracies of 92.62% for males and 91.96% for females, respectively, versus an accuracy of 87.84% from the refined comprehensive model, further highlighting the value of sex-specific analysis. Based on these findings, we created Gap-App, a web application that enables the use of individual gene expression profiles combined with sex information for personalized survival predictions. Gap-App, the first online tool aiming to bridge the gap between complex genomic data and clinical application and facilitating more precise and individualized cancer care, marks a significant advancement in personalized prognosis. The study not only underscores the importance of acknowledging sex differences in personalized prognosis, but also sets the stage for the shift from traditional one-size-fits-all to more personalized and targeted medicine. The GAP-App service is freely available at www.gap-app.org.
Keywords: pancreatic ductal adenocarcinoma (PDAC), RNA-Seq, machine learning, feature selection, gene expression, survival, personalized prognosis, Gap-App.

Kaylee Scarnati

Case Report: Palliative care for metastatic triple negative breast cancer with cutaneous involvement

Kaylee Scarnati, Katie Beier, Katherine Esser, Thanuja Neerukonda, MD, Siddharth Kunte, MD

Introduction: Metastatic triple-negative breast cancer (TNBC) is a highly aggressive subtype of breast cancer, characterized by the absence of estrogen and progesterone receptors and the lack of HER2 protein overexpression. Cutaneous metastasis in breast cancer indicates a more advanced stage of the disease and is often associated with considerable morbidity. While palliative care in general aims to improve the quality of life for patients with advanced diseases, there is limited research on the most effective methods for managing the specific symptoms and complications arising from metastatic triple-negative medullary carcinoma with extensive skin involvement.
Case Presentation: We present a case of a 60-year-old female diagnosed with metastatic triple negative medullary carcinoma of the breast, complicated by extensive malignant involvement of the skin. The patient underwent all currently recommended therapies for cutaneous skin metastases including palliative radiation, chemotherapy, antibiotic regimens, and frequent debridement of the skin lesions, but these therapies were unsuccessful in controlling this patient's pain and disease progression, ultimately leading to her passing from disease-related complications. Figure 1 depicts the state of her lesion during a hospitalization for sepsis in August 2023.
Conclusion: Despite utilizing the most commonly recommended therapies for managing aggressive cancer with cutaneous involvement, our patient's symptoms remained uncontrolled. Electrochemotherapy is a widely recognized treatment modality for patients with malignant cutaneous involvement, offering significant benefits, particularly for smaller tumors less than three centimeters in size. However, its efficacy diminishes with larger tumors, such as the 8 cm lesion presented in this case. Despite employing a multi-modal approach, including palliative chemotherapy with Sacituzumab, palliative radiation, and regular debridement coupled with silver dressings, the patient's symptoms were not effectively managed. The persistent pain and progression of the disease underscore the limitations of current palliative care strategies for patients with extensive and aggressive cutaneous metastasis.

Michael R. Stuckert BS

A case of cardiac papillary fibroelastoma: A primary cardiac tumor

Michael R. Stuckert BS, Rawnag El Sheik BS, Claire Popovich BS, Ahmed Elzanaty MD, Hazem Malas DO

Primary cardiac tumors are a rare occurrence in the general population. With an incidence of <0.1%, management of these conditions remains a topic of discussion as their relative rarity limits the ability to conduct clinical trials. Such neoplasms can cause significant morbidity and mortality with the most common presentations being cardiac dysfunction and cardioembolic events. Cardiac papillary fibroelastoma (PFE) is the most common benign primary cardiac neoplasm with an unknown etiology. PFEs are frequently found in the aortic valve and have been increasingly recognized due to advancements in imaging modalities. Herein, we present a case of an 81-year-old female presenting for a cerebrovascular accident. She was found to have a mass in the right coronary cusp of the aortic valve via transthoracic echocardiogram. Subsequent imaging using more sensitive diagnostic modalities including transesophageal echocardiogram and cardiac MRI revealed findings consistent with neoplastic characteristics of PFE and highlighted the tumor's unique mobile nature without a pedicle. Given this patient's presentation with an embolic event, surgical excision of the mass was ultimately performed for definitive treatment. Subsequent pathological evaluation confirmed the suspected diagnosis of cardiac papillary fibroelastoma. Overall, this case provides valuable insight into the diagnostic workup and management of PFEs, highlighting the necessity of a multidisciplinary approach when treating patients with such rarely encountered cardiac neoplasms.

Faraz N Zia BS

Wegener's granulomatosis with polyangiitis with gynecological manifestation

Faraz N Zia BS, Jessica Sedlak BS, Yusuf Mohammad BS, Mohammad Z Khan BS, Isaac Arefi BS, Chmsalddin Alkhas MD, Divya Vijendra MD

Introduction: Granulomatosis with Polyangiitis (GPA), previously known as Wegener's Granulomatosis, is a potentially life-threatening autoimmune disorder. Systemic blood vessel inflammation in GPA can lead to granulomas causing symptoms including focal segmental glomerulonephritis, interstitial lung disease and common systemic vasculitis symptoms like sinus-bleeding. Diagnosing GPA can be challenging due to overlap with other diseases. Positive C-ANCA antibodies are sensitive blood-markers, which are followed by tissue biopsies that show inflammation with granulomatous changes and necrotizing vasculitis affecting small to medium-sized vessels.
Case Presentation: A 59-year-old-female with a 4-year history of GPA had a novel presentation of severe progressing pelvic pain. Patient was sexually inactive since 2011 and denied dysuria, however, liquid-contact to the perineum caused significant pain. Initial diagnosis was bacterial vaginosis and yeast. Shortly after beginning appropriate BV medicine regimen, moderate vaginal bleeding was observed, initially using 4-pads/day, progressing to spotting eventually. Endometrial ultrasound was not performed due to patient pain-intolerance and CT did not comment on endometrial thickness. GPA was in remission with the patient not on any treatment regimen at this time. Vulvar biopsy was then performed confirming vulvar cellulitis and leukocytoclastic vasculitis after which antibiotics, norco and rituximab were initiated. Visual inspection showed a rectovaginal fistula however the surgeon did not attempt repair due to fear of complication and limited access. To prevent infection from bowel leakage, a colostomy bag was placed.
Discussion/Conclusion: Gynecological complications of GPA are exceedingly rare with less than 1% of patients presenting with gynecological symptoms, most frequently bleeding. The cervix and vagina are the most commonly affected genital areas. GPA should be considered when biopsies of malignant-appearing gynecological tissues are negative for malignancy. Treatment is effective and typically includes glucocorticoids and either cyclophosphamide, methotrexate, or azathioprine. Rituximab can also be used alone, as seen in this case study [Pereira, 2022].

INFECTIOUS DISEASES

Roaa Aljunaidy MD

Case Report: A unique course of severe Community-acquired Methicillin-Resistant Staphylococcus Aureus (CA-MRSA) cavitary pneumonia with skipped phenomenon

Roaa Aljunaidy MD, Qutaiba Qafisheh MD, Bisher Sawaf MD, Nezam Altorok MD

Community-acquired Methicillin-resistant Staphylococcus aureus (CA-MRSA) is a less common but increasingly recognized cause of severe pneumonia, particularly necrotizing pneumonia, in otherwise healthy individuals. The antibiotic resistance associated with CA-MRSA often leads to prolonged hospital stays and increased mortality. A unique feature of this pathogen, the "skipped phenomenon," is characterized by intermittent negative blood cultures and is linked to poor prognosis, complicating treatment decisions. We report the case of a 60-year-old male with a history of chronic obstructive pulmonary disease (COPD) and a significant smoking history, who presented with severe CA-MRSA cavitary pneumonia. Initially, the patient exhibited mild respiratory symptoms that rapidly progressed to severe pneumonia, confirmed by imaging studies showing cavitary lesions. Despite initial treatment with vancomycin, the patient experienced persistent MRSA bacteremia for more than 14 days, leading to the addition of ceftaroline to the therapeutic regimen. The patient's course was further complicated by the skipped phenomenon, with intermittent negative blood cultures followed by positive results, even as clinical symptoms began to improve. The skipped phenomenon, though rare, is a critical diagnostic challenge in the management of CA-MRSA infections, necessitating careful monitoring and repeated blood cultures to confirm bacterial clearance, as delayed or incomplete treatment can lead to severe complications. Our patient's presentation underscores the importance of considering CA-MRSA in cases of cavitary pneumonia, even in the absence of traditional risk factors, and highlights the potential benefits of combination antibiotic therapy in managing persistent bacteremia. This case emphasizes the need for high clinical suspicion for CA-MRSA pneumonia in patients with cavitary lung lesions, particularly in those with severe presentations. The presence of the skipped phenomenon requires vigilant monitoring to ensure complete bacterial eradication and successful patient outcomes. Early and aggressive treatment, guided by repeated cultures, is crucial in managing this life-threatening infection.

Eun Seo Kwak MD

Impact of Clostridium Difficile infection on inpatient outcomes of acute pancreatitis: A nationwide study

Eun Seo Kwak MD, Nahush Bansal MD, Keith Burns MD, Nooraldin Merza MD, Sahithi Chinnam DO, Tony Dong, Emily Moore, Yaseen S. Y. Alastal MD

Background: Clostridium difficile infection (CDI) is linked to unfavorable outcomes in hospitalized adults. Patients with acute pancreatitis (AP) are frequently admitted to the hospital and may be at risk for CDI due to antibiotic exposure. We investigated the healthcare outcomes of CDI in individuals with AP.
Methods: The National Inpatient Sample (NIS) 2020 Database was analyzed for adult patients with acute pancreatitis as the primary discharge diagnosis and clostridium difficile infection as a secondary discharge diagnosis, identified using ICD-10 codes. The primary outcome measured was inpatient mortality, with secondary outcomes including length of stay (LOS), hospitalization charges, acute kidney injury, acute respiratory failure, severe sepsis, and septic shock. Multivariate logistic and linear regression analyses were employed to adjust for confounders. Statistical analyses were conducted using STATA software.
Results: Out of 258,965 patients admitted with acute pancreatitis, 1632 (0.64%) were identified as having clostridium difficile infection. The inpatient mortality in AP patients with CDI, compared to those without CDI, was adjusted odds ratio, 2.14; 95% CI (1.18-6.39, p=0.019). AP patient with CDI had longer length of stay 11.51 (10.19-12.83, p<0.001) and hospitalization charges $125846.9 (103885.1-147808.6, p<0.001), as well as increased odds of acute kidney injury 2.11 (1.60-2.78, p<0.001), acute respiratory failure 5.56 (4.11-7.53, p<0.001), severe sepsis 9.34 (5.85-14.91, p<0.001) and septic shock 9.33 (5.39-16.12, p<0.001).

Conclusions: These results suggest that acute pancreatitis patients with clostridium difficile infection have significantly higher odds of mortality, acute kidney injury, acute respiratory failure, severe sepsis, and septic shock compared to those without clostridium difficile infection.

Stephen Prevoznik

Hemophagocytic lymphohistiocytosis Secondary to Epstein–Barr Virus presenting as rhabdomyolysis

Stephen Prevoznik, Zachary Holtzapple MD, Joshua-Paolo Calibag Reyes, Mohanad Qwaider MD, Hoda Shabpiray MD, Mani Askari MD

Background: Hemophagocytic lymphohistiocytosis (HLH) is a severe systemic inflammatory disorder driven by the excessive activation of dysregulated cytotoxic T lymphocytes, macrophages, and natural killer cells. This hyperactivation can result in tissue infiltration by lymphohistiocytes, leading to multiorgan failure and potentially fatal outcomes. The primary mechanism that leads to further fatality is believed to be associated with the excessive cytokine storm.
Case Report: A 27-year-old male without any significant past medical history and no medication use was admitted with a chief complaint of nausea, vomiting, and diarrhea with cyclical febrile episodes at home ongoing for three days prior to admission. The patient was noted to be tachycardic on admission with a heart rate in the 140s but otherwise normal vital signs. Other significant lab work revealed acute kidney injury with creatinine of 3.59 mg/dL and creatine kinase (CK) of 14255 IU/L peaking at 46057 IU/L. EBV and cytomegalovirus (CMV) were ordered and were found to be positive, and the patient was started on ganciclovir. Following further fluid resuscitation, acute kidney injury and rhabdomyolysis drastically improved. Follow-up soluble CD25 (sCD25) was positive. The patient was subsequently diagnosed with HLH and prompt therapy was started with dexamethasone. The patient was treated with steroids and valacyclovir on discharge for CMV, with follow-up in the outpatient setting revealing the resolution of symptoms without any long-term complications.
Conclusion: HLH is a significant systemic inflammatory state that should be treated swiftly, as mortality is high without appropriate treatment. As seen in our case, rhabdomyolysis as a presenting feature of HLH is a novel presentation. This along with the infection of EBV should be a raise concerns about an underlying etiology, which in our case, led to the discovery and prompt treatment of HLH.

Bisher Sawaf, MD

Rare case of metronidazole-induced encephalopathy in a multiple transplant recipient: Clinical and radiological insights

Bisher Sawaf MD, Yusuf Hallak MD, Mohamad Alsakka MD, Shahem Abbarh MBBS, MRCP, Yaseen Alastal MD, MPH

Introduction: Metronidazole is a widely used antibiotic used to treat various anaerobic infections. Metronidazole-induced encephalopathy (MIE) is a rare but significant central nervous system (CNS) adverse effect.
Case presentation: We report the case of an 18-year-old male with a history of liver, small bowel, and pancreas transplantation and chronic liver failure, maintained on long-term metronidazole for recurrent C. diff colitis and post-transplant ulcerative ileitis. The patient developed slurred speech and unsteadiness following a recent increase in metronidazole dosage. A magnetic resonance imaging (MRI) of the head showed multifocal areas of diffusion restriction and T2 hyperintensity in the splenium of the corpus callosum, dentate nuclei, inferior colliculi of the midbrain, and pontine tegmentum bilaterally, consistent with MIE. [figure 1] Metronidazole was discontinued, leading to a gradual improvement in symptoms and complete resolution of MRI abnormalities on follow-up. [figure 2]
Discussion: This case highlights the importance of recognizing MIE as a potential adverse effect of metronidazole, particularly in patients on long-term therapy with recent dosage increases. Further studies are needed to better understand the mechanisms, risk factors, and optimal management of MIE.

Conclusion: Early discontinuation of metronidazole can lead to significant clinical and radiological improvement.

Katarina Tomac, BS

A case of skin necrosis during severe sepsis complicated by disseminated intravascular coagulation

Katarina Tomac, BS, Andrew R. Campbell, MD

Background: Purpura fulminans is a skin manifestation of a thrombotic microangiopathy known as diffuse intravascular coagulation (DIC) that occurs in severe infection. It is characterized by microvascular thrombi affecting the skin of the extremities, causing skin necrosis and threatening limbs or digits. Purpura fulminans is relatively uncommon, but the presence of these skin findings implies certain management strategies that can improve coagulopathy and possibly save a patient's limb.
Case Presentation: Here we present a case of a woman with severe sepsis who developed skin necrosis and distal ischemia while undergoing aggressive treatment in the medical ICU. Surgical debridement revealed non-bleeding skin, soft tissue and skin necrosis that spared the underlying fascia. The veins of the skin were thrombosed, and the skin culture was negative for infection. In the patient's lab work, she had elevated INR, low fibrinogen, thrombocytopenia, and an elevated d-dimer level.
Conclusion: Purpura fulminans is diagnosed based on characteristic skin findings in the setting of sepsis and coagulopathy. This finding has unique implications for management, affecting choices of vasopressor, anticoagulation, and blood products. Its pathophysiology is thought to be driven by consumption of protein C, crucial to preventing excessive thrombosis in maintaining homeostasis in the coagulation system. Conservative measures such as topical vasodilators may be used but commonly, patients require surgical debridement and supportive measures that resemble the care of burn victims. Awareness of this life-threatening form of thrombotic microangiopathy, and understanding its treatment implications, may decrease morbidity in patients with severe sepsis.

NEPHROLOGY

Zohaib Ahmed, MD

Non-germinal center diffuse large B-cell lymphoma of the liver in a renal transplant patient: A case report

Zohaib Ahmed, MD, Connor Campbell MS, Emma Bolyard BS, Kiya Shazadeh Safavi MD, Manthanbhai Patel MD, Abdallah Kobeissy MD, MPH

Introduction: Diffuse large B-cell lymphoma (DLBCL) is a relatively rare lymphoproliferative disorder affecting more than 18,000 people per year. Extranodal involvement occurs in up to 40% of cases with DLBCL. While extranodal involvement most commonly occurs in the GI tract, liver involvement is particularly uncommon and may portend a poor prognosis. We present a case of an immunosuppressed patient with non-germinal center B-cell (non-GCB) DLBCL.
Methods: Literature review of reported cases was performed using PubMed.
Case Report: A 58-year-old male with history of right renal transplant, on immunosuppression, initially presented to the ED with several days of fever, chills, nausea, vomiting, and RUQ pain. CT of the abdomen and pelvis displayed a 2 cm lesion in the right hepatic lobe, which was a new finding compared to abdominopelvic CT scans done 4 days prior and 3 months prior. He was started on empiric antibiotics for suspected hepatic abscess. MRI showed several ring-enhancing lesions, all displaying T2 hyperintensity and increased DWI signal. CT-guided percutaneous biopsy demonstrated negative culture results, but pathology showed a monomorphic, EBV positive, CD20 positive, diffuse large B-cell lymphoma with a non-germinal center phenotype showing large areas of necrosis. The patient was admitted for weekly rituximab infusions, with plans for restaging 2-4 weeks later; full R-CHOP regimen was foregone at that time due to concerns for concomitant infectious etiology. However, after much consideration, CVP regimen was started shortly after. While it was

thought that the patient may have done well on this regimen, his condition quickly deteriorated from an episode of fulminant *C. difficile* colitis resulting in ileal perforation and septic shock, and he passed away shortly after.
Conclusion: Malignancy should always be a consideration in patients presenting with RUQ pain, constitutional symptoms, and liver lesions, particularly in immunosuppressed patients. In cases of rapid onset, as in our patient, clinicians must take care to differentiate DLBCL of the liver from hepatic abscess and more common primary or metastatic liver malignancies. This can be particularly difficult given the overlap of clinical presentation involving B-symptoms and an undifferentiated hepatic lesion. The relatively rapid deterioration of our patient is a rare case of non-GCB DLBCL in the liver.

Brianna N. Bailey MS
Acute interstitial nephritis following repeated daptomycin treatment for recurrent joint infection: A case of delayed identification of infective endocarditis
Brianna N. Bailey MS, Serena A. Maag MS, Mathieu K. Holt BS, Danyal S. Butt MD, Bibek M. Shrestha MD, Ayman Iqbal MD, Davonte Willis MD, Srini K. Hejeebu DO

Introduction: Acute interstitial nephritis (AIN) is characterized by inflammation of the renal interstitium, often triggered by drug exposure. While vancomycin is commonly associated with AIN due to its known nephrotoxicity, other agents like daptomycin can also induce this condition, potentially leading to severe renal impairment.
Case Presentation: A 68-year-old female with stage IIIA chronic kidney disease and hypertrophic obstructive cardiomyopathy, who had a dual-chamber implantable cardioverter-defibrillator (ICD) placed in March 2024, presented to the emergency department following her fourth joint infection drainage procedure in six months. Each infection, caused by *Pseudomonas aeruginosa*, was treated with repeated courses of daptomycin. During hospitalization, her renal function deteriorated, indicated by a significant increase in serum creatinine and BUN levels, leading to the need for hemodialysis, which continued after discharge. The ICD was identified as the source of recurrent infections and was promptly removed, but the patient remains on outpatient dialysis.
Discussion: Although daptomycin is generally considered less nephrotoxic than vancomycin, it can still cause acute interstitial nephritis (AIN), particularly with repeated or prolonged use, which increases the risk of acute kidney injury (AKI). This case highlights the importance of vigilant renal function monitoring in patients with chronic kidney disease who are undergoing multiple treatments with nephrotoxic agents to prevent severe outcomes, such as long-term dialysis. Clinicians must carefully weigh the benefits of daptomycin against its risks and remain alert for signs of AIN in patients presenting with unexplained renal impairment.
Conclusion: Clinicians should maintain a high level of awareness regarding the potential side effects of medications, particularly when repeated courses are prescribed. Proactive monitoring of renal function and a thorough understanding of drug side effects are essential in preventing serious complications.

Lena S. Bercz BS
Acute renal failure in a patient with Waldenström's macroglobulinemia: Case report and literature review
Lena S. Bercz BS, Andrew Campbell MD

Introduction: Waldenström's macroglobulinemia (WM) is a rare lymphoid neoplasm, making up around 2% of all hematologic malignancies. While patients with WM often present with symptoms like cytopenias and hyperviscosity, renal insufficiency is less common compared to multiple myeloma (MM). We report a case of acute renal failure in a woman with newly diagnosed plasma cell dyscrasia.
Case Presentation: CB, a 70-year-old woman with a history of NASH cirrhosis and hypertension, presented to the ER in Spring 2023 after her primary care provider noticed elevated creatinine levels (3.48 mg/dL) during routine tests. She complained of fatigue but denied other symptoms such as chest pain, dyspnea, lower extremity edema, or oliguria. Additional lab results showed BUN of 35, protein to creatinine ratio of 2.4 g/g, hemoglobin of 9.1 g/dL, and platelet count of 87,000. Serum free light chains showed a kappa/lambda ratio of 0.07. Monoclonal IgM lambda was detected (2.3 g/dL), with elevated urine free light chains. A bone marrow

biopsy revealed lymphoid aggregates and interstitial plasmacytosis. Flow cytometry indicated monoclonal lambda light chain-restricted B-cell and plasma cell populations. PET/CT revealed diffuse osseous uptake, but no focal malignancy. The patient was diagnosed with WM and started on Zanubrutinib. Before treatment initiation, she became oliguric and required hemodialysis.
Conclusion: Though rare, renal involvement in WM has been increasingly reported. Unlike MM, there is no single defining renal lesion for WM nephropathy, which can present as proteinuria, hematuria, or light chain deposition disease. In this case, despite coexisting liver disease, her renal dysfunction was attributed to WM due to the presence of light chains in the urine. Factors associated with poor prognosis in renal WM include age over 60, anemia, neutropenia, and elevated beta 2-microglobulin. Immediate treatment is recommended for WM-related kidney injury.

Mengxuan Chen

Glycogen synthase kinase (GSK) 3beta hyperactivity impairs glomerular podocyte insulin signaling via IRS1 modulation in diabetic kidney disease

Mengxuan Chen, Yan Ge, Lance D. Dworkin, Rujun Gong

Background: Insulin signaling in kidney cells, in particular podocytes, is essential for maintaining kidney homeostasis, independent of glycemic levels. As a critical transducer of insulin signaling, GSK3beta also acts as a convergent point for myriad pathways implicated in kidney injury. However, its role in DKD remains elusive.
Methods: Mouse podocytes were exposed to insulin or a type 2 diabetic milieu, following GSK3beta silencing, ectopic expression of a constitutively active GSK3beta mutant (S9A), or treatment with tideglusib, a GSK3beta inhibitor. Podocyte injury was assessed, and results validated in kidneys from db/db mice.
Results: Upon insulin stimulation, insulin signaling mediators like Akt and GSK3beta, were phosphorylated, associated with increased glucose uptake and expression of GLUT. GSK3beta silencing sensitized insulin signaling, marked by potentiated induction of p-Akt and p-ERK1/2 and enhanced glucose uptake and GLUT expression. Conversely, S9A de-sensitized insulin signaling and mitigated GLUT induction and glucose uptake. Among the many insulin-signaling transducers, IRS1 co-precipitated and interacted with GSK3beta. Moreover, in silico analysis indicated that IRS1S332, resides in the consensus motifs for phosphorylation by GSK3beta. Indeed, insulin-induced p-IRS1S332 was suppressed by GSK3beta silencing but was enhanced by S9A. Furthermore, in podocytes exposed to a type 2 diabetic milieu, inhibitory p-GSK3betaS9 was suppressed, denoting GSK3beta hyperactivity. This was associated with enhanced p-IRS1S332. Tideglusib treatment counteracted this effect, re-sensitized insulin signaling, and averted diabetic podocyte injury. In db/db mice, expression of p-IRS1S332 was augmented in glomerular podocytes. Based on immunoblotting, the expression ratio of p-GSK3betaS9/GSK3beta in glomeruli was repressed in db/db mice as compared with control mice, denoting GSK3beta hyperactivity, which negatively correlated with the level of p-IRS1S332.
Conclusion: Diabetes-associated GSK3beta hyperactivity promotes IRS1 phosphorylation, contributing to insulin signaling desensitization in podocytes. Therapeutic targeting of GSK3beta could re-sensitize insulin signaling in podocytes via regulation of IRS1.

Emily R Crossley

Ultra-conserved non-coding elements in the human genome: Their possible functions and association with diseases

Emily R Crossley, Larisa Fedorova, Oleh A Mulyar, Shuhao Qiu, Ryan Freeman, Alexei Fedorov

Thousands of prolonged sequences of human ultra-conserved non-coding elements (UCNEs) share only one common feature: peculiarities in the unique com-position of their dinucleotides. Here we investigate whether the numerous weak signals emanating from these dinucleotide arrangements can be used for computational identification of UCNEs within the human genome. For this purpose, we analyzed 4272 UCNE sequences, encompassing 1,393,448 nucleotides, alongside equally sized control samples of randomly selected human genomic sequences. Our research identified nine different features of dinucleotide arrangements that enable

differentiation of UCNEs from the rest of the genome. We employed these nine features, implementing three Machine Learning techniques -- Support Vector Machine, Random Forest, and Artificial Neural Networks -- to classify UCNEs, achieving an accuracy rate of 82-84%, with specific conditions allowing for over 90% accuracy. Notably, the strongest feature for UCNE identification was the frequency ratio between GpC dinucleotides and the sum of GpG and CpC dinucleotides. Additionally, we investigated the entire pool of 31,046 SNPs located within UCNEs for their representation in the ClinVar database, which catalogs human SNPs with known phenotypic effects. The presence of UCNE-associated SNPs in ClinVar aligns with the expectation of a random distribution, emphasizing the enigmatic nature of UCNE phenotypic manifestation. We propose that the key to the cryptic properties of UCNEs is hidden in their specific DNA conformations. Our hypothesis is that specific non-canonical DNA conformation of UCNEs may be integral to the homologous pairing of double-stranded DNAs during meiosis.

Tony Dong, MS4

Delayed bile leak in the setting of grade V blunt liver trauma

Tony Dong, MS4, Emily Moore, MS4, Eun Seo Kwak, M.D., Keith Burns, M.D., Nooraldin Merza, M.D., Yaseen Alastal, M.D.

Background: Bile leakage is a known, but serious complication of abdominal surgery or trauma to the biliary system. The consequence of bile leaks can be serious and can lead to complications including infection resulting in sepsis. Furthermore, cases of delayed bile leaks are not common. Here, we describe a rare case of delayed bile leak in the setting of trauma following a motor vehicle accident (MVA).
Case Presentation: The patient is a 32-year-old female who initially presented for polytrauma secondary to MVA. Notably, the patient suffered multiple fractures, pneumothorax, and lacerations of the liver and spleen. Initial imaging described grade V hepatic trauma on the American Association for the Surgery of Trauma (AAST) scale with likely injury to the portal vein and traumatic proximal pancreatic laceration with no signs of bile leak. Magnetic resonance cholangiopancreatography (MRCP) was subsequently performed showing laceration of the pancreas without hemorrhage or fluid collection, with no indication of ductal disruption. Although she was initially recovering with liver enzymes trending downwards, repeat abdominal Computed Tomography (CT) performed two days after MRCP for abdominal distention showed full-thickness laceration of the pancreatic neck, peritoneal enhancement, and liver laceration with new concerns of pancreatic leak. Endoscopic retrograde cholangiopancreatography performed one week after admission confirmed pancreatic leak, and the patient underwent pancreatic and biliary sphincterotomy with pancreatic and common bile duct stent placement. The patient recovered and was discharged after seventeen days of admission.
Conclusion: Urgent diagnosis and treatment of bile leaks can prevent adverse outcomes. This case highlights the importance of close clinical monitoring and meticulous physical exams while keeping ductal injury on the differential, even after initial negative imaging. Due to the correct diagnosis and prompt treatment, the patient recovered uneventfully and was discharged without further gastroenterological complications.

Athena Y Gong

Vinyl carbamate activates the alternative complement pathway in glomerular endothelial cells and induces membranoproliferative glomerulonephritis

Athena Y Gong, Lance Dworkin, William T Gunning, Mengxuan Chen

Background: Vinyl carbamate (VC) is a carcinogenic metabolite of ethyl carbamate (EC), which is a process contaminant in fermented foods and alcoholic beverages. While EC and VC are recognized for their tumorigenic effects, their impact on the kidney has not been previously studied.
Methods: A/J inbred mice received a single i.p. injection of VC (60 mg/kg). Kidney injury was evaluated. A *post hoc* analysis was performed on a publicly available RNA-Seq transcriptome of kidneys from rats treated with fermented wine containing high levels of EC.
Results**:** Beginning 5 weeks post VC injection, mice showed signs of moribund state and were killed. By 12

weeks, a total of 97 of the 240 treated mice had died or were killed. Necropsies revealed evident renal disease, characterized by glomerular lobularization, mesangial hypercellularity and expansion, endocapillary proliferation, and capillary wall thickening by light microscopy. Electron microscopy showed subendothelial deposits, new basement membrane formation, and extensive podocyte foot process effacement. Immunofluorescence indicated abundant granular C3 staining in the mesangium and coarse linear capillary staining, resembling membranoproliferative glomerulonephritis (MPGN). Additionally, Kyoto Encyclopedia of Genes and Genomes pathway enrichment analyses were performed on differentially expressed genes between high EC-treated and control rats and showed that complement and coagulation cascades are top predicted biological processes implicated. Furthermore, pathway-based data integration and visualization using Pathview demonstrated that key regulators of complement activation pathways were altered by high EC treatment. Notably, complement factor (CF) D and H, critical positive and negative regulators of the alternative pathway, respectively, were the most affected, with CFD induced by 3.49-fold and CFH repressed by 5.88-fold, underscoring a hyperactive alternative pathway.
Conclusion: VC, a metabolite of EC, induces complement fixation in glomeruli and MPGN in mice. Complement overactivation due to CFD induction and CFH repression may be an underlying pathomechanism.

Jing Liu

Activation of podocyte-specific MC5R signaling by melanocortin therapy protects against THSD7A-associated membranous nephropathy

Jing Liu, Yan Ge, Lance Dworkin, Rujun Gong

Backgrounds: Melanocortins, exemplified by adrenocorticotropic hormone, have demonstrated a unique beneficial effect in membranous nephropathy (MN). The underlying mechanism remains elusive, and this study tested the role of melanocortin 5 receptor (MC5R), one of the five MCRs of the melanocortin system.
Methods: Wild-type (WT) and MC5R knockout (KO) mice were injected with a rabbit anti-THSD7A antibody to develop MN. Beforehand, some KO mice received hydrodynamic transfer of a plasmid encoding MC5R driven by *Nphs2* promoter. Subsequently, melanocortins were given, including repository corticotropin injection (RCI), the nonsteroidogenic pan-MCR agonist NDP-MSH, and the selective MC5R agonist PG901. *In vitro*, primary podocytes from WT or KO mice were exposed to the anti-THSD7A antibody in the presence or absence of melanocortins. Glomerular and cellular injury was assessed.
Results: After anti-THSD7A antibody insult, WT mice developed massive proteinuria and a pathology resembling human MN. Despite granular subepithelial deposition of the rabbit IgG in glomeruli to a comparable extent, KO mice sustained more severe glomerular injury, as evidenced by heavier proteinuria, worsened podocytopathy, and increased expression of the podocyte injury marker. Melanocortin treatment with RCI, NDP-MSH or PG901 ameliorated proteinuria and glomerular damage in WT mice, coinciding with an improvement in podocyte injury. The beneficial efficacy of melanocortins was drastically blunted in KO mice. Mechanistically, MC5R is expressed in glomeruli in WT mice, and co-localized with podocyte markers. Melanocortin treatment directly protected the WT podocytes against the antibody-elicited cytopathic changes, including cytoskeleton disruption, cellular hypermotility, oxidative stress, and apoptosis. This protective effect was abolished in cultured KO podocytes. In contrast, glomerular podocyte-specific reconstitution of MC5R in KO mice attenuated the experimental MN and restored the beneficial efficacy of melanocortins.
Conclusions: Our findings suggest that podocyte-specific MC5R signaling protects against glomerular injury and proteinuria in MN and may serve as a novel therapeutic target for treating MN.

Jing Liu

THSD7A-associated membranous nephropathy involves both complement-mediated and autonomous podocyte injury

Jing Liu, Deepak Malhotra, Yan Ge, William Gunning, Lance Dworkin, Rujun Gong

Backgrounds: As a distinctive subtype in the serology-based classification of membranous nephropathy (MN), thrombospondin type 1 domain containing 7A (THSD7A)-associated MN has attracted increasing interest because THSD7A is expressed in preclinical species, facilitating the study of its role in MN. This study aimed to establish models of THSD7A-associated MN by using a commercial antibody. The potential pathomechanisms and the therapeutics efficacy of repository corticotropin injection (RCI) were tested in this model.
Methods: Primary mouse podocytes were cultured in regular complete medium containing complements or in medium pre-heated to inactivate heat-labile complements, followed by exposure to a rabbit anti-THSD7A antibody. *In vivo,* mice were injected with the anti-THSD7A antibody and treated with RCI or vehicle. To deplete complement, some mice were treated with cobra venom factor (CVF). Podocyte injury and glomerular disease was evaluated.
Results: After anti-THSD7A antibody insult, mice developed massive proteinuria, concomitant with histologic lesions of glomerular injury, including epimembranous or intramembranous electron-dense deposits in glomeruli as well as variable podocyte foot process effacement, reminiscent of glomerular ultrastructural changes in human MN. Complement depletion with CVF only partially attenuated proteinuria and glomerular injury, suggesting that complement-independent pathomechanisms also contribute. Consistently, in primary podocytes, exposure to the anti-THSD7A antibody caused evident podocytopathic changes, such as disruption of the actin cytoskeleton integrity, podocyte hypermobility, oxidative stress and apoptosis. These signs of podocyte injury were preserved, although to a lesser extent, following complement inactivation, denoting an autonomous podocytopathic activity of this antibody. As an FDA-approved treatment option for primary nephrotic glomerulopathies including MN, RCI appeared to be beneficial in this model.
Conclusions: Both complement-dependent and autonomous podocytopathy are involved in the mouse model of THSD7A-associated MN, which could be attenuated by RCI. This model, based on the use of a commercially available anti-THSD7A antibody, could be an important tool for MN research.

Wei-Shin Lu BS

Gardnerella vaginalis urinary tract infection in male patient with renal allograft transplant

Wei-Shin Lu BS, Michael A. Kleman BS, Vaishnavi Aradhyula BS, Dinkar Kaw MD, Caleb Spencer MD

Patients with a history of renal transplants are often immunocompromised and at risk for infection. *Gardnerella vaginalis* is an anaerobic gram variable organism that rarely causes infection in men. The few reported cases primarily involve urinary tract infection. The incidence of bacteremia is even more rare and there have been no reported cases of *G Vaginalis* infection from renal allograft transplant.
We present a case of a 45-year-old male patient with a history of renal allograft transplant 4 years prior to admission who presented with acute kidney injury. We had initial concerns for acute kidney rejection. Urine cultures were positive for *G vaginalis*, and labs were negative for BK virus, CMV, and donor specific antigen. Renal biopsy showed chronic inflammation in the fibrotic areas of the interstitium and acute inflammation involving a calyceal urothelial lining. The findings were concerning for chronic pyelonephritis. The patient developed sepsis during the hospital course. He was initially treated with metronidazole and broad-spectrum antibiotics. Broad spectrum antibiotics were quickly discontinued, and the patient improved with prolonged metronidazole treatment. The patient was discharged on request to follow up for dialysis and long-term antibiotic therapy. Previous cases of *G vaginalis* in men have demonstrated susceptibility of the bacteria to Metronidazole but emphasize the unlikeliness of detection due to delay in isolation and identification. Furthermore, G vaginalis bacteremia is rarely found in men and there are even fewer reports of bacteremia in an immunocompromised patient such as in our case. This case highlights the importance of considering *G vaginalis* in patients, male or female, with renal allograft transplants who present with urinary tract infections.

Daniyal A. Saeed MD

From Lungs to Kidneys: A case of mycoplasma pneumonia complicated by acute kidney injury and hemolytic anemia

Daniyal A. Saeed MD, Dinkar Kaw MD, Jonathan G. Irvin, Muhammad U. Ali MD

Introduction: Cold agglutinin disease is an established hematologic manifestation of Mycoplasma pneumoniae infection. There are cases describing this process also resulting in acute renal failure via processes such as glomelorunephritis and interstitial nephritis.
Case: We present a case of a 59-year-old male who presented with shortness of breath, fever and diagnosed with bilateral pulmonary emboli along with pneumonia. Patient subsequently developed hemolytic anemia and noted to have positive urine mycoplasma antigen. His hospital course was complicated by worsening kidney function as well. He was treated with plasmapheresis and dialysis while admitted to the hospital with improvement in hemolysis. He experienced prompt recovery of renal function, and dialysis was then discontinued.
Conclusion: Mycoplasma Pneumonia infection rarely leads to severe hemolytic anemia, thrombosis, and worsening kidney function and has been described in the literature.

Mitchell Salke MD

Use of avacopan as a steroid-sparing medication in ANCA-associated vasculitis patients with renal impairment

Mitchell Salke MD, Tahrima Ferdous MD, Nezam Altorok MD

Background: Alveolar hemorrhage can be a significant cause of mortality in patients hospitalized with ANCA-vasculitis and will often necessitate use of high-dose glucocorticoids early on in the hospital course. When considering a transition to steroid-sparing medications, options may be limited in patients with renal impairment. This case highlights the use of the C5a receptor inhibitor avacopan as an option in such patient populations.
Case Presentation: A 69-year-old female with a history of CKD stage IIIA, insulin-dependent type 2 diabetes mellitus, congestive heart failure, and hypertension was admitted to the hospital following a 1–2-week history of fatigue and weakness after outpatient lab studies were significant for a hemoglobin of 7.1. The initial chest x-ray showed only mild bibasilar opacities, but over the next couple of days, the patient began to experience worsening respiratory distress, ultimately requiring intubation. Due to significant fluid overload and worsening creatinine, the patient was started on hemodialysis. Bedside bronchoscopy showed erythematous mucosa of the bilateral bronchial trees with multiple foci or oozing blood concerning for alveolar hemorrhage **[Figures 1-2]**. Rheumatologic work-up was significant for ANA at 1:1280 with homogenous pattern, normal C3/C4, elevated MPO at 260 and PR3 at 36 with a positive p-ANCA. The patient was immediately started on high-dose IV glucocorticoids. When the time came to wean down steroids, cyclophosphamide was considered as an adjunct steroid-sparing therapy. However, due to concerns for renal toxicity, a plan was made to start avacopan instead. Prior to initiation of avacopan, the patient's family ultimately decided to pursue comfort measures.
Conclusion: Since alternative pathway complement activation has been shown to play a role in the pathophysiology of ANCA-associated vasculitis[1], pharmaceuticals such as avacopan that inhibit this pathway may be considered as part of the treatment plan. This is especially true in patients with renal impairment, which is a common sequela of ANCA-associated vasculitis.

PULMONOLOGY

Andrew R. Boring

TP53 somatic mutation prevalence in airway epithelial cells as a potential biomarker for COPD risk

Andrew R. Boring MS, Erin L. Crawford MS, Daniel J. Craig MD, PhD, Heidi Chen PhD, Rami Ahmad MD, Mohamed Omballi MD, Eric L. Grogan MD MPH, Steven A. Deppen MD, James C. Willey MD

Background: Approximately 10% of current smokers are at risk for developing Chronic Obstructive Pulmonary Disease (COPD). COPD follows an insidious disease course prior to diagnosis by a pulmonary function test (PFT). A PFT measures an obstructive defect due to lung damage that has progressed over time prior to diagnosis. There is need for a biomarker that identifies COPD risk well before obstruction develops to enable effective prevention. We recently reported that in the airway epithelium of smokers, there is an increased prevalence of somatic TP53 mutations. Further, among heavy smokers a higher TP53 mutation prevalence acted as a biomarker for lung cancer (CA). Due to the known association between COPD and CA risk we investigated whether this TP53 biomarker is an independent biomarker for COPD risk.
Methods: Patients undergoing bronchoscopy were recruited into an IRB-approved research study wherein soft brush biopsies of airway epithelial cells (AEC) from the large airways were collected. DNA extracted from bronchial brush specimens was sequenced by PCR-amplicon library NOS. Using synthetic internal standards to compensate for sequencing error, VAF was observable down to 0.0 I%. The TP53 biomarker was measured in AEC DNA from 29 non-cancer subjects, 7 COPD and 22 non-COPD.
Results: The TP53 biomarker was significantly associated ($p<0.01$) with COPD, yielding 95% specificity, 57% sensitivity, 80% positive predictive value, 87.5% negative predictive value, and an accuracy of 86.2% using Pearsons' chi-square analysis with Yates correction.
Conclusions: The TP53 biomarker is associated with COPD diagnosis among non-cancer subjects in this small discovery set. We plan to validate the association in larger case-control studies. If validated this biomarker may enable early detection of COPD while providing mechanistic insight regarding the biological processes driving COPD.

Erin Crawford MS

The TP53 biomarker in nasal brush biopsy samples shows promise as a relatively non-invasive test for lung cancer risk

Erin L. Crawford MS, Daniel J. Craig PhD/MD, Mohamed Omballi MD, Rami Ahmad MD, Andrew Boring MS, Eric L. Grogan MD/MPH, Stephen A. Deppen PhD, James C. Willey MD

Background and Purpose: Annual lung cancer screening with low-dose computed tomography (LDCT) scans enables earlier detection allowing for potentially curative treatments and a reduction in mortality. However, eligibility for LDCT screening is based primarily on age and smoking history and many lung cancers occur among individuals who currently are ineligible. Recently we demonstrated that a biomarker measuring TP53 somatic mutations in grossly normal airway epithelium was significantly associated with cancer status independent of age and smoking history and was synergistic with traditional risk score models. The goal of this pilot study was to test the TP53 biomarker in nasal brush biopsy specimens, a potential surrogate tissue obtained using less invasive collection methods.
Methods: Nasal brushings from 27 lung cancer and 24 control subjects were collected at the University of Toledo and Vanderbilt University Medical Center under approved institutional protocols. Genomic DNA (gDNA) was extracted with the Qiagen AllPrep DNA/RNA kit using a modified protocol. gDNA from each subject was combined with competitive TP53 internal standards and a complexity control, then PCR amplified. Next, samples were barcoded and pooled to create NGS libraries and sequenced on an Illumina MiSeq (V3 flow cells, 2 x 250 paired-end). Qiagen CLC Workbench was utilized for bioinformatic analyses. The Basic Variant Detection Tool was used to call variants and the significance of endogenous variants relative to internal standard variants at the same base position was determined using Poisson Exact Test. A Bonferroni correction was applied to minimize false discovery. Total significant variants/subject was compared between cases and controls using an f-test followed by a paired t-test.
Results and Conclusions: The TP53 mutation biomarker measured in nasal brushing was associated with lung cancer ($p=0.0085$) in an initial set of 10 cases and 11 controls. Measurement of the remaining nasal brush specimens currently is underway.

Mathieu K. Holt, BS

Pulmonary infection with irpex laceratus in asthmatic using steroid inhaler

Mathieu K. Holt, BS, Danyal S. Butt, MD, Serena A. Maag MS, Brianna N. Bailey, MS, Bibek M. Shrestha, MD, Ayman Iqbal, MD, Davontae Willis, MD, Srini K. Hejeebu, DO

Introduction: Irpex laceratus, a wood rotting basidiomycete, was identified through bronchoscopy in an adult female with pneumonia who uses an inhaled corticosteroids for asthma. There are currently no guidelines for the treatment of I. laceratus for pulmonary infections.
Case Presentation: A 54-year-old female with previous medical history of asthma, rhinitis, migraines, nausea, vomiting and one year history of cough due to fungal pneumonia treated with IV Amphotericin B liposome after outpatient oral treatment presents with change in appetite, fatigue, cough, shortness of breath, and serum creatinine elevation found on outpatient labs. Physical exam is positive for wheezing. Labs show hypomagnesemia, hypokalemia, elevated BUN, and elevated serum creatinine. Amphotericin was reduced and IV fluid boluses were added pre- and post- to improve tolerability. Reported cases of Irpex lacteus in immunocompromised patients have been treated with Amphotericin, so those cases guided the treatment of I. laceratus due to both belonging to the Irpex species. The persistent infection and elevation of serum creatinine coinciding with the use of Amphotericin warranted hospitalization while evaluating the elevated serum creatinine and determining appropriate treatment.
Discussion: Existing literature does not provide guidelines for the treatment of I. laceratus, leaving case reports of I. lacteus as examples to follow. Cases document the use of Amphotericin B to treat I. lacteus. This case serves as a reference for the treatment of persistent I. laceratus with Amphotericin.
Conclusion: Irpex laceratus pulmonary infections are rare and no guidelines outline treatment of this infection, so physicians must refer to case reports of I. lacteus for guidance of emerging cases. I. laceratus treatment warrants further to establish treatment guidelines.

Bivek Timalsina

Aerosolized microcystin exposure triggered a significant inflammatory response in both healthy and asthmatic human airway epithelial cells

Bivek Timalsina, Evan M Benson, Benjamin French, Steven Haller, David Kennedy

Background: Cyanobacterial harmful algal blooms (cHABs) are on the rise, leading to higher production of microcystin toxins as secondary metabolites, which are toxic to humans and animals. Among the 300 different congeners, microcystin - leucine arginine (MC-LR) has recently been shown to have one of the highest concentrations in lake aerosol particles. We have demonstrated that exposure to aerosolized microcystin induces inflammatory responses, but a thorough understanding of the differences in response to different congeners among healthy individuals and those with pre-existing disease conditions remains unclear.
Objectives: We aimed to determine the specific physiologic and inflammatory effects of aerosolized microcystins in lung airway epithelium.
Methods: We used human primary airway epithelial cells isolated from both healthy and asthmatic donors. The cells were seeded in 12 well Transwell culture plates and allowed to fully differentiate in an air-liquid interface where the basal side is submerged in media, while the apical side is exposed to air. This setup mimics the airway environment and promotes the development of a polarized, pseudostratified epithelial layer, with ciliated, goblet, and basal cells similar to those found in human airways. These differentiated cells were exposed to vehicle control (saline water), 1 µMand 10 µM of MC-LR for 5 minutes per day for 3 days using the expoCube environmental exposure system. The mRNA expression of various inflammatory gene markers was determined using qRT-PCR and analyzed for the fold change.
Results: The primary cells differentiated fully with characteristics of cilia beating and mucociliary clearance. There were minimal changes in cellular morphology with 1 0µM MC-LR exposure and no changes with 1 µMMC-LR. Exposure to 1 µM MC-LR led to a 1.8-fold increase in TNF-alpha, and a 1.9-fold increase in IL-6

in healthy group ($p<0.001$). These increments were significantly higher in asthmatic group of airway epithelial cells, with a 3.5-fold increase in TNF-alpha and a 2.6-fold increase in IL-6 ($p<0.001$).
Conclusion: Our findings demonstrate that exposure to aerosolized microcystin-leucine arginine (MC-LR) induces a significant inflammatory response in airway epithelial cells, with more pronounced effects in cells derived from asthmatic individuals compared to healthy controls. The observed increases in TNF-alpha and IL-6 expression highlight the potential exacerbation of airway inflammation in vulnerable populations exposed to cyanotoxin-containing aerosols, underscoring the need for further investigation into the long-term health impacts of these environmental exposures, especially among individuals

RHEUMATOLOGY/IMMUNOLOGY/ALLERGY

Mohammed Abu-Rumaileh MD
Occipital strokes and bilateral oculomotor palsy due to bilateral giant cell arteritis
Mohammed Abu-Rumaileh MD, Nezam Altorok MD

Introduction: Giant cell arteritis (GCA) is a vasculitis affecting large and medium arteries, it commonly involves temporal arteries and can lead to severe complications such as vision loss and stroke. Oculomotor palsy is a very rare but serious manifestation. This case report discusses a 79-year-old female with GCA, occipital strokes, and bilateral oculomotor palsy, emphasizing the need for early recognition and treatment.
Case Report: A 79-year-old woman with a history of migraine presented with a two-day history of worsening frontal headache, sinus pain, blurry and double vision, fatigue, dizziness, chills, night sweats, nausea, vomiting, dry cough, and decreased oral intake. Her headache was different from her usual migraines and unresponsive to ibuprofen. Physical exam revealed double vision and diffuse facial tenderness. Labs showed elevated WBC, creatinine, procalcitonin, CRP, ESR, and lactate. Initial imaging and tests showed left occipital strokes and enterocolitis. Initial ophthalmology exam showed vision loss due to occipital stroke and oculomotor palsy. Despite starting pulse-dose steroids after CSF ruled out meningitis, her vision deteriorated, resulting in total vision loss in the right eye. Repeat ophthalmology exams confirmed GCA. Bilateral temporal artery biopsy was positive for GCA. She was discharged on a 6-week prednisone taper. A follow-up ophthalmology exam showed similar right eye findings, however left eye oculomotor palsy resolved.
Discussion: GCA requires prompt diagnosis and treatment to prevent severe complications. This case illustrates the diagnostic challenges, especially with overlapping symptoms like sepsis-like presentations, and blurry/double vision in the setting of occipital strokes and oculomotor palsy. The progression to complete vision loss despite treatment highlights the aggressive nature of GCA. Multidisciplinary management involving neurologists, ophthalmologists, and rheumatologists is crucial. This case aims to increase awareness of GCA's atypical presentation, severe manifestations, and the need for timely intervention.

Mohammed Abu-Rumaileh MD
Recurrent COVID-19 induced warm autoimmune hemolytic anemia
Mohammed Abu-Rumaileh MD, Momin Shah MD, Tahrima Ferdous MD, Clare Miller MD, Rashmi Goyal MD, Nezam Altorok MD

Introduction: COVID-19 has revealed numerous complications, including hematologic issues such as Warm Autoimmune Hemolytic Anemia (WAIHA), where the immune system mistakenly attacks red blood cells. While COVID-19 is linked to the onset of WAIHA, this case presents a unique scenario for a patient experiencing recurrent COVID-19-induced WAIHA, with differing antibodies identified in each infection.
Case Report: In April 2021, an 18-year-old female with sickle cell trait (Hgb A 58%, Hgb S 39%) presented with shortness of breath, jaundice, and severe anemia, with a hemoglobin level of 5.5 g/dL. Lab results showed a positive direct antiglobulin test (DAT) for complement but negative for IgG, consistent with a diagnosis of WAIHA. She was treated with Prednisone and Rituximab, resulting in an improvement of her hemoglobin to 7.0 g/dL before discharge, and subsequently to 11-13 g/dL after completing treatment. For the next 18 months,

her hemoglobin remained stable between 13-13.9 g/dL without signs of hemolysis. In December 2023, she presented again with symptoms following a COVID-19 infection, including severe anemia with a hemoglobin level dropping from 7.8 g/dL to 6.1 g/dL within hours. This time, her DAT was positive for IgG but negative for complement, a change from her previous episode. The patient required blood transfusion and was treated with IV Methylprednisolone, leading to an improvement in her hemoglobin. Unlike her first episode, Rituximab was not needed. Notably, the WAIHA in this patient occurred exclusively during COVID-19 infections, with different antibody profiles in each episode.
Discussion: This case highlights the complex relationship between COVID-19 and WAIHA, where the virus appears to trigger autoimmune hemolysis. The shift in antibody profiles between episodes, with complement positivity in the first instance and IgG positivity in the second, suggests a dynamic immune response influenced by the viral infection. Understanding these variations is critical for managing these cases.

Taryn Hibshman, BS
A complex case of the role of rhinosinusitis in pediatric stroke
Taryn Hibshman, BS, David Garcia, MD, Oscar Salichs, BS, Nahush Bansal, MD

Introduction: Stroke in the pediatric population is a rare but important cause of morbidity and mortality in children with a variety of understudied etiologies.
Case: A 5 year old previously healthy female presented with acute right sided headache, weakness, facial droop, aphasia. A stroke alert was called with an NIH score of 9. A CT angiogram (CTA) carotid and CT brain showed moderate focal narrowing of the M1 segment of left middle cerebral artery (MCA). A respiratory panel revealed human metapneumovirus, and she was started on antibiotics and transferred to the pediatric intensive care unit (PICU) for monitoring. Initial management included aspirin as an anticoagulant, levetiracetam as seizure prophylaxis and methylprednisolone for anti-inflammation. An MRI showed acute infarct of the left basal ganglia without hemorrhage, as well as pansinusitis in the left maxillary, sphenoid and ethmoid sinuses along with a left upper molar signal hyperintensity. In searching for stroke etiology, an echocardiogram, lumbar puncture, EKG, full lab panel and video electroencephalogram were done but all resulted unremarkable. At the time, differentials included cardioembolism, vasospasm from extensive pansinusitis, moyamoya disease, arteriopathy from vasospasm or hematologic pathology. A repeat MRI 5 days later revealed no acute changes. The patient remained hemodynamically stable and her mobility increased with physical therapy. She was transferred to the floor after 8 days in the PICU. After a total of 15 days in hospital, the patient was discharged home in stable condition.
Conclusion: The rare MCA infarct that presented itself abruptly in this healthy child is likely secondary to vasospasm due to a viral infection. Thorough hemorrhagic, thrombotic, hematologic and autoimmune workups were all negative. The patient still follows with neurology for right sided weakness but has had no events since.

Saira Khan BS
Case Report: A mystery case of incidental transaminitis in the setting of rheumatologic disease
Saira Khan BS, Lauren Rager BS, Zachary Schreckenberger MS, Mani Askari MD

Introduction: Transaminitis, characterized by elevated liver transaminases, can stem from numerous underlying causes, posing challenges in diagnosis and management. In this case, we describe a patient case with unclear etiology amidst multiple chronic conditions and nonspecific symptoms.
Case Presentation: A 66-year-old Caucasian female presented to the ED after a fall, with symptoms of increased somnolence, forgetfulness, and weakness over months. Her medical history includes CHF, COPD, GERD, pulmonary hypertension, and uveitis. Initial lab results showed elevated AST (1994 U/L), ALT (780 U/L), and ALP (195 U/L). Imaging was negative. Vital signs included elevated BP and low oxygen saturation. She reported mild chest pain and dyspnea due to CHF exacerbation, and later developed abdominal pain. Her history included intermittent elevated transaminases, swollen fingers, peripheral numbness, arthralgias, and dysphagia, with a past positive anti-RNP titer. Differential diagnoses included drug-induced toxicity,

autoimmune hepatitis, infectious hepatitis, and ischemic shock liver. Testing revealed positive anti-RNP, ANA, p-ANCA antibodies, and low C4. She was treated for CHF with steroids, leading to stabilization and down-trending LFTs. Suspected of having MCTD, she was referred to outpatient rheumatology.
Conclusion: Mixed Connective Tissue Disease (MCTD) is a rare condition characterized by a mix of symptoms from systemic sclerosis, systemic lupus erythematosus, and polymyositis, with high-titer anti-U1-RNP antibodies. Diagnosis is difficult due to nonspecific symptoms and varying criteria. A 2020 study found the Kasukawa criteria most sensitive, requiring one common symptom (e.g., Raynaud's phenomenon), positive anti-RNP antibodies, and signs of at least two mixed syndromes. Although autoimmune hepatitis is rare in MCTD, it should be considered in patients with unexplained liver issues. This case highlights the importance of considering autoimmune causes like MCTD in complex transaminitis cases, highlighting the need for a thorough patient history and differential diagnosis.

Rida Z. Naqvi BS

Gout vs Rheumatoid Arthritis: A diagnostic dilemma

Rida Z. Naqvi BS, Nathaniel Gilbert MD, Aya Abugharbyeh MD

Background: Gout is an inflammatory arthritis caused by monosodium urate crystal deposition in joints, leading to acute, painful episodes (1). While typically presenting as a monoarticular arthritis, often in the first metatarsophalangeal joint, it can sometimes resemble rheumatoid arthritis (RA), a chronic autoimmune disorder causing symmetric, inflammatory polyarthritis (1, 2). The clinical overlap between gout and RA, particularly in cases of polyarticular involvement, can complicate diagnosis and management.
Case Presentation: A 50-year-old male initially presented with symptoms including metacarpophalangeal, knee, and hip swelling, erythema, and stiffness. Initial labs demonstrated elevated CRP (20.6) and normal ESR, RF and CCP. Ultrasound revealed excess synovium in the left wrist, but no erosions or inflammation in the wrist or 2nd-3rd MCP joints bilaterally. Imaging included a left-hand x-ray which showed degenerative changes in the wrist, particularly in the mid-carpal space laterally (see image 1). Based on these findings, an initial diagnosis of RA was considered, and the patient was started on a prednisone taper, however his symptoms persisted. An MRI of the left hand later suggested gout, with findings of erosive changes involving the distal scaphoid and scaphoid-trapezium articulation, along with a non-marginal aggressive enhancing erosion (see image 2). Uric acid was elevated at 7.9, for which treatment initially included allopurinol, later discontinued due to rash. As an alternative, the patient received febuxostat, in addition to corticosteroid injections bilaterally in his first MCPs and for De Quervain's tenosynovitis on the left, leading to improvement of his symptoms.
Conclusion: This case highlights the diagnostic complexity of gout and RA. This patient's initial presentation of symmetric polyarthritis with synovial excess was misleading, suggesting RA. A definitive diagnosis of gout was made when MRI demonstrated a non-marginal aggressive enhancing erosion. This case emphasizes the need for accurate diagnosis through clinical assessment, laboratory tests, and advanced imaging to guide effective management.

Rupesh Ramtel MD

Radiological diagnosis of SAPHO syndrome- A case report

Rupesh Ramtel MD, Nathaniel Gilbert MD, Bashar Kahaleh MD

SAPHO syndrome, which includes synovitis, acne, pustulosis, hyperostosis, and osteitis, is an uncommon chronic inflammatory disorder affecting bones, joints, and skin. We report a case of a 31-year-old woman with a prolonged history of left clavicular pain without any associated skin changes. 31 years old female presented with chronic pain in the left clavicle for 3-4 years, with no relief from physical therapy. A CT scan revealed sclerosis in the medial head of the left clavicle, while an MRI showed inflammation and sclerosis of the sternoclavicular joint. A bone scan indicated symmetrically increased activity in both sternoclavicular joints and negative HLA-B27 test. The patient had a history of well-controlled acne, which later recurred on her back. Initially, NSAIDs provided pain relief but were discontinued due to NSAID-induced colitis. Treatment with

methotrexate was also halted due to side effects. Subsequently, the patient was started on weekly Etanercept, which led to clinical improvement. While NSAIDs and intra-articular injections are initial options for symptom relief, Etanercept has proven highly effective in cases of treatment-resistant SAPHO syndrome. Early diagnosis and treatment of SAPHO syndrome can significantly enhance the patient's quality of life. Radiological imaging is valuable in diagnosing SAPHO in the absence of dermatological symptoms and can help avoid unnecessary tests.

Bisher Sawaf MD

Causal association between rheumatoid arthritis and inflammatory bowel disease: NHANES III cross-sectional study

Bisher Sawaf MD, Yusuf Hallak MD, Nezam Altorok MD MPH

Background: Rheumatoid arthritis (RA) and inflammatory bowel disease (IBD) are prevalent autoimmune disorders affecting joints and the digestive tract. Despite distinct manifestations, both share genetic and immune complexities, impacting a significant portion of the U.S. population.
Objectives: We conducted this cross-sectional study using the NHANES data to explore the association between IBD and RA between the years 2009-2010.
Methods: Our study utilized NHANES data between 2009 and 2010. We analyzed a dataset of 37,857 participants, excluding those under 20 years old and missing data. We conducted various statistical analyses, including descriptive statistics, chi-squared tests, and logistic regression models to predict the likelihood of IBD in individuals with RA**.**
Results: Our analysis included 5,085 participants, among whom 499 had rheumatoid arthritis and 62 had IBD. Our results showed that various covariates significantly influenced the presence of arthritis, including race, marital status, vigorous work activity, smoking, hypertension, diabetes mellitus, congestive heart failure, coronary heart disease, stroke, emphysema, cancer, and uveitis ($P<0.05$). Only 26 arthritis patients had IBD, whereas 36 patients without arthritis had IBD ($P<0.001$). In addition, individuals with rheumatoid arthritis and other types of arthritis exhibited a higher risk of IBD compared to those without arthritis (p-value < 0.05, OR: 1.9-2.9).
Conclusion: Our American dataset analysis confirmed a substantial association between rheumatoid arthritis and inflammatory bowel disease.

Julianna M Sim

Xanthogranulomatous pyelonephritis presenting as elevated inflammatory markers

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Introduction: Xanthogranulomatous pyelonephritis is a rare form of pyelonephritis characterized by chronic granulomatous inflammation in which the renal parenchyma is replaced by sheets of lipid-laden macrophages. It mainly affects middle-aged women but has been reported in men and all ages including children (1). Symptoms are largely non-specific and include flank pain, weight loss, fever, lower urinary tract symptoms, and palpable masses (1). Mainstay diagnosis is made by CT, although MRI also be used (1, 2). Standard treatment includes antibiotics, percutaneous decompression, and radical nephrectomy (3).
Case Presentation: A 32-year-old female was referred to rheumatology for evaluation of elevated C-reactive protein at 130 mg/L, elevated Sed rate at 82 mm/hr, and positive rheumatoid factor. She reported a 1-month history of joint pain affecting the ankles, posterior ribs, and lower back, as well as a 22 lb. weight loss over 3 months, fatigue, and hypotension with dizziness and lightheadedness. She was initially diagnosed with systemic inflammatory response syndrome of unknown etiology, and extensive further workup was pursued. Labs showed persistent leukocytosis with a white blood cell count of 15.79-19.61 10*3/uL and anemia with hemoglobin 6.7-8.0 g/dL. No clear rheumatologic etiology was discovered. CT abdomen and pelvis then revealed an enlarged right kidney with a cystic lesion measuring 13.8 x 9.8 x 11.6 cm. She was diagnosed with xanthogranulomatous pyelonephritis. Two right percutaneous nephrostomy tubes were placed, followed by a

right ureteral stent due to staghorn calculus. Urine culture was positive for Proteus, and antibiotics were initiated. She ultimately underwent a curative right nephrectomy. Pathology showed severe acute and chronic pyelonephritis with xanthogranulomatous inflammation likely secondary to obstructing calculus.
Conclusion: We present a case with elevated inflammatory markers that ended up with non-rheumatologic diagnosis. Xanthogranulomatous pyelonephritis is an elusive diagnosis that should be considered in patients with flank pain and non-specific inflammatory signs.

Tiffany Yu

Thromboangiitis obliterans presenting with atypical manifestation as persistent tenosynovitis of the wrist

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Introduction: Thromboangiitis obliterans (TAO), also known as Buerger's disease, is a rare inflammatory disease affecting approximately 0.02% of the population (1). Classically, it presents in young male smokers with distal extremity ischemia, ischemic digital ulcers, or digit gangrene (1).
Case Presentation: A 49-year-old man with a past medical history positive for osteoarthritis, carpal tunnel, and a significant smoking history presented for pain and swelling of the right wrist and thumb. Along with TAO, sarcoidosis and rheumatoid arthritis were suspected due to elevated ACE and rheumatoid factor. His symptoms, however, were unresponsive to steroids. After excluding other inflammatory or autoimmune joint pain causes, a diagnosis of Buerger's disease was made from MRI which showed thrombophlebitis of the radial artery.
Conclusion: This case underscores the need for clinicians to consider TAO in the differential diagnosis of vascular inflammation, especially in patients with a history of smoking, even in the absence of classic symptoms. TAO often presents with atypical manifestations, including thrombophlebitis and joint pain, which can complicate the diagnostic process. The rarity of TAO and its overlap with other inflammatory conditions make it crucial for healthcare providers to maintain a high index of suspicion. Current literature suggests that early diagnosis and smoking cessation are pivotal in managing TAO. Delayed diagnosis can lead to significant morbidity, including the need for amputations due to progressive ischemia (2). A study by Khandekar et al. (2019) highlights that the prognosis of TAO is directly linked to smoking cessation, with patients who quit smoking having a markedly improved outcome (3) Thus, educating patients about the risks associated with smoking and the importance of early intervention is essential in mitigating the disease's impact.

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