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Editorial

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This edition of *Translation* contains the abstracts submitted to the Third Annual installment Annual Research Symposium of the Department of Medicine, University of Toledo College of Medicine & Life Sciences. I wish to thank the editors and staff of the Journal for making this edition possible. It is the first time the abstracts of that meeting are being formally published and we greatly appreciate the opportunity.

The Annual Research Symposium serves multiple important purposes for our department and the College. First, it calls attention to the depth and breadth of biomedical investigation, basic laboratory science, clinical translational, and quality and outcomes research that exists, but can be overshadowed by our clinical and educational missions. The research programs involve people at every level, including faculty, staff, post-doctoral fellows, clinical fellows, graduate students, residents, medical and undergraduate students, all working collaboratively on diverse projects in each of our 11 divisions. This year, approximately 140 abstracts were submitted to the symposium, the great majority of which have trainees as first or presenting authors.

Each year as part of the symposium, we invite in a world class scientist to provide a keynote address. Bringing outstanding investigators on campus helps to energize us and to remind us what can be accomplished through science to better understand our world and to advance medical therapeutics. The opportunities I had as a trainee to listen and interact with leading investigators who came on campus are still some of my favorite memories from my entire academic career.

Publishing the abstracts is also a critical component of the program. Even in a single department like Medicine, individual research efforts can become siloed and investigators with overlapping interests may be unaware of each other's work. The published abstracts serve as a resource and database that investigators can access throughout the year to be better informed about ongoing work close to home and to identify potential collaborators.

On a personal level, I am extremely proud of our trainees, faculty, and staff for their commitment to scholarship and to the active exchange of ideas demonstrated here. These are fundamental values for any academic department, and that I believe are clearly on display in these published proceedings.

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Safety and Efficacy of Anifrolumab in Systemic Lupus Erythematosus: Systematic Review with Network Meta-analysis

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Introduction: Enhanced cold sensitivity is an early and consistent phenomenon in scleroderma (SSc). Introduction: Anifrolumab is a human monoclonal antibody targeting type 1 interferon receptor subunit 1 for treatment of systemic lupus erythematosus (SLE) with varying results. We performed a systematic review and network meta-analysis comparing varying doses of Anifrolumab versus placebo for treatment of SLE.

Methods: A comprehensive search of different databases was undertaken through May 31, 2022. The primary outcome was British Isles Lupus Assessment Group (BILAG)–based Composite Lupus Assessment (BICLA) score at 52 weeks. Secondary outcomes assessed included overall flares at 52 weeks, adverse events and serious adverse events. Network meta-analysis was conducted using random effects model and frequentist approach.

Results: A total of 3 RCTs with 4 unique intervention arms were included (Placebo, Anifrolumab 150mg, Anifrolumab 300mg, and Anifrolumab 1000 mg). A total of 1129 patients were randomized, of which 953 (84.4%) completed the study. The mean age of patient was 41.2 ± 1.3 years and female proportion was 1045/1129 (92.5%). Significantly higher 'BICLA response' was noted for Anifrolumab 300mg compared to placebo (RR: 1.61, CI: 1.30-1.99) (Figure 1A). The overall 'flares' were also significantly lower for Anifrolumab 300mg compared to placebo (RR: 0.76, CI: 0.65-0.90) (Figure 1B). The adverse events were evaluated by 4 groups. Significantly higher 'any adverse events' were noted for Anifrolumab 300mg (RR: 1.10, CI: 1.04-1.16) and Anifrolumab 1000mg (RR: 1.14, CI: 1.02-1.26) (Figure 1C). None of the groups of Anifrolumab showed significantly higher adverse events compared to Placebo (Figure 1D). Using the P-score, Anifrolumab 300mg was ranked higher for improved BICLA

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response and lower flares, while the placebo group ranked higher for lower overall and serious adverse events.

Conclusion: Anifrolumab 300mg showed significantly better response at 52 weeks and lower overall flare events for SLE. The drug can be employed in clinical practice for SLE patients.

Clinical Characteristics, Management, and Outcomes of CLIPPERS: A Comprehensive Systematic Review of 140 patients from 100 Studies

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Introduction: Chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) is a rare inflammatory disorder of the central nervous system, characterized by symptoms referable to the brainstem and cerebellum such as, diplopia, gait ataxia and cerebellar dysarthria. The features and outcomes of CLIPPERS remains uncertain. Wwe conducted this comprehensive systematic review to summarize the existing studies that described CLIPPERS in the literature and to provide a quantitative assessment on the clinical characteristics, management, and outcomes of this rare syndrome.

Methods: A search of PubMed and Web of Science databases was conducted from inception until January 15, 2022, was conducted. We included the cases that reported probable or definite diagnosis of CLIPPERS based on Taieb et al.'s criteria. The quality of the included studies was assessed using the JBI Critical Appraisal Tool. Descriptive statistics were performed to analyze the studies.

Results: We identified 140 patients with CLIPPERS (mean age: 46±18 years and males were 60%). The average follow-up duration was 32.27±57.8 months. Ataxia was the most common presenting symptom. Sixteen percent of the cases were associated with malignancy, mostly hematologic malignancies. The overall relapse rate was 59.2%, and the duration of steroid therapy was considerably shorter in the relapsed cases than in the non-relapsed (mean 6.19±7.9 vs. 10.14±12.1 days, respectively, P=0.04). The overall mortality rate was 10%, but mortality in patients with malignancy was 30% and it was 12% in patients with relapses.

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Relapsing Polychondritis: A Case Report of the Use of Adalimumab in Steroid Dependent Disease

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Introduction: Relapsing polychondritis is a rare chronic immune mediated disease characterized by inflammation in cartilaginous structures. The disease has traditionally been managed with systemic glucocorticoids and immunosuppressive agents such as methotrexate, cyclophosphamide, and mycophenoloate.

Case Presentation: A 54 year old male with relapsoing polychondritis characterized by bilateral conjunctivitis and chondritis of the ear. The addition of adalimumab aided in tapering of high dose steroids after attempts with immunosuppressive agents were unsuccessful.

Conclusion: Biologic therapy with TNF-alpa inhibition can be considered in patients with refractory or steroid dependent relapsing polychondritis.

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Activation of the Transient Receptor Potential Ion Channel TRMP8 Mediates Upregulation 0f Profibrotic Genes, A New Pathway to Tissue Fibrosis

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Introduction: Enhanced cold sensitivity is an early and consistent phenomenon in scleroderma (SSc). TRPM8 protein is cold-and menthol-sensing calcium (Ca2+) ion channel. In this study, we evaluated TRPM8 expression, the effects of TRPM8 activation on fibroblast (FB) fibrotic gene expression, and intracellular signaling.

Methods: FBs were isolated from involved SSc skin and matched control subjects. TRPM8 activation in FBs was triggered by the TRPM8 agonist menthol (MT) or by exposure of cells to cold (18C°). Intracellular calcium concentration ([Ca2+] i) was determined using Fura-2 or Fura-4. The mRNA and protein expression levels were determined by qPCR and WB . The production of ROS was detected by dihydroethidium (DHE). SMAD3 binding to the CTGF promoter region was detected by chromatin immunoprecipitation assay (ChIP).

Results: TRPM8 is expressed in dermal FBs. The expression levels of TRPM8 were significantly higher in SSc-FBs and SSc-skin biopsies. MT or cold exposure increased [Ca2+]}i, enhanced expression of COL1A1, aSMA, FN, and CTGF, and also evoked production of intracellular ROS. SSc-FBs were more sensitive to MT or cold than normal FBs. These effects were blocked by the addition of Capsazepine, or TRPM8 siRNA, or antioxidants. Moreover, MT induced SMAD3 phosphorylation and nuclear accumulation. Chip assay confirmed that SMAD3 is recruited to the CTGF promoter after MT stimulation in FBs.

Conclusion: Functional TRPM8 is expressed in human dermal FBs and enhanced expression was observed in SSc FBs and skin. The activation of TRPM8 mediated enhanced expression of the profibrotic genes in FBs via the calcium-ROS-SMAD3 signaling pathway.

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Downregulation of Microrna-126 in Scleroderma is Associated with Epigenetically Mediated Nitric Oxide Synthase Repression and Enhanced Platelet/Endothelial Interaction

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Introduction: SSc vasculopathy is characterized by deficient endothelial nitric oxide (eNOS) and enhanced platelet adhesion to endothelial cells. In this study, we examined the epigenetic regulation involved in enhanced platelet adhesion, deficient eNOS expression, and the role of miRNA-126 in this process.

Methods: Platelet adhesion to MVECs was determined by the Calcein AM method. eNOS, NOS3, miR-126, DNA methyltransferase-1 (Dnmt1) expression were measured by qPCR and WB. L-NAME was used as NO antagonist. MiR-126 expression was inhibited by hsa-miR-126 inhibitor and enhanced by hsa-miR-126 Mimic.

Results: MiR-126 expression levels were significantly downregulated in SSc-MVECs. SSc MVECs supported platelet adhesion at a higher level than control cells (10.16+/-2.8 platelet/ EC vs. 3.3 +/-0.94 in control cells, mean +/-SD, P<0.001). Addition of L-NAME to control MVECs resulted in enhanced platelet adhesion in a dose-dependent fashion. NOS3 expression levels were significantly reduced in SSc cells, Dnmt1 expression levels were significantly higher in SSc cells. NOS3 under expression in SSc cells was related to heavy DNA methylation of the promoter CpG islands as shown by promoter sequence analysis of DNA after bisulfite modification. Upregulation of MiR126 in SSc MVECs resulted in the reduction of Dnmt1 and upregulation of NOS3 expression levels, while the inhibition of MiR 126 expression levels in control MVECs resulted in decreased NOS3 levels and enhanced Dmnt1 levels.

Conclusion: The data demonstrate that defective miR-126 expression in SSc MVES leads to upregulation of Dmnt1 expression and downregulation of NOS3 expression that is associated with defective NO release and enhanced platelet/endothelial interaction.

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IgA Vasculitis Associated with COVID-19 Infection Successfully Treated with Corticosteroid Regimen without Relapse

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Introduction: Immunoglobulin A (IgA) vasculitis is an autoimmune disease associated with bacterial and viral infections and characterized by palpable purpura, arthralgia, abdominal pain, and renal involvement. COVID-19 can trigger numerous autoimmune conditions, including IgA vasculitis.

Case: We report a 33-year-old male with COVID-19 infection two weeks before developing worsening palpable purpura for one week then severe abdominal pain, nausea, emesis, diarrhea, hematochezia, and arthralgia. Outpatient prednisone for two days improved his lesions. Examination revealed diffuse severe abdominal tenderness, extensive palpable purpura including legs, pelvis, and buttocks, and petechiae on the bilateral arms. Labs revealed mildly elevated ALT, leukocytosis from corticosteroids, D-dimer at 808 ng/mL, CRP at 1.6 mg/dL, and ESR at 22 mm/h. Lipase and CMP were otherwise unremarkable. ANA, ANCA, anti-chromatin IgG, anti-smith, and antinuclear ribonucleoprotein antibodies were negative. Total complement, C3, and C4 levels were normal. Urinalysis revealed glucosuria, proteinuria, and ketonuria; no RBCs or WBCs on microscopy. Positive COVID-19 PCR and IgG antibodies indicated recent infection. Mycoplasma pneumoniae IgM antibodies and stool studies were negative. Right thigh punch biopsy with direct immunofluorescence revealed granular IgA and C3 deposition plus homogeneous fibrinogen deposition within many superficial dermal vessel walls, consistent with IgA vasculitis. Patient received intravenous methylprednisolone 80 mg daily for three days, followed by oral prednisone 60 mg daily with significant improvement. Steroids were tapered and discontinued at six weeks without relapse.

Conclusion: This case demonstrates active COVID-19 infection precipitated biopsy-proven IgA vasculitis. Treatment with six weeks of tapered corticosteroids resolved symptoms and skin lesions without relapse.

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Vasopressin Modulates Endothelial and Fibroblast Gene Expression

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Introduction: SSc vasculopathy is characterized by deficient endothelial nitric oxide (eNOS) and enhanced platelet adhesion to endothelial cells. In this study, we examined the epigenetic regulation involved in enhanced platelet adhesion, deficient eNOS expression, and the role of miRNA-126 in this process.

Methods: Platelet adhesion to MVECs was determined by the Calcein AM method. eNOS, NOS3, miR-126, DNA methyltransferase-1 (Dnmt1) expression were measured by qPCR and WB. L-NAME was used as NO antagonist. MiR-126 expression was inhibited by hsa-miR-126 inhibitor and enhanced by hsa-miR-126 Mimic.

Results: MiR-126 expression levels were significantly downregulated in SSc-MVECs. SSc MVECs supported platelet adhesion at a higher level than control cells (10.16+/-2.8 platelet/ EC vs. 3.3 +/-0.94 in control cells, mean +/-SD, $P<0.001$). Addition of L-NAME to control MVECs resulted in enhanced platelet adhesion in a dose-dependent fashion. NOS3 expression levels were significantly reduced in SSc cells, Dnmt1 expression levels were significantly higher in SSc cells. NOS3 under expression in SSc cells was related to heavy DNA methylation of the promoter CpG islands as shown by promoter sequence analysis of DNA after bisulfite modification. Upregulation of MiR126 in SSc MVECs resulted in the reduction of Dnmt1 and upregulation of NOS3 expression levels, while the inhibition of MiR 126 expression levels in control MVECs resulted in decreased NOS3 levels and enhanced Dmnt1 levels.

Conclusion: The data demonstrate that defective miR-126 expression in SSc MVES leads to upregulation of Dmnt1 expression and downregulation of NOS3 expression that is associated with defective NO release and enhanced platelet/endothelial interaction.

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Decreased Prevalence of Autoimmune Connective Tissue Diseases in Type 1 and Type 2 Diabetes

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Background/Purpose: Evidence suggest that some autoimmune diseases coexist at a higher rate than expected, reflecting common pathogenetic pathway, while an inverse association is also reported . In this study we investigate the co-occurrence of systemic sclerosis (SSc), Systemic lupus Erythematosus (SLE) and Sjogren Syndrome (SS) In patient with type 1 and type 2 diabetes mellitus (DM).

Methods: Health Care and Utilization Project (HCUP) data for the year 2019 was searched. We identified patients with Type 1 and Type 2 DM, SSc with and without lung involvement, patients with SS, and SLE with and without lupus nephritis (LN). We used weighted logistic regression to examine the association between each of these diseases and DM.

Results: The prevalence of SSc among patients with Type 1 and 2 DM was significantly lower than that for the non-DM control group. Also, the prevalence of SSc with lung involvement was lower among patients with Type 1 and type 2 DM. The prevalence of SLE and SLE-LN were lower among patients with type 1 and in type 2 DM. A decrease prevalence of SS in patients with type 1 and type 2 DM was also seen.

Conclusion: The data demonstrates an inverse relation between SSc, lupus, and SS in patients with DM. This suggests that these diseases and DM may have different immune pathogenesis. There was also significantly lower incidence of organ complications such as lupus nephritis and SSc lung disease among patients with diabetes suggesting that diabetes and treatment of diabetes may alter the clinical expression of these disorders.

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Intermittent High Grade AV-Block and Atrial Flutter Associated with Lyme Carditis: A Case Report

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Introduction: Lyme disease is the most common tick-borne infection caused by spirochetes in the Borreliacidal family. In USA, infection is caused primary by Borrelia burgdorferi. Lyme disease typically progresses in phases. The clinical manifestations progress from early localized to early disseminated disease and then finally late disease. Lyme carditis occurs in 1% of untreated patients in the early disseminated phase. While complete AV-block is most common, atrial flutter is a rarer manifestation.

Case Report: Otherwise healthy 43-year-old man presented with new onset dizziness, fatigue, and syncope. Initial EKG showed complete heart block. Telemetry showed he developed underlying atrial flutter with episodes of ventricular standstill. Echocardiogram and cardiac MRI were unremarkable. Troponin was negative. Serologies for borrelia burgdorferi as well Lyme IgG and IgM western blot were positive. He was treated with IV Ceftriaxone and discharged with an active fixation pacemaker.

Discussion: Cardiac involvement occurs during the early disseminated phase of the disease usually within weeks after the onset of infection. 90% of Lyme carditis presents as high-degree atrioventricular block (AVB), whereas the other 10% is represented by myocarditis, pancarditis or other types of arrhythmias and conduction disorders. Other abnormalities that may occur include prolonged QTc, asystolic pauses and other supraventricular tachyarrhythmias. The mechanism of atrial flutter in Lyme carditis isn't fully understood.

Conclusion: It is important for physicians to understand the cardiac manifestations of Lyme disease. Patients who are otherwise young and healthy, who present acutely in an otherwise unexplained cardiac rhythm should have Lyme carditis ruled out or at least considered.

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Suspected Doxycycline Induced Acute Interstitial Nephritis

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Introduction: This report describes a case of a patient presenting with diabetic ketoacidosis who experienced progressively worsening acute kidney injury after exposure to multiple nephrotoxic agents during hospital course. The patient's presentation led to a relatively broad differential for acute kidney injury (AKI), which included contrast-induced nephropathy, vancomycin-induced nephrotoxicity, and interstitial nephritis secondary to antibiotic use. Interstitial nephritis associated with doxycycline use is poorly described in the literature, which delayed cessation of suspected offending agent.

Case Presentation: A 28-year-old male with past medical history of diabetes mellitus type 2 presented with diabetic ketoacidosis. On admission, patient underwent CT neck with contrast for evaluation of cellulitis and was placed on empiric antibiotic therapy (vancomycin, piperacillin-tazobactam and metronidazole). Patient was later transitioned to oral doxycycline. Within 24 hours of starting doxycycline, the patient developed AKI. Despite fluid resuscitation and oral prednisone, the patient's kidney function rapidly worsened. Doxycycline was discontinued, and 48 hours after the last dose, renal function began to steadily improve. Electron microscopy findings from renal biopsy exhibited severe acute interstitial nephritis.

Discussion: Pathology findings confirm acute interstitial nephritis, ruling out other potential causes including contrast-induced nephropathy and vancomycin-induced tubular necrosis. The patient experienced a decline in renal function less than 7 days from introduction of an offending agent, which would indicate a repeat exposure. The patient received doxycycline in the week prior to admission. Drug-induced acute interstitial nephritis characteristically improves after withdraw of the offending drug. Doxycycline was the only agent for which kidney function improved after withdraw.

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Primary Esophageal Extra-Gonadal Yolk Sac Tumor Metastasized to the Liver

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Introduction: Extra-gonadal germ cell tumors (EGCTs) usually arise from midline structures such as the retroperitoneum, mediastinum, and sacrococcygeal region. EGCTs originating from the gastrointestinal system such as the stomach and esophagus are rarely reported. No reported case of primary esophageal yolk sac tumor (YST) has been published yet in the literature.

Case Presentation: A 62-year-old male presented with difficulty swallowing and feeling of food stuck in the middle of his chest for two months. There were associated right upper-quadrant abdominal pain, early satiety, and weight loss (25 pounds) in the last three months. Abdominal CT demonstrated abnormal thickening in the distal esophagus and metastatic disease in the liver adjacent to the distal esophagus. Biopsy of the liver lesions showed poorly differentiated carcinoma with features consistent with YST (positive isochromosome 12p FISH). EGD showed partially obstructing tumor in the lower third of the esophagus. Biopsy of the esophageal mass also showed findings consistent with the YST. PET scan showed increased activity in the lower esophagus but did not identify testicular activity. Blood tests showed AFP of 12,752, HCG of 11, and LDH of 1039. Brain MRI and testicular ultrasound findings were unremarkable. Eventually, he was diagnosed with stage IIIc M1b (liver metastasis) primary esophageal YSK. The patient was started on a chemotherapy regimen with etoposide, ifosfamide, and cisplatin.

Discussion: Primary gastrointestinal germ cell tumors have been very rarely reported in the literature. To the best of our knowledge, our case is the first extra-gonadal yolk sac tumor that originated from the esophagus and metastasized to the liver.

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Midostaurin in Advanced Systemic Mastocytosis: A Systematic Review and Meta-analysis

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Background: Midostaurin, an oral multikinase inhibitor, is approved for the treatment of advanced systemic mastocytosis (SM).

Methods: We systematically searched the following databases: PubMed/MEDLINE, Embase, and Cochrane through February 02, 2022, to include all studies that assessed the effect of midostaurin on clinical outcomes of patients with advanced SM. Our primary outcome was the overall response rate (ORR). All statistical analyses were performed using Open Meta Analyst (CEBM, University of Oxford). Pooled rates and corresponding 95% confidence intervals (CI) were calculated using DerSimonian-Laird/Random-effects approach.

Results: Four studies (two clinical trials and two observational studies) with a total of 156 patients with advanced SM were included in the pooled analysis. The mean age of the patients was 59.6±15.8 years, and males represented 64.7% of total patients. The most common subtype of advanced SM was SM associated with hematological neoplasm (59%) followed by aggressive SM (23.1%). Three studies reported the KIT D816V mutation status, and 85.2% of patients were positive for KIT D816V mutation. The mean duration of treatment with midostaurin was 10±15.3 months. The pooled ORR was 60% (95% CI 46.5%-73.5%) over a mean follow-up duration of 41.1±38.7 months. The PD and SD rates were 12.8% (95% CI 7.6%-18%) and 10.6% (5.3%-15.9%), respectively. Treatment discontinuation due to AEs occurred in 25.6% (95% CI 18.8%-32.4%). The most common hematological grade ≥3 treatment-related AE was anemia (29%), while fatigue (7.1%) was the most common non-hematological grade ≥3 treatment-related AE.

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Conclusion: Our study demonstrated that midostaurin could achieve a durable response in patients with advanced SM with an acceptable safety profile.

A Novel Lipidomics Approach to Predicting Pulmonary Hypertension in Human Heart Failure

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Pulmonary hypertension (PH) in heart failure with preserved ejection fraction (HFpEF) is associated with high morbidity and mortality; however, the pathophysiology of disease is unknown. Polyunsaturated Fatty Acid (PUFA) metabolites play a vital role in cardiovascular health by regulating balance between anti-inflammation and pro-resolution processes. An imbalance of these metabolites can lead to PH. We hypothesize that a PUFA-derived mediator score can be created using lipidomics analysis to accurately predict PH in patients with HFpEF. Pulmonary venous and arterial serum samples were collected during right heart catheterization from 88 HFpEF patients without PH (control, n=40), HFpEF with isolated postcapillary PH (pc-PH, n=30), and HFpEF with combined post- and precapillary PH (cpc-PH, n=18). A total of 143 PUFA metabolites were analyzed by mass spectroscopy with Multiple Reaction Monitoring. A series of regression models was conducted to assess which metabolites were predictive of PH. Low arterial 7(S)-Maresin1, a pro-resolution molecule, was significantly more predictive of HFpEF with pc-PH (p=0.0003) and HFpEF with cpc-PH (p=0.004) when compared to control. Low venous 11(12)-EpETrE, an anti-inflammatory molecule, was more predictive of HFpEF with pc-PH (p=0.02) compared to control. Elevated arterial 19(R)- OH PGF2 alpha and 20-OH PGF2 alpha both pro- and anti-inflammatory molecules, were more significant predictors of HFpEF with cpc-PH compared to pc-PH (p=0.006). These findings support the hypothesis that distinct PUFA metabolites play a significant role in mediating PH in HFpEF. Our study introduces a novel lipidomics framework and approach for the diagnostic assessment of PH in patients with HFpEF.

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Aerosolized Harmful Algal Bloom Toxin Microcystin-LR Induces Inflammatory Signaling in Human Airway Epithelial Cells

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Introduction: Harmful algal blooms plague bodies of freshwater globally. These blooms are often composed of outgrowths of cyanobacteria capable of producing the heptapeptide Microcystin-LR (MC-LR) which is a well-known hepatotoxin. Recently, MC-LR has been detected in aerosols generated from lake water. However, the risk for human health effects due to MC-LR inhalation exposure have not been extensively investigated.

Methods: In this study, we exposed a fully differentiated 3D human airway epithelium derived from 14 healthy donors to MC-LR-containing aerosol for 3 minutes per day for 3 days. Concentrations of MC-LR ranged from 100 pM to 1 μM.

Results: Although there were little to no detrimental alterations in measures of the airway epithelial function (i.e. cell survival, tissue integrity, mucociliary clearance, or cilia beating frequency), a distinct shift in the transcriptional activity was found. Genes related to inflammation were found to be upregulated such as C-C motif chemokine 5 (CCL5; log2FC = 0.56 , p = 0.02) and C-C chemokine receptor type 7 (CCR7; log2FC = 0.83, p = 0.03). Functionally, conditioned media from MC-LR exposed airway epithelium was also found to have significant chemo-attractive properties for primary

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human neutrophils. Additionally, increases were found in the concentration of secreted chemokine proteins in the conditioned media such as CCL1 (log2FC = 5.07 , p = 0.0001) and CCL5 (log2FC = 1.02, p = 0.046).

Conclusion: These results suggest that MC-LR exposure to the human airway epithelium is capable of inducing an inflammatory response that may potentiate acute or chronic disease.

Harmful Algal Bloom Impacts on Human Health: An Analysis of National Emergency Department Data in the U.S. from 2016 to 2018

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Introduction: Harmful algal bloom (HAB) cyanobacterial species produce cyanotoxins that disrupt ecosystems and are harmful to both human and animal health. These HAB events are increasingly common around the world and have been recorded in every continental state. HAB cyanotoxins released by cyanobacteria affect a wide range of tissues, including the skin, nervous system, liver, and lungs. We sought to determine trends and patterns in diagnostic codes relating to HAB exposures from the Healthcare Cost and Utilization Project's (HCUP) Nationwide Emergency Department Sample (NEDS).

Methods: We analyzed HCUP NEDS data from years 2016 to 2018 as these represented the years in which complete data was available using the World Health Organization (WHO) International Classification of Diseases-10 diagnosis codes for HAB exposure. For each year's grouping, statistical analysis was performed to uncover patterns and trends. Each patient occurrence was screened for the most prevalent comorbidities associated with HAB exposures.

Results: Over the 3-year period studied, there were 118 reported patient admissions to the Emergency Department. Respiratory related illness accounted for the majority of comorbidities and were present in 53% of patients, including 30% as the primary diagnostic code.

Conclusion: These data represent one of the first attempts to analyze HAB exposure related illness presenting to Emergency Departments in the United States. The predominance of respiratory related diagnostic codes in these patients suggests greater attention to these conditions in the risk characterization of HAB exposure in the development of evidence-based prevention and treatment strategies.

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Cardioprotective Effects of Paraoxanase 3 in a Dahl Salt-Sensitive Rat Model of Chronic Kidney Disease

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Objective: Paraoxanases (Pon) are hydrolytic enzymes with three distinct isoforms. Decreased circulating Pon activity is associated with increased oxidant stress and adverse clinical outcomes in the setting of chronic kidney disease (CKD), yet the mechanism of action is unknown. We tested the hypothesis that Pon-3 is cardioprotective in a Dahl salt-sensitive model of hypertensive renal disease.

Methods: Ten week old, age-matched, Dahl salt-sensitive wildtype and Pon3 mutant male and female rats were maintained on eight percent high salt diets for eight weeks to initiate the salt-sensitive hypertensive renal disease characteristic of this model. After eight weeks, animals were euthanized and hearts were processed for histology. Echocardiography was performed to measure left ventricular function.

Results: By 8 weeks, mortality was observed in 18.2% of male SS-Pon3 KO rats on high salt; no mortality was observed in male SS male rats on high salt. In female rats, by 8 weeks 100% mortality was observed in SS-Pon3 KO rats on high salt diet while no mortality was observed in SS rats on high salt. High salt fed SS-Pon3 KO male rats that survived the echocardiography study demonstrated significantly decreased left ventricular end-systolic diameter and end-diastolic diameter, as well as significant increases in left ventricular relative wall thickness compared to age matched SS rats. Furthermore, SS-Pon3 KO rats demonstrated significantly increased heart-weight-to-body-weight ratio compared to age matched SS rats.

Conclusion: These findings suggest a cardioprotective role for PON-3 in the setting of salt-sensitive hypertensive renal disease.

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Harmful Algal Bloom Toxin Microcystin-LR Induces Macrophage Inflammation of Lung Tissues

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Introduction: Harmful Algal Blooms, or HABs, are rapidly growing algae or cyanobacteria that may produce toxins, which are dangerous for humans and animals. They arise from warm temperatures and nutrient pollution. HAB toxins, such as Microcystin-LR (MC-LR) present public health concerns, such as the transmission of HAB toxins via the generation of aerosols. Exposure to aerosolized HAB toxins may even potentially be linked to hazardous health consequences, such as airway inflammation. In previous studies, oral exposure to MC-LR in rodents led to macrophage infiltration of the colon. Therefore, the objective of this study was to investigate the role of macrophages in the airways in response to MC-LR exposure.

Methods: C57BL/6J and BALB/c mice were exposed to MC-LR aerosols at a concentration designed to mimic potential environmental exposure. Lung tissues were analyzed for exposure dependent changes in gene expression, cytokine concentrations, and immune cell infiltration.

Results: Gene expression profiles of mice exposed to HAB toxin aerosols demonstrated a significant increase in the CD68 gene expressed by macrophages in C57BL/6J mice. Cytokine and chemokine protein concentration profiles also showed significant increases in multiple macrophage associated

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markers. Furthermore, IHC stains of lung tissue also revealed higher numbers of macrophages in C57BL/6J, but not BALB/c mice.

Conclusion: It appears that airways exposed to MC-LR aerosols respond with an increase in macrophage inflammation. These findings warrant further investigation into the impact of this toxin in populations with pre-existing airway inflammation.

Paraoxanase-1 Modulates Cardiotonic Steroid Induced Cardiac Inflammation and Fibrosis in Dahl Salt Sensitive Model of Chronic Kidney Disease

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Objective: Cardiotonic steroids (CTS) are known ligands of the Na+/K+-ATPase (NKA) and chronic elevations in volume expanded conditions such as hypertension and chronic kidney disease (CKD). Paraoxonase-1 (PON1) is a lactonase enzyme that can hydrolyze CTS to inactive open-ring forms making them incapable of stimulating NKA and initiating pro-inflammatory signaling cascades. We hypothesized that PON-1 can attenuate the progression of cardiac inflammation in CKD via modulating the pathogenic pathways induced by CTS signaling using a well characterized Dahl salt-sensitive rat model of hypertensive renal disease and elevated CTS.

Methods: Dahl salt-sensitive wild type, PON1 knockout, and PON1 knockout rats that were treated with 3E9 anti-CTS monoclonal antibody were fed a high salt diet for five weeks to induce hypertensive renal disease and elevate CTS levels. Hematoxylin and Eosin (H&E) staining was performed on hearts to analyze immune cell infiltration. Real-time PCR analysis was performed for markers of inflammation (IL-6, IL1β, and CCL2), hypertrophy (Myh7, NPPA, and Slc8a), and fibrosis (Timp-1).

Results: RT-PCR analysis revealed significantly increased expression of cardiac inflammatory, hypertrophy, and fibrotic markers in SS-PON1 KO compared to SS-WT rats after high salt feeding. Treatment of SS-PON-1 KO rats with 3E9 mAb significantly decreased expression of Timp-1, IL-6, Ccl2, IL1β, NPPA, Myh7 and Slc8a. H&E analysis of hearts revealed significantly decreased immune cell infiltration in SS-PON-1KO rats treated with 3E9 mAb.

Conclusion: Our findings suggest that PON-1 via its counter-regulatory mechanism of the CTS signaling axis exhibits a cardioprotective role in chronic kidney disease.

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Paraoxanase 1 Deletion Leads to Increased Cardiac Remodeling and Cardiac Fibrosis in a Dahl Salt-Sensitive Rat Model of Chronic Kidney Disease

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Introduction: Paraoxanase 1 (Pon-1) synthesis occurs in liver and circulates bound to high-density lipoproteins (HDL), contributing to HDL's antioxidant, anti-inflammatory and anti-atherogenic properties. Decreased circulating Pon-1 activity is associated with increased oxidant stress and adverse clinical outcomes in the setting of chronic kidney disease (CKD). Whether decreased Pon-1 is mechanistically linked to adverse cardiovascular outcomes in CKD, however, remains unclear. We tested the hypothesis that Pon-1 is cardioprotective in a Dahl salt-sensitive model of hypertensive renal disease.

Methods: Ten-week-old, age-matched male and female control Dahl salt-sensitive rats (SS) and Pon1 mutant rats (SS-Pon1 KO) were maintained on high salt diet (8% NaCl) for up to 12 weeks to initiate salt-sensitive hypertensive renal disease. Left ventricular geometry and function were assessed in male SS and SS-Pon1 KO rats at the end of week four of high salt diet via echocardiography and animals were euthanized and hearts processed for histology.

Results: SS-Pon1 KO male rats demonstrated a significantly increased relative cardiac wall thickness (0.77+/-0.05 vs. 0.58+/-0.02) and fractional shortening (0.62+/-0.02 vs. 0.53+/-0.01), as well as significantly increased mean velocity of circumferential fiber shortening (circ/s, 6.37+/-0.33 vs. 5.52+/-0.17) and cardiac index (ml/min/kg, 184+/-18 vs. 136+/-11) vs age matched SS rats. No difference in heart rates was observed. Upon histological examination, heart sections of SS-Pon1 KO male rats showed a significant increase in fibrosis and heart-weight-to-body-weight ratio compared to the age matched SS rats.

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Conclusion: Our findings suggest that loss of PON-1 in salt-sensitive hypertensive rats leads to a cardiac phenotype consistent with compensated heart failure.

Paraoxanase 1 Regulation of Cardiac Inflammation and Fibrosis in a Dahl Salt-Sensitive Rat Model of Chronic Kidney Disease

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Objective: Paraoxonase-1 (PON1) is a lactonase enzyme associated with high-density liproteins (HDL), contributing to its antioxidant, anti-inflammatory and anti-atherogenic properties. Deficiencies in PON1 result in oxidative stress and adverse clinical outcomes in chronic kidney disease (CKD), however the link to cardiovascular pathology in CKD is unknown. We investigated the hypothesis that PON1 is cardioprotective in a Dahl Salt-Sensitive model of hypertensive renal disease.

Methods: Age matched 10-week-old Dahl salt-sensitive (SS) and mutant PON1 knock-out (SS-PON-1 KO) male rats were maintained high salt diet (8% NaCl) for five weeks to induce hypertensive renal disease. Echocardiography was performed 1 week prior to euthanasia and hearts were processed for histopathologic and real-time (RT) PCR analysis of cardiac hypertrophy and fibrosis.

Results: RT PCR analysis of cardiac left ventricular tissue revealed an increase in the expression of natriuretic peptide A ($p< 0.0001$) and myosin heavy chain 7 ($p< 0.0001$), suggesting cardiac hypertrophy in SS-PON-1 KO male rats compared to controls (SS). A decrease in sarcoplasmic/endoplasmic reticulum Ca2+ ATPase ($p< 0.0001$) expression was observed. CD68 staining showed an increase in macrophage infiltration in both perivascular ($p< 0.0277$) and interstitial ($p< 0.005$) regions within the heart sections of SS-PON-1 KO male rats. Furthermore, upregulation of tissue inhibitor of metalloproteases 1 ($p< 0.0001$) expression was seen.

Results are consistent with the echocardiography analysis and trichrome analysis indicating increased cardiac fibrosis in SS-PON-1 KO vs SS rats.

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Conclusion: Our findings indicate that loss of PON1 in salt-sensitive hypertensive rats results in compromised left ventricular function and hypertrophy, increased cardiac fibrosis and macrophage infiltration.

Venous Stent Migration to the Heart: Case Report and Review of the Literature

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Background: Venous stent migration (VSM) to the heart is considered a rare complication. Several case reports and case series have documented this event. A large percentage of reported cases were asymptomatic and discovered incidentally; additionally, there is no standardized database tracking stent migration occurrences. Therefore, the true incidence of VSM is likely higher than thought. Diagnosing this complication is obfuscated by its general presentation, which can include dyspnea, chest pain and arrhythmia. The diagnosis is often missed because of its non-specific presentation and the belief that it is a rare occurrence. We present a case of bilateral iliac vein stent migrations into the right ventricle and interlobar artery.

Case presentation: A 74 year old woman with history of heart block and venous thromboembolism presented with dyspnea, atrial flutter and nonsustained ventricular tachycardia. Bilateral iliac vein stents were placed five years prior and a pacemaker six weeks prior. She was on warfarin and diltiazem. Physical exam demonstrated jugular distension, murmur, and lower extremity edema. Electrocardiogram revealed AV paced rhythm. 2-D transthoracic echo revealed a hyperechoic mass in the right ventricular outflow tract. A follow up CT revealed one iliac vein stent lodged in the right ventricular outflow tract and the other in a right interlobar pulmonary artery. Cardiothoracic surgery was consulted, and the patient later underwent uneventful surgical removal of both stents.

Conclusion: VSM is considered a rare complication; however, its true incidence is likely higher than commonly thought because many cases go undiagnosed and there is no standardized reporting process.

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Exposure to Nanoplastics Induces an Inflammatory Response in Healthy and Type 2 Diabetic Primary Human Proximal Tubular Epithelial Cells

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Introduction: As environmental pollutants, micro- and nanoplastics are increasingly prevalent in ocean and freshwater ecosystems. Nanoplastics (NPs) are particles generated when microplastics inevitably degrade into particles ≤100 nm. Recent evidence from experimental models suggests that exposure to NPs induces renal injury and oxidative stress. We sought to determine if exposure to NPs induces an inflammatory response in healthy and type 2 diabetic (T2D) primary human proximal tubular epithelial cells (PTEC).

Methods: Healthy and T2D primary human PTECs were cultured in 96 well-plates and exposed to 0.026%, 0.052% w/v 0.05 µm monodisperse polystyrene microspheres (or vehicle) for 24 hours. After the 24 hour exposure, cells were subject to RT-PCR assessing markers of inflammation.

Results: Nanoplastic beads induced significant increases in tumor necrosis factor-alpha (TNF-alpha), transforming growth factor-beta (TGF-beta), and the TNF super family receptor molecule, CD40. In regard to TGF-beta, cells isolated from diabetic individuals demonstrated an elevated response compared to cells isolated from healthy individuals.

Conclusion: Our results suggest that NPs induce an inflammatory response in human PTECs, which may be enhanced in prevalent, pre-existing conditions, such as T2D, with important implications for human health that warrant further investigation.

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Hypercalcemia in the Inpatient Setting: A Case Report

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A 57-year-old female with a history of bipolar disease, depression, diabetes, and hypothyroidism presents with worsening mental status changes, visual hallucinations, and depressive symptoms. Symptoms started six months ago and have worsened over the past two months. Her husband reports she has been talking "gibberish" and has started displaying acts of aggression, such as punching him in the face. Her husband also notes a decrease in the patient's motor control. The morning of the ED visit, the patient fell down five stairs and hit her head. She denied any loss of consciousness (LOC) during the fall. After admission, she was restrained as she was agitated and confused. She believed she had been abducted and that her husband didn't know her location. Initial imaging included a head and cervical spine CT that showed no acute processes. However, CT of the chest showed abnormal adenopathy. Notable labs included a BUN of 37, Cr of 4.34, Ca of 15 mg/dl, and an ionized Ca of 2.01. Elevated calcium and adenopathy then led physicians to believe the altered mental status could be due to hypercalcemia secondary to a possible lymphoma/granulomatous disease. She was then treated with calcitonin and started on dialysis. Deterioration can occur in both physical and mental functions of hypercalcemic patients acutely. Thus, identifying and correcting hypercalcemia, while taking care to identify and treat any underlying pathology is crucial. A thorough workup focusing on laboratory findings and imaging can be crucial to quickly identifying the cause and treating the patient.

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Double Negative T Cell Proportion of CD3+ Cells Present in the Thyroid Microenvironment is an Immunogenomic Marker for Predicting Thyroid Cancer

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Thyroid cancer is becoming increasingly relevant in the growing population and has been seeing a greater incidence of diagnosis since the early 1980s. While there has been an increase in diagnosis, there has not been any significant advancement in the quality or sensitivity of screening methods. Current guidelines recommend repeat biopsy in these patients because they lack any guidance if patients continue to yield unclear or contradictory pathology. Current ATA recommendations state that these patients should receive diagnostic surgery which results in the removal of the entire thyroid gland. It is estimated that 60-75% of these surgeries end up removing benign lesions. Yet with the current methods of diagnosis, it is impossible to determine the prognostic status of every thyroid nodule without thyroidectomy for patients with unspecified pathology. We have found a diagnostic profile that lends a greater sensitivity and specificity using the microenvironments of the tumor cells. A fine needle aspirate sample from patients with thyroid nodules was analyzed via flow cytometry. Using this data, we characterized the lymphocytic environment of malignant tumors expressing a large population of T cells which are neither expressing CD4 nor CD8 (CD3+CD4-CD8-) known as double negative lymphocytes (DN T) cells. A profile of >9.14% DNT cells was shown to indicate malignancy with a sensitivity of 96.6% and specificity of 100%. Therefore, measurement of tumor microenvironment cell populations serves as an extremely effective method for thyroid nodule risk assessment. This would be instrumental in cutting back the number of unnecessary surgeries and avoiding excessive patient hardship resulting from surgery or postsurgical care. Clearly, the microenvironment holds significance in the instance of malignant modules, and they reflect the behavior of the tumor. Using High-throughput gene expression analysis, we will analyze the mRNA expression of DN T cells present in the microenvironment. Using the information gathered, we will design a profile of markers that indicate malignancy. Furthermore, our group is working on amplifying DN T cell markers on a PCR-based platform to allow a more economically viable diagnostic test.

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Comparison of Artificial Intelligence with other interventions to improve Adenoma Detection Rate for Colonoscopy: A Network Meta-analysis

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Introduction: Recent randomized controlled trials (RCTs) and meta-analysis have demonstrated improved adenoma detection rate (ADR) for colonoscopy with artificial intelligence (AI) compared to high-definition (HD) colonoscopy without AI. We aimed to perform a systematic review and network meta-analysis of all RCTs to assess the impact of AI compared to other endoscopic interventions aimed at increasing ADR such as distal attachment devices, dye-based/virtual chromoendoscopy, water-based techniques and balloon-assisted devices.

Methods: A comprehensive literature search of PubMed/Medline, Embase, and Cochrane was performed through May 6, 2022 to include RCTs comparing ADR for any endoscopic intervention mentioned above. Network meta-analysis was conducted using a frequentist approach and random effects model. Relative risk (RR) and 95% confidence interval (CI) were calculated for proportional outcome.

Results: A total of 94 RCTs with 61172 patients (mean age 59.1±5.2 years, females 45.8%) and 20 discrete study interventions were included. Network meta-analysis demonstrated significantly improved ADR for AI compared to Autofluorescence imaging (RR: 1.33, CI: 1.06-1.66), dye-based chromoendoscopy (RR: 1.22, CI: 1.06-1.40), Endocap (RR: 1.32, CI: 1.17-1.50), Endocuff (RR: 1.19, CI: 1.04-1.35), Endocuff-Vision (RR: 1.26, CI: 1.13-1.41), Endoring (RR: 1.30, CI: 1.10-1.52), flexible spectral imaging color enhancement (RR: 1.26, CI: 1.09-1.46), Full-spectrum Endoscopy (RR: 1.40, CI: 1.19-1.65), High-Definition (RR: 1.41, CI: 1.28-1.54), Linked Color Imaging (RR: 1.21, CI: 1.08-1.36), Narrow Band Imaging (RR: 1.33, CI: 1.18-1.48), Water-Exchange (RR: 1.22, CI: 1.06-1.42), and Water-Immersion (RR: 1.47, CI: 1.19-1.82).

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Conclusion: AI demonstrated significantly improved ADR when compared to most endoscopic interventions. Future RCTs directly assessing these associations are encouraged.

Does I-Scan Improve Adenoma Detection Rate Compared to High-Definition Colonoscopy? A Systematic Review and Meta-Analysis

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Background and study aims: Recent studies evaluated the impact of i-scan in improving the adenoma detection rate (ADR) compared to high-definition (HD) colonoscopy. We aimed to systematically review and analyze the impact of this technique.

Methods: A thorough search of the following databases was undertaken: PubMed/Medline, EMBASE, Cochrane and Web of Science. Full-text RCTs and cohort studies directly comparing i-scan and HD colonoscopy were deemed eligible for inclusion. Dichotomous outcomes were pooled and compared using random effects model and DerSimonian-Laird approach. For each outcome, relative risk (RR), 95 % confidence interval (CI), and P value was generated. $P < 0.05$ was considered statistically significant.

Results: A total of five studies with six arms were included in this analysis. A total of 2620 patients (mean age 58.6 ± 7.2 years and female proportion 44.8 %) completed the study and were included in our analysis. ADR was significantly higher with any i-scan (RR: 1.20, [CI: 1.06-1.34], P = 0.003) compared to HD colonoscopy. Subgroup analysis demonstrated that ADR was significantly higher using i-scan with surface and contrast enhancement Gonly (RR: 1.25, [CI: 1.07-1.47], P = 0.004).

Conclusion: I-scan has the potential to increase ADR using the surface and contrast enhancement method. Future studies evaluating other outcomes of interest such as proximal adenomas and serrated lesions are warranted.

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Cyanotoxin Degrading Lake Bacteria Significantly Alleviate Microcystin-LR Induced Hepatotoxicity in Both In Vitro and In Vivo Models

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Introduction: Harmful algal blooms are a potential threat to human health due to the release of cyanotoxins. Our recent reports have shown that exposure to the prevalent cyanotoxin microcystin-LR (MC-LR) exacerbates development of pre-existing liver disease as well as alters gut microbiota that may significantly impact development of hepatotoxicity. We have isolated naturally occurring novel MC-LR degrading bacteria from Lake Erie, OH and hypothesize that they may alleviate MC-LR toxicity.

Methods: Human Hep3B hepatocytes were treated with various ratios of hepatocyte:bacterial cells – 1:10, 1:50 and 1:100 for 30 min. prior to exposure with 10 µM MC-LR. After 24 hrs, cells and supernatants were collected for qPCR and mass spectrometric analysis. Age-matched Balb/c female mice were either given normal or a mix of MC-degrading bacteria (105 CFU/ml) in drinking water for four weeks followed by a single gavage with vehicle or 500 µg/kg of MC-LR and then euthanized 2 or 24 hrs post-exposure. Urine and organs were collected for qPCR and mass spectrometric analysis.

Results: Genetic analysis for markers of hepatotoxicity and inflammation in both in vivo and in vitro settings were significantly downregulated in the presence of MC-degrading bacteria compared to the untreated groups. Mass spectrometric analysis of urine from mice pre-treated with the bacteria prior to MC-LR exposure, revealed significant reduction in urine MC-LR levels and elevated levels of the detoxified metabolite - MC-LR Cysteine as compared to the untreated control group.

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Conclusion: These results suggest a potential novel therapeutic approach that can be developed for MC-LR induced toxicity.

Lactated Ringer's Vs Normal Saline for Acute Pancreatitis: An Updated Systematic Review and Meta-Analysis

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Introduction: Recent studies have evaluated and compared the efficacy of normal saline (NS) and lactated Ringer's (LR) in reducing the severity of acute pancreatitis (AP) and improving outcomes such as length of stay, the occurrence of the systemic inflammatory response syndrome (SIRS), ICU admission and mortality. We performed an updated systematic review and meta-analysis of the available studies to assess the impact of these fluids on outcomes secondary to AP.

Methods: We systematically searched the following databases: PubMed/Medline, Embase, Cochrane, and Web of Science through February 8th, 2021 to include randomized controlled trials (RCTs) and cohort studies. Random effects model using DerSimonian-Laird approach was employed and risk ratios (RR) and mean difference (MD) with 95% confidence interval (CI) were calculated for binary and continuous outcomes, respectively.

Results: 6 studies (4 RCTs and 2 cohort studies) with 549 (230 in LR and 319 in NS) were included. The overall mortality (RR: 0.73, CI: 0.31-1.69) and SIRS at 24 h (RR: 0.69, CI: 0.32-1.51) was not significantly different. The overall ICU admission was lower in LR group compared to NS group (RR: 0.43, CI: 0.22-0.84). Subgroup analysis of RCTs demonstrated lower length of hospital stay for LR group compared to NS group (MD: 0.77 days, CI: 1.44 -0.09 days).

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Conclusion: Our study demonstrated that LR improved outcomes (ICU admission and length of stay) in patients with AP compared to NS. There was no difference in rate of SIRS development and mortality between LR and NS treatments.

Severe Transaminitis in Allopurinol-Induced DILI presenting as DRESS Syndrome

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Introduction: Patient is an 81-year-old male who presented for significant dyspnea and rash. Further workup demonstrated morbilliform rash, severe transaminitis, elevated alkaline phosphatase, acute kidney injury, and mild eosinophilia.

Case Description: Four weeks prior to admission, the patient was placed on allopurinol for acute gouty arthritis and developed the erythematous, pruritic rash shortly before admission. The rash presented over the trunk and bilateral upper and lower extremities. Patient was given betamethasone cream and Benadryl three times daily with no relief. Upon cessation of allopurinol and initiation of high-dose corticosteroids in the hospital, the transaminitis began resolving within two days and the rash stabilized.

Discussion: We reviewed the PubMed database to identify cases of allopurinol-induced drug-induced liver injury. The patient's LFTs, especially ALT, were significantly higher than the LFTs in a previous case series (median ALT: 500s). This patient's ALT peaked at 1818 U/L, while AST (278) and Alk Phos (339) were also elevated. Liver injury pattern in drug reaction with eosinophilia and systemic symptoms (DRESS) is either cholestatic or hepatocellular. The patient we present demonstrates a hepatocellular pattern of liver injury. In a case series of 16 patients with DRESS and acute liver injury, six patients underwent emergency liver transplantation. It is extremely important to closely monitor LFTs and determine the grade of severity as acute liver failure may manifest, although rare. Overall, this patient presented with severe allopurinol-induced drug-induced liver injury (DILI) with Grade 4 AIDS CTG criteria ALT and AST elevations.

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Analysis of Demographic and Staging Characteristics in Patients with Colorectal Cancer Using the SEER Registry

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Screening for colorectal cancer (CRC) was previously started at age 50, with recent guidelines suggesting age 45 for earlier detection. CRC incidence data from NCI's SEER registry was utilized for this study. Data from 2014-2018 was analyzed for ages 50-64, 64-74, and 75+. Localized, regional and distant metastasis were coded in the database. The incidence of CRC increased with age where ages 75+ had the highest incidence at 211.8 per 100,000, compared to 70.7 for ages 50-64. In the age group of 75+, the incidence of localized CRC was 70.1 (95% CI: 69.2-71.0) and regional CRC was 69.2 (68.4-70.1) which was not statistically significant. Female patients have a lower chance of presenting with CRC at 59.5, 107.6, 192.1 for the age groups 50-64, 65-74, and 75+ respectively, whereas male counterparts have rates of 82.7, 152.9, and 240.2. White males had statistically significant higher odds of localized compared to regional cancer in all age groups. Asian females showed no difference in incidence of local and regional disease for ages 50-74. For ages 75+, the incidence of regional disease at 54.6 (51.3-58.1) was much higher than local disease at 45.3 (42.3- 48.5). Of note, Asian females aged 50-64, Hispanic females ages 65 and older, and Black and White females ages 75+ were equally likely to present with local or regional disease. Ensuring equitable access to screening may be beneficial in improving cancer-related mortality in certain demographics. This analysis was limited to incidence, and future studies with presentation at diagnosis could be insightful.

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Metastatic Renal Cell Carcinoma to the Descending Colon Presenting as Recurrent Hematochezia

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Renal Cell Carcinoma (RCC) metastasis to the colorectal region is a rare occurrence. This report documents a case of an individual with solitary metastasis of RCC to the descending colon presenting with recurrent hematochezia. Per literature review, it is the first case of metastasis to the descending colon after negative diagnostic colonoscopy less than a year prior. Management of the patient's hematochezia was challenging given poor surgical candidacy, no option for palliative radiation given non-visualization of the lesion on CT, and no target was present for IR guided embolization. The patient's rectal bleeding was partially improved with cessation of his Apixaban indicated for atrial fibrillation stroke prophylaxis. Our case demonstrates that interval metastasis should always be on the differential for persistent GI bleeding in the setting of RCC and it highlights challenges in management of hematochezia related to colorectal metastasis of RCC.

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Iron Deficiency Anemia Secondary to Colonic Diaphragm Disease

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Introduction: The chronic use of NSAIDs has many well-established effects on the digestive system specifically within the upper GI tract. One uncommon complication of chronic NSAID use is the formation of diaphragm-like strictures, characterized by the circumferential narrowing of mucosal membranes. These diaphragm-like strictures are most encountered in the small intestine, and there exists a limited number of cases reporting occurrence of such lesions within the colon. Our case highlights one such example and the importance of considering NSAID-induced colopathy as a causative factor for iron deficiency anemia.

Case Report: A 69-year-old female with history of chronic low back pain and associated long-term use of diclofenac 75 mg twice daily (**do we know the dose and for how long**) presented to the hospital with a hemoglobin of 6.2 g/dL discovered on outpatient lab work. Addional labs showed iron saturation 5% and ferritin 2 ng/ml at that time, consistent with iron deficiency anemia. She endorsed dyspnea on exertion, fatigue and lightheadedness for one month duration and denied symptoms of overt GI bleeding. The patient had a colonoscopy five years prior to presentation which revealed several benign polyps and diverticulosis with no strictures. EGD and colonoscopy were subsequently pursued. EGD showed mild erosive gastritis and colonoscopy revealed 5 diaphragm-like strictures with ulcerative edges located in the ascending and proximal transverse colon requiring CRE balloon dilation up to 15 mm to allow passage of the scope. The ileocecal valve could not be traversed due to significant narrowing. Biopsy of the diaphragm lesions showed benign colonic mucosa with chronic architectural distortion and ulcer bed. NSAID-induced colopathy was suspected to be the cause of anemia, for which she was counseled to discontinue NSAID use.

Discussion: NSAID-induced diaphragm-like strictures are encountered most often in the small intestine, specifically at the ileum. Colonic diaphragm disease (CDD) remains a lesser recognized entity and their prevalence remains unknown, occurring predominantly in the proximal ascending colon. Poor recognition of NSAID-induced colopathy has led to misdiagnosis with conditions such as Crohn's disease. Therefore, in providing another example of this rarer finding, it is one aim of this case report to

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encourage NSAID-induced colopathy to be considered in differential diagnosis for iron deficiency anemia among different other GI pathologies.

Rectal Ischemia Status Post EVAR and COVID-19

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Introduction: Ischemic proctitis is a rare, but serious, source of GI bleeding as mortality rates approach 20-40%. Patients for which ischemia should be considered are those with previous surgery, older patients, and those with known peripheral arterial disease.

Case Description: 80-year-old male with history of hyperlipidemia and hypertension presented to the hospital for shortness of breath secondary to COVID-19 pneumonia. His respiratory status continued to decline requiring mechanical ventilation and ICU admission. During his admission, he was found to have acute left lower extremity ischemia requiring stenting of his superficial femoral artery and abdominal endovascular aneurysm repair (EVAR). He was started on anticoagulation with heparin infusion. His hospital course was further complicated large volume maroon-colored stools concerning for lower GI bleed. Colonoscopy was performed at the bedside to further evaluate. In the rectum, there were circumferential ulcerations with inflammation and exudate, extending 10cm from the anal verge. Biopsies were consistent with rectal ischemia.

Discussion: Rectal ischemia is rare as the rectum has blood supply from the inferior mesenteric and bilateral iliac arteries. In our patient, during EVAR graft repair, the IMA was occluded by a stent, the iliac arteries however, remained intact providing the middle rectal and pudendal artery as sources of collateral blood supply. It is hypothesized that a hypercoagulable state caused by COVID-19 infection coupled with ongoing hypotension in the setting of critical illness in our patient with significant peripheral arterial disease led to the low flow state in bilateral iliac arteries causing ischemic proctitis.

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Use of Endoscopic Vacuum Therapy to Repair Colonic Anastomotic Leaks: A Meta Analysis

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Introduction: Endoscopic vacuum therapy (EVT) has recently emerged as a treatment modality for patients who experience anastomotic leak after surgery with an incidence of 6-30%. Treatment of anastomotic leaks using EVT in the upper gastrointestinal tract has been well documented. However, EVT for colorectal leaks remains a less studied entity. EVT is based on applying sponges to the area of the leak and negative pressure is applied to draw off fluid from the leak and help promote granulation tissue formation and healing. Our study aims to use prospective studies to assess the success and rates of adverse events using EVT for colo-rectal anastomotic leaks.

Methods: Pubmed, Embase and Cochrane were searched from inception to April 2022 for prospective studies reporting success and adverse event rates for EVT used for colo-rectal anastomotic leaks. Using I2 we assessed heterogeneity and calculated 95% confidence intervals using fixed or random effect models.

Results: Seven studies involving 368 patients were included in our analysis. Indication for surgery was malignancy in all cases. The total clinical success rate was 90.5% (CI: 87.6-93.5. I2 = 0%). The adverse event rate among all studies was 7% (95% CI: 4.4-9.5%, I2 = 0%). 6 patients required further surgical intervention and 2 required CT guided drain placement. No mortality was reported.

Conclusion: EVT is an emerging treatment option for anastomotic leak. Our study demonstrates the safety and efficacy of EVT as an option for patients who experience colorectal anastomotic leak, however large prospective studies are warranted for further evaluation.

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ERCP in Patient with Situs Inversus Totalis

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Introduction: Situs inversus (SI) is a congenital anomaly resulting in transposition of thoracic and abdominal organs. This case details a patient found to have situs inversus totalis (SIT) while being evaluated for abdominal pain and ultimately requiring ERCP for choledocholithiasis.

Case Description/Methods: An 89-year-old male presented with a history of epigastric abdominal pain for one month associated with nausea and non-bloody, non-bilious vomiting. The patient was found to have elevated lipase and a CT abdomen showed an obstructing stone at the ampulla accompanied by inflammatory changes consistent with pancreatitis and situs inversus totalis. ERCP was indicated for choledocholithiasis and was subsequently performed. The side-viewing duodenoscope was advanced into the stomach, and a slight clockwise rotation of the scope was needed to advance towards the antrum, subsequently the scope was advanced in the long position into the first and second part of the duodenum and maintained in the long position. The major papilla was visualized in the upper right quadrant of the screen and noted to be bulging, and deep biliary cannulation was difficult due to anatomical variation and bulging papilla. A pancreatic duct stent was placed first to aid in biliary cannulation and subsequently biliary cannulation was achieved with biliary sphincterotomy and balloon sweep performed.

Discussion: SI is found in approximately 1 in 10,000 which can obscure the diagnosis of abdominal pathology. In our case SIT was noted on CT along with the culprit stone. In such patients careful planning to minimize adverse events and maximize success is essential.

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Do Topical Corticosteroids Induce Histologic Remission and Improve Clinical Symptoms in Eosinophilic Esophagitis? - A Systematic Review and Meta-Analysis

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Introduction: Eosinophilic esophagitis is a chronic esophageal disease characterized histologically by eosinophil-predominant inflammation and clinically by symptoms related to esophageal dysfunction. The management of the disease commonly involves elimination diet, acid suppression, topical corticosteroids, and esophageal dilation.

Methods: We conducted a systematic review and meta-analysis of studies that investigated the efficacy and safety of topical corticosteroids compared with placebo in eosinophilic esophagitis. We performed a comprehensive search in the databases of PubMed/MEDLINE, Embase, and Cochrane from inception through October 18, 2021. Our outcomes were histologic remission, symptomatic clinical improvement, and the occurrence of oral or esophageal candidiasis. The random-effects model was used. A p value <0.05 was considered statistically significant. Heterogeneity was assessed using the Higgins I2 index.

Results: Nine randomized controlled trials involving 483 patients were included in the meta-analysis. Compared to placebo, patients who received steroids were more likely to achieve histologic remission (RR 12.50, 95% CI 6.04 – 25.88, p < 0.00001, I2 = 0%) and report symptomatic clinical improvement (RR 1.84, 95% CI 1.02 – 3.32, p = 0.04, I2 = 64%). Oral or esophageal candidiasis was more likely to occur in patients who received steroids (RR 4.31, 95% CI 1.53 – 12.18, p = 0.006, I2 = 0%).

Conclusion: Our meta-analysis demonstrated that topical corticosteroids were more effective than placebo in achieving histologic remission and improving clinical symptoms. However, they are more likely to cause oral or esophageal candidiasis.

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Early Versus Delayed Minimally Invasive Intervention for Infected Pancreatic Necrosis – A Systematic Review and Meta-Analysis

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Introduction: Pancreatic necrosis complicates 20% of acute pancreatitis cases, and 30-40% of those become infected. Current guidelines recommend that invasive intervention for pancreatic necrosis should be delayed to 4 or more weeks from disease onset. However, recent studies have challenged the optimal timing of intervention.

Methods: We conducted a systematic review and meta-analysis. We performed a comprehensive search in the databases of PubMed/MEDLINE, Embase, and the Cochrane from inception through April 11, 2022. We collected the number of patients who underwent early and late interventions for infected pancreatic necrosis. Outcomes were mortality, gastrointestinal fistula or perforation, bleeding, and length of hospital stay. The random-effects model was used. A p value <0.05 was considered statistically significant. Heterogeneity was assessed using the Higgins I2 index.

Results: Seven studies involving 742 patients were included in the meta-analysis. Timing of intervention had no statistically significant effect on mortality (RR 1.49, 95% CI 0.87 – 2.55, p = 0.15, I2 = 15%) or bleeding (RR 1.54, 95% CI 0.74 – 3.21, p = 0.24, I2 = 67%). However, early intervention was associated with a statistically significant higher risk of gastrointestinal fistula or perforation (RR 1.52, 95% CI 1.04 – 2.21, p = 0.03, I2 = 0%) and a longer hospital length of stay (MD 10.25 days, 95% CI 0.41 – 20.10, p = 0.04, I2 = 52%).

Discussion: Our meta-analysis demonstrated that the timing of intervention had no effect on mortality or bleeding. Early intervention resulted in higher risk of gastrointestinal fistula or perforation and longer length of stay.

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Bilateral Accessory (Aberrant) Renal Arteries Associated With Uncontrolled Hypertension—Role of Renin-Angiotensin-Aldosterone Antagonist Drugs for Treatment Goal: A Case Report

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Introduction: Accessory (aberrant) renal arteries (ARAs) are extra vessels that supply the kidneys in addition to the usual single arteries. They typically arise from the abdominal aorta but can also originate from other abdominal/pelvic arterial systems. They can be seen in up to 30% of adults, can complicate various urological, abdominal surgery, interventional radiological, and transplantation procedures.

Case Report: A 49-year-old woman had developed elevated blood pressure during her previous pregnancies, and hypertension persisted after pregnancy. Angiotensin- converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARB) could not be used at the time because of teratogenic considerations. Antihypertensive drugs as calcium channel antagonists, beta-blockers, direct vasodilators, and thiazide-based diuretics did not control the blood pressure to goal. Renal Doppler studies showed a slight increase in peak velocity on the right renal artery. A computed tomographic angiography (CTA) and magnetic resonance angiography (MRA) showed accessory renal arteries in both the right and left kidneys. Laboratory tests showed persistent hypokalemia and plasma renin activity was significantly elevated. The addition of Losartan 100 mg daily and Spironolactone 50 mg daily was needed to get blood pressure to goal.

Conclusion: Accessory renal arteries could lead to perfusion abnormalities, contribute to or exacerbate maintenance and control of blood pressure. Drugs affecting the renin-angiotensin-aldosterone pathway are important in the treatment of patients with accessory (aberrant) renal arteries if hypertension is renin mediated.

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Use of Smartphone Applications to Augment Colonoscopy Preparation Instructions and Effect on Quality of Colonoscopy Preparation and Adenoma Detection Rate – A Systematic Review and Meta-Analysis

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Introduction: Adequate preparation of the large bowel is essential for a successful colonoscopy. Patients should be provided with clear instructions prior to the procedure, which can be achieved by verbal, written, and more recently, digital tools. A few studies have evaluated the role of smartphone applications to augment colonoscopy preparation instructions.

Methods: We conducted a systematic review and meta-analysis. We performed a comprehensive search in the databases of PubMed/MEDLINE, Embase, and the Cochrane from inception through October 11, 2021. The primary outcome was adequate bowel preparation, defined as per Boston bowel preparation scale (BBPS). The secondary outcome was adenoma detection rate (ADR), which was defined as patients with ≥1 adenoma detected on colonoscopy. The random-effects model was used. A p value <0.05 was considered statistically significant. Heterogeneity was assessed using the Higgins I2 index.

Results: Nine randomized controlled trials involving 2933 patients were included in the meta-analysis. Eight studies reported adequate bowel preparation, which was significantly higher in patients who used smartphone applications compared with controls (RR 1.17, 95% CI 1.06 – 1.30, $p < 0.003$, I2 = 90%). Five studies reported ADR, which was also significantly higher in patients who used smartphone applications compared with controls (RR 1.37, 95% CI 1.19 – 1.58, $p < 0.0001$, I2 = 0%).

Conclusion: Our meta-analysis demonstrated that the use of smartphone applications to augment colonoscopy preparation instructions improves the quality of colonoscopy preparation and adenoma detection rate. Further randomized controlled trials are needed to confirm our findings.

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A Case of Rhabdomyolysis with Rigors

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Introduction: Rhabdomyolysis is a potential life- threatening condition caused by extensive skeletal muscle breakdown with leakage of toxic muscle contents into the circulation. The most dreaded complication is acute renal failure caused by toxic effects of myoglobin in the kidneys. The causes of rhabdomyolysis are classified into traumatic, non-traumatic exertional, and non-traumatic rhabdomyolysis. The pathophysiologic hallmark of rhabdomyolysis regardless of etiology is increased free ionized calcium due to cellular energy depletion (ATP) or direct plasma membrane rupture and consequent intensified muscle contractility, mitochondrial dysfunction, and production of oxygen radicals.

Case Report: We report a case of a middle-aged black woman with rhabdomyolysis that was caused by intense shivering chills, and rigor from pneumonitis. She had no personal or family history of muscle disorder and was admitted to the hospital after a weeklong history of upper and lower respiratory symptoms that led to the worse shivering and shaking chills she ever had. She was noted to have elevated creatine phosphokinase (CPK) of 200,000 uL (26–192 uL) and creatinine level of 5.52 (0.81–1.2 mg/dL). She was started on intravenous fluid with half-isotonic saline (0.45%) or 77 mmol/L sodium, 75 mmol/L sodium bicarbonate, and hemodialysis with progressive improvement in kidney function that took up to seven weeks to full recovery.

Conclusion: Shivering and shaking chills from respiratory infection can cause rhabdomyolysis with severe muscle damage and renal failure in a patient with no known underlying muscular-skeletal disorder condition but has good recovery with fluid management and hemodialysis. Renal function has returned back to normal.

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Discovery of Gastric Adenocarcinoma during PEG Tube Placement in Patient with Epiglottic Squamous Cell Carcinoma

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Introduction: Multiple primary neoplasms constitute up to 2-17% of cancer diagnoses. We report a patient who was diagnosed with gastric adenocarcinoma at the time of percutaneous endoscopic gastrostomy (PEG) tube placement for dysphagia secondary to squamous cell carcinoma of the anterior epiglottis.

Case Description: A 77-year old male presented for upper endoscopy with PEG tube placement. Two months prior, the patient was diagnosed with p16 negative invasive squamous cell carcinoma of the anterior epiglottis. He was referred for PEG tube placement for nutrition supplementation due to 5 months of progressive dysphagia, malnutrition, and unintentional weight loss. Social history was significant for tobacco dependence with 52 pack years and alcohol dependence. At the time of PEG tube placement, a 1.5 cm excavated lesion at the gastric incisura was identified. Biopsy was performed to rule out malignancy. PEG tube was successfully placed. Biopsy was consistent with diffuse type signet ring gastric adenocarcinoma. PET scan 1 month prior to PEG tube placement showed no foci of abnormal FDG uptake outside of the primary lesion in the epiglottis. Patient is undergoing treatment for laryngeal carcinoma with chemotherapy and radiation. Assessment and treatment for gastric cancer diagnosis will be deferred until completion of treatment for laryngeal carcinoma.

Discussion: Concurrent laryngeal and gastric cancer is a unique diagnosis not well reported. Literature shows that signet ring cell carcinomas has significantly lower 18F-FDG uptake than other forms of gastric cancer. These findings highlight the importance of completing a full endoscopic evaluation in all patients undergoing endoscopy.

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Hepatic Sarcoidosis Presenting as Cholestatic Liver Injury Exacerbated by Nitrofurantoin Use

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Introduction: The liver is a common site of involvement in patients with sarcoidosis with 50-80% of patients having hepatic involvement at diagnosis. However, it is largely asymptomatic and <15% of patients present with symptoms of hepatic injury. We report a patient with hepatic sarcoidosis presenting as cholestatic liver injury exacerbated by nitrofurantoin use.

Case Presentation: A 67-year-old African American female presented due to 1 week of diffuse itching, shortness of breath, and scleral icterus with darkened urine. Medical history was significant for type 2 diabetes, hypertension, and hyperlipidemia. Patient denied alcohol use and was a lifetime non-smoker. Family history was significant for sarcoidosis in father. Notably, the patient took nitrofurantoin for a UTI one week prior to presentation. Lab results showed elevated direct bilirubin 5.2, total bilirubin 8.8, ALK PHOS 950, ALT 126, and AST 229. Ultrasound of the liver and MRCP showed hepatic steatosis and gallbladder sludge. Liver biopsy showed cholestatic granulomatous hepatitis with stage 2-3 bridging fibrosis. This patient's presentation was deemed most consistent with hepatic sarcoidosis. Nitrofurantoin is a well-known cause of hepatic injury, but has rarely been reported as causing granulomatous disease exacerbating underlying sarcoidosis.

Discussion: While the liver is a common site of involvement for sarcoidosis, the majority of patients are asymptomatic. Hepatotoxic drugs can exacerbate symptoms and lead to diagnosis. In those with clinical symptoms, a cholestatic pattern is most common. Glucocorticoids and methotrexate are common treatments. However, there is currently a lack of randomized controlled studies regarding treatment and surveillance of hepatic sarcoidosis.

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Impact of Guidewire Caliber on ERCP Outcomes: Systematic Review and Meta-Analysis Comparing 0.025- and 0.035-Inch Guidewires

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Background and Study Aims: The impact of guidewire caliber on endoscopic retrograde pancreatography (ERCP) outcomes are not clear. Recent studies have compared two guidewires, 0.035- and 0.025-inch, in randomized controlled trials (RCTs). We performed a systematic review and meta-analysis of available RCTs to assess if different caliber would change the outcomes in ERCP.

Patients and Methods: A systematic search of PubMed/Medline, Embase, Cochrane, SciELO, Global Index Medicus and Web of Science was undertaken through November 23, 2021 to identify relevant RCTs comparing the two guidewires. Binary variables were compared using random effects model and DerSimonian-Laird approach. For each outcome, risk-ratio (RR), 95 % confidence interval (CI), and P values were generated. $P < 0.05$ was considered significant.

Results: Three RCTs with 1079 patients (556 in the 0.035-inch group and 523 in the 0.025-inch group) were included. The primary biliary cannulation was similar in both groups (RR: 1.02, CI: 0.96-1.08, P = 0.60). The overall rates of PEP were also similar between the two groups (RR: 1.15, CI: 0.73-1.81, P = 0.56). Other outcomes (overall cannulation rate, cholangitis, perforation, bleeding, use of adjunct techniques) were also comparable.

Conclusion: The results of our analysis did not demonstrate a clear benefit of using one guidewire over other. The endoscopist should consider using the guidewire based on his technical skills and convenience.

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Primary Gastric Squamous Cell Carcinoma with Concurrent H. Pylori Infection and Colonic Metastasis

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Introduction: Primary gastric squamous cell carcinoma (PGSCC) is a rare, aggressive, malignancy that requires EGD with biopsy and pathology for diagnosis. H. pylori infection is a known risk factor for gastric malignancies but, only one case has been reported with an association between the two.

Case Information: This is a 66-year-old male, with no significant history, presented to the hospital with syncope, melena, fatigue, exertional dyspnea, and 50lb weight loss. Patient was found to have HGB of 3.2. CT abdomen showed a mass in the antrum of the stomach, most prominent posteriorly and around the greater curvature. EGD revealed normal esophagus and a 15cm, oozing, fungating, and partially circumferential gastric mass located in the antrum, involving the entire posterior wall with extension into the greater curvature. The gastric mass was 5cm below the GE junction, without evidence of esophageal involvement. Biopsy of the mass revealed poorly differentiated SCC and Helicobacter pylori infection. Colonoscopy then revealed a 4 cm lesion which was confirmed to also be poorly differentiated SCC. PET scan showed known gastric and colonic mass with multiple enlarged and hypermetabolic perigastric and retroperitoneal lymph nodes consistent with metastasis.

Discussion: PGSCC is a rare form of gastric malignancy accounting for roughly 0.2% of primary gastric cancer reported. Compared to the more common gastric adenocarcinoma, SCC tends to be more aggressive with poorer outcomes. Unfortunately, the pathogenesis remains obscure, making early detection difficult. Additionally, metastasis to the colon is exceptionally rare with most cases metastasizing to liver, peritoneum, lung and bone.

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Safety and Effectiveness of Endoluminal Vacuum-Assisted Closure for Esophageal Defects: Systematic Review and Meta-Analysis

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Background: Esophageal defects (leaks, fistulas, and perforations) are associated with significant morbidity and mortality. Endoluminal vacuum-assisted closure (EVAC) is a novel intervention that entails the use of sponges in the defect along with negative pressure to achieve granulation tissue formation and healing and has been gaining popularity. We performed a systematic review and pooled analysis of available literature to assess the safety and effectiveness of EVAC for esophageal defects.

Methods: We queried PubMed/Medline, Embase, Cochrane, and Web of Science through September 25, 2020 to include all pertinent articles highlighting the safety and effectiveness profile of EVAC for esophageal defects. Pooled rates, 95 % confidence intervals (CIs), and heterogeneity (I2) were assessed for each outcome.

Results: A total of 18 studies with 423 patients were included (mean age 64.3 years and males 74.4 %). The technical success for EVAC was 97.1 % (CI: 95.4 %-98.7 %, I 2 = 0 %). The clinical success was 89.4 % (CI: 85.6 %-93.1 %, I 2 = 36.8 %). The overall all-cause mortality and adverse events (AEs) noted were 7.1 % (CI: 4.7 %-9.5 %, I 2 = 0 %) and 13.6 % (CI: 8.0 %-19.1 %, I 2 = 68.9 %), respectively. The pooled need for adjuvant therapy was 15.7 % (CI: 9.8 %-21.6 %, I 2 = 71.1 %).

Conclusion: This systematic review and meta-analysis showed high rates of technical success, clinical success, and low all-cause mortality and AEs using EVAC. Although the technique is a promising alternative, the lack of comparative studies poses a challenge in making definite conclusions regarding use of EVAC compared to other endoscopic modalities, such as clips and stents.

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Gastrointestinal Ulceration as a Manifestation of Severe Dermatomyositis - A Case Report

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Introduction: A 32-year-old female with a history of adult-onset dermatomyositis presented to the emergency department with symptoms of fever and altered mental status. The patient was admitted for septic shock and multi-organismal pneumonia.

Case Description: Ten months prior, the patient began having back aches, generalized myalgia, and a wide-spread rash. Three months later, a diagnosis of acute fulminant dermatomyositis was made with NXP-2, GAD-65 positivity on biopsy. Her course of illness required long-term use of systemic steroids, IVIG, methotrexate, mycophenolate mofetil, and rituximab alongside tracheostomy and PEGJ tube placement due to chronic respiratory and neuromuscular failure. With onset of melena and anemia, the patient underwent upper endoscopy. Ulceration was present throughout the esophagus, stomach and duodenum. While more profound ulceration was seen in the esophagus, two small ulcers in the duodenum containing visible, bleeding vessels required clipping. A repeat EGD under general anesthesia was completed for further evaluation and biopsy. Same-day colonoscopy was unremarkable. Esophageal and gastric biopsies revealed focal granulation tissue without evidence of malignancy, fungal elements, or viral inclusions.

Discussion: Dermatomyositis is an inflammatory condition which largely affects skin and striated muscle, commonly presenting with proximal muscle weakness. Although the etiology is unclear, an autoimmune pathogenesis has been highly implicated. Pathogenic involvement of the gastrointestinal tract is rare. When it does occur, symptoms primarily include dysphagia, reflux, and gastroparesis. We present a case of severe dermatomyositis with esophageal, gastric, and duodenal ulceration.

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Anaplastic Large Cell Lymphoma Presenting as Ulcerative Facial Mass: A Case Report

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Introduction: Anaplastic large cell lymphoma (ALCL) is a rare form of non-Hodgkin lymphoma (NHL) that can be aggressive with rapid speed, thus mandating a timely diagnosis to optimize treatment and deter progression. NHL classically presents with lymphadenopathy and constitutional symptoms. However, ALCL can present with nonspecific cutaneous manifestations with minimal or absent constitutional symptoms. The cutaneous involvement may resemble common dermatologic conditions, delaying diagnosis. We present a case of an aggressive cutaneous ALCL lesion mimicking facial cellulitis that rapidly progressed from a small comedone to a large, exophytic mass over the course of 6 weeks.

Case Report: A 59-year-old female with current smoking history (40 pack years) and history of COPD presented to the emergency department with a painful enlarging forehead lesion that grew over 6 weeks, with later appearance of multiple tender lymph nodes on the head and neck. She had four previous ED visits and was treated with empiric intravenous antibiotics for suspected bacterial infection without improvement. Core needle biopsy of the forehead lesion confirmed the diagnosis of anaplastic lymphoma kinase-negative ALCL. Chemotherapy with brentuximab vedotin, cyclophosphamide, doxorubicin, and prednisone was planned for a total of 6–8 cycles with curative intent. By cycle 5, positron emission tomography and computed tomography demonstrated response to therapy with no enlarged or metabolically active lymph nodes appreciated.

Conclusion: Our case report highlights the importance of developing a broad differential diagnosis for ulcerative facial masses, particularly when unresponsive to antimicrobial therapies. Lymphomas should be included in the differential diagnosis of patients with rapidly growing facial lesions.

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EUS Guided Through the Needle Biopsy Versus Fine Needle Aspiration for Pancreatic Cystic Lesions: A Systemic Review and Meta-analysis.

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Introduction: EUS guided FNA has been widely used to collect samples from pancreatic cystic lesions (PCLs) for cytology and fluid analysis. However, EUS guided FNA has relatively lower sensitivity in discriminating the types of lesions. Recent studies have investigated the EUS guided through the needle biopsy (EUS-TTNB) as an alternative method.

Methods: We performed a comprehensive search of the databases: PubMed/MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials from inception through May 10th, 2022. We considered randomized controlled trials, cohort studies, and case-control studies. The primary outcome was sample adequacy which is defined as the presence of enough sample for histopathological evaluation. The secondary outcome was sample accuracy which is defined as the ability to have a definite diagnosis. 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.

Results: Nine observational studies involving 520 patients were included in the meta-analysis. The rate of sample adequacy was significantly higher in the EUS-TTNB group (RR 1.64, 95% CI 1.19-2.26, p =0.003, I2 = 95%) (Figure 1a). The diagnostic accuracy was significantly higher in the same group (RR 2.03, 95% CI 1.13-3.65, p = 0.02, I2 = 87%) (Figure 1 b).

Discussion: Our meta-analysis demonstrated that the rates of both sample adequacy and accuracy were higher in the EUS-TTNB group compared to the EUS-FNA group. EUS-TTNB should be considered

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where applicable clinically for improving the diagnostic yield in patients undergoing evaluation of PCLs.

Epididymo-orchitis Secondary to Colovesical Fistula

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Introduction: Acute epididymo-orchitis is a common cause of scrotal pain in adults. It is most often caused by a retrograde spread of cystitis into the epididymis and testicles via the vas deferens. Epididymo-orchitis is most often seen in older patients with prostate hypertrophy with increased post residual urine volume. In younger patients it may result as a consequence of sexual practices. We present a unique case of epididymo-orchitis secondary to colovesical fistula caused by chronic diverticulitis.

Case Report: A middle aged male presented with subacute left testicular pain, back pain, and pneumaturia. Pertinent medical history included type II diabetes, obesity and multiple prior incidences of diverticulitis. Physical exam revealed a soft abdomen without tenderness, normal bowel sounds, and left scrotal swelling. CBC demonstrated neutrophilia with left shift. Urinalysis was urine nitrite positive, urine esterase 1+, WBC too numerous to count, and urine bacteria many. Urine culture was greater than 100,00 col/mL E.coli. CT abdomen and pelvis demonstrated sigmoid diverticulitis, left sided bladder wall thickening, urinary bladder gas and a colovesical fistula. Scrotal US findings were consistent with epididymo-orchitis. Cystoscopy confirmed the presence of the fistula.The patient was admitted and underwent a two week course of augmentin, which resulted in pain and swelling resolution. The patient underwent robotic assisted sigmoidectomy and takedown of the colovesical fistula. The patient was subsequently discharged and was doing well at one month's follow up.

Conclusion: We present a unique case of epididymo-orchitis and its medical and surgical management.

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EUS Guided Gastroenterostomy Vs Surgical Gastrojejunostomy for the Palliation of Malignant Gastric Outlet Obstruction: A Systemic Review and Meta-analysis

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Background: Gastric Outlet Obstruction (GOO) was traditionally treated palliatively with surgical gastrojejunostomy (SGJ). However, very few studies were done on less aggressive procedures including EUS guided gastroenterostomy (EUS-GE).

Methods: We performed a comprehensive search in the databases of PubMed/MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials from inception through October 10, 2021. We considered only randomized controlled trials. The primary outcome was the technical success. The secondary outcomes were the occurrence of adverse events and the 30 days mortality rate. The random-effects model was used to calculate the risk ratios (RR), mean differences (MD), and confidence intervals (CI). A p value <0.05 was considered statistically significant.

Results: Four randomized controlled trials involving 271 patients were included in the meta-analysis. The rate of the technical success was significantly lower in the EUS-GE compared to the SGJ (91.4% vs. 100%, RR 0.92, 95% CI 0.87 – 0.98, p =0.001, I2 = 0%). However, no statistical significance was noted in the rate of adverse events and the 30 days mortality rate between the two groups (11.7% vs 10.4%, RR 0.90, 95% CI 0.20 – 4.10, p =0.89, I2 = 59%) and (4.6% vs. 1.4%, RR 1.61, 95% CI 0.31 – 8.31, p =0.57, I2 = 0%).

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Conclusion: Our meta-analysis demonstrated that the technical success was significantly higher in the SGJ compared to the EUS-GE. However, there was no significant difference between the two groups in the rates of clinical success, 30 days mortality rate and the rate of adverse events.

Early Feeding Versus Delayed Feeding after Therapeutic Endoscopic Intervention in Upper GI Bleeding: A Systematic Review and Meta-analysis

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Introduction: Multiple endoscopic interventions are used to treat upper GI bleeding. Early feeding after endoscopic intervention in upper GI bleeding was always thought to be associated with higher mortality rate and worse outcomes.

Methods: We performed a comprehensive search in the databases of PubMed/MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials from inception through May 25th, 2022. We considered only randomized controlled trials. The primary outcome was the mortality rate. The secondary outcomes were the occurrence of early bleeding, late bleeding and the length of hospital stay. The random-effects model was used to calculate the risk ratios (RR), mean differences (MD), and confidence intervals (CI).

Results: Eight randomized controlled trials involving 818 patients were included in the meta-analysis. The mortality rate was not statistically different between the two groups (RR 0.60, 95% CI 0.32-1.14, p =0.12, I2 = 0%) (Figure 1a). Also, the rates of both early and late bleeding were not statistically different (RR 1.17, 95% CI 0.60-2.26, p =0.64, I2 = 0%) and (RR 0.74, 95% CI 0.25-2.14, p =0.58, I2 = 17%), respectively. The length of hospital stay was significantly shorter in the early feeding group (MD -0.99 days, 95% CI -1.15- -0.83, p <0.00001, I2 = 70%) (Figure 1b).

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Discussion: Our meta-analysis demonstrated that early feeding after endoscopic interventions in patients with upper GI bleeding appears to be relatively safe. There was no statistical difference in mortality rates and in early or late bleeding rates. Moreover, it was associated with a shorter hospital stay.

Rare Occurrence of Primary Gastric Lymphoma: A Case Report

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Introduction: Primary gastric lymphoma (PGL), a rare gastrointestinal cancer, arises from lymphocytes found in the lamina propria of the stomach because of chronic inflammation. PGLs can range from mucosa-associated lymphoid tissue (MALT) lymphoma to diffuse large B-cell lymphoma, which is a more aggressive form. The majority of PGLs are of B-cell lineage, and they are the most common extranodal non-Hodgkin lymphomas. We present a unique case of primary gastrointestinal lymphoma.

Case Report: An elderly woman presented to the emergency department for intermittent lower left quadrant pain over the prior several weeks. She also reported constipation, fatigue and weight loss over the prior several months. Physical exam findings were unremarkable. CBC demonstrated neutrophilia, thrombocytosis and neutrophilia. Computed tomographic (CT) imaging demonstrated an ulcerating gastric mass, and later PET-CT imaging demonstrated hypermetabolic activity in the gastric mass. With subsequent biopsy and pathological analysis, the diagnosis of a gastric B-cell lymphoma was made.

Conclusion: Primary gastric lymphoma is a rare cause of gastric mass. Initial presentations are similar to pancreatic disorders or functional disorders of the stomach, potentially obfuscating the diagnosis and deferring treatment. Therefore, it is important to consider gastric lymphoma as part of the differential diagnosis.

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Recurrent Pancreatitis Secondary to Common Channel Volvulus through Petersen's Space Defect in a Patient with Roux-En-Y Bypass

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Introduction: Petersen's space hernia is an internal hernia that can occur after Roux-en-Y gastrojejunostomy. The intestinal loops herniate through a defect between the retroperitoneum, the transverse mesocolon and the small bowel limbs. We present a case of recurrent pancreatitis in a patient with Roux-En-Y bypass found to have common channel hernia through a Petersen's space defect.

Case Description/Methods: Case Description/Methods: We present the case of a 34-year-old female with a history of Roux-en-Y surgery in 2018 and subsequent recurrent pancreatitis who presented to the emergency department with a chief complaint of severe epigastric and left lower quadrant abdominal pain associated with hematemesis. Patient reported 3 episodes of pancreatitis within 1 year previously. CT abdomen and pelvis showed mildly dilated common bile duct and intrahepatic biliary dilatation with no evidence of pancreatitis. Significant lab work included elevated lipase at 184 U/L. Patient was admitted to the medical service. Gallbladder ultrasound revealed no evidence of cholelithiasis, a prominent CBD of 9 mm and redemonstrated mild intrahepatic biliary dilatation. MRCP revealed a mesenteric swirl in the mid abdomen which was suspicious for an internal hernia in the setting of antecolic Roux-en-Y gastric bypass. It also showed focally dilated intrahepatic with underlying segmental atrophy. General surgery consultation was sought, with eventual plans for diagnostic laparoscopy after ruling out marginal ulcer via EGD. An EGD was performed which did not show evidence of marginal ulcer. Patient then underwent diagnostic laparoscopy which revealed a 360-degree volvulus of the common channel through a Petersen's space defect; this was carefully reduced, and the Petersen's space defect was closed. Patient also underwent laparoscopic cholecystectomy. Patient did not have any further episodes of pancreatitis after surgery.

Discussion: This case demonstrates recurrent pancreatitis in a patient with a history of Roux-En-Y bypass found to have a common channel volvulus through a Petersen's space defect. It is our understanding that the volvulus likely caused compression of the pancreaticobiliary system, thus causing

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recurrent pancreatitis. Reduction of the volvulus and closing of the Petersen's defect resulted in complete resolution of recurrent pancreatitis in the patient.

Comparative Efficacy of Treatment Options for Prevention of Post-TIPS Hepatic Encephalopathy: A Systematic Review and Network Meta-analysis

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Introduction: Transjugular intrahepatic portosystemic shunt (TIPS) is commonly used to treat complications of portal hypertension including refractory ascites, as well as secondary prophylaxis of variceal bleeding in patients with liver cirrhosis. Unfortunately, 35-50% of patients develop overt hepatic encephalopathy (HE) after TIPS. However, data on the utility of lactulose and rifaximin to prevent post-TIPS HE are limited. Therefore, we conducted a network meta-analysis to investigate the efficacy of multiple pharmacological regimens in preventing post-TIPS HE.

Methods: A comprehensive search strategy to identify reports of studies of rifaximin use and post-TIPS hepatic encephalopathy was developed in Embase (Embase.com, Elsevier) by an experienced health sciences librarian [WL-S], using truncated keywords, phrases, and subject headings. This strategy was translated to MEDLINE (PubMed platform, NCBI), Cochrane Central Register of Controlled Trials (CochraneLibrary.com, Wiley), and the Web of Science Core Collection (Web of Science platform, Clarivate) with all searches performed on 10 February 2022 (see Supplementary Information for detailed search strategies). No publication date or language limits were used.

Results: The results of this meta-analysis demonstrate no benefit from prophylactic administration of either a non-absorbable disaccharide (lactulose/lactitol) alone or a non-absorbable antibiotic (rifaximin) alone compared to placebo/no prophylaxis for the prevention of post-TIPS HE. However, there is weak evidence supporting the combination of lactulose and rifaximin in preventing post-TIPS HE based on the P-score rankings in our network meta-analysis.

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Conclusion: In conclusion, lactulose/lactitol or rifaximin alone did not prevent post-TIPS HE. Despite this, there is weak evidence that the combination of lactulose and rifaximin is superior at preventing post-TIPS HE. Further research is warranted to determine if there is an ideal time for therapy initiation and duration of treatment in order to appreciate significant benefit of administering pharmacological prophylaxis to prevent post-TIPS HE.

Efficacy and Safety of Cap Assisted vs. Conventional Endoscopic Esophageal Foreign Body Removal- Systematic Review and Meta-analysis

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Introduction: Foreign body impaction (FBI) is a common endoscopic emergency in clinical practice. FBI can be food (also known as a "food bolus (FB)") or other impactions (non-food). We conducted a comprehensive systematic review and meta-analysis to compare cap-assisted and conventional endoscopic techniques for removing esophageal foreign body impaction.

Methods: A comprehensive search technique was utilized to identify studies that used capped endoscopic devices to remove food boluses or other esophageal foreign bodies. The primary outcomes were the technical success rate, rate of en bloc retrieval, and procedure time. Secondary outcomes were overall complications, mucosal tear, bleeding, and perforation. Odds Ratio (OR) with 95% confidence intervals (CI) were estimated using random effects models and the DerSimonian-Laird technique.

Results: Seven studies with a total of 1407 patients were included. The included patients' mean age was 55.3+/- 7.2 years, and the male percentage was 44.8%. There were two RCTs and five observational studies among the included studies. The technical success rate was significantly higher in the cap-assisted group compared to the conventional group (OR: 3.47, CI: 1.68-7.168, I2=0%, p=<0.001). The en bloc retrieval rate was significantly higher in the cap-assisted group compared to the conventional group (OR: 26.90, CI: 17.82-40.60, I2=0%, p=0.001). The overall adverse events were significantly lower in the cap-assisted group compared to the conventional group (OR: 0.118, CI: 0.018-0.792, I2=81.79%, p=0.02).

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Conclusion: This systematic review and meta-analysis showed that the cap-assisted technique has higher efficacy and better safety than conventional techniques. However, larger randomized control trials are needed to validate these results.

Lung Cancer Metastasis to the Pituitary Gland

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Introduction: Common sites of lung cancer metastasis include the bone, brain, liver, and adrenal gland. Cancer metastasis to the pituitary gland or sellar region is a rare finding. Here, we present a case of pituitary gland metastasis from underlying lung cancer in a patient presenting with a predominance of pituitary symptoms.

Case Report: A 48-year-old white female with a 36 pack-year smoking history presented to the hospital with chief complaints of worsening fatigue, intractable headaches, and blurred vision over the past three months. Associated symptoms included daily nausea, progressive anorexia with 25-lb weight loss, lightheadedness, exertional shortness of breath, cold intolerance, hair loss, dry skin, polyuria, polydipsia, abdominal pain, and diarrhea. She smoked one pack of cigarettes daily since the age of 12, and she did not drink alcohol. Mother died of lung cancer at age 58. A brain MRI done two months earlier revealed a large mass in the pituitary gland and sella turcica area. Biochemical test abnormalities consistent with pituitary hormonal insufficiencies were noted, and subsequent imaging showed an enlarging pituitary mass and extensive metastases to the bones, brain, liver, adrenal gland, and lymph nodes. CT Scan of the lungs with contrast showed a macrolobulated mass 2.5 x 2.4 x 2.3cm in the left upper lung. Bone biopsy was consistent with poorly differentiated adenocarcinoma of the lung as the primary site.

Conclusion: Cancer metastasis to the pituitary gland is rare. Worsening pituitary symptoms with an enlarging pituitary mass and widespread metastases should alert consideration for pituitary metastasis and a search for a primary cancer site.

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Prevalence and Clinical Significance of Antiphospholipid Antibodies in Hospitalized Patients with COVID-19 Infection

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Introduction: The pathophysiology of coronavirus disease 2019 (COVID-19) may involve both arterial and venous thromboembolic events; however, current literature shows variance in incidence. Previous literature suggests that the presence of antiphospholipid antibodies (APA) is an important factor for thrombosis in COVID-19 patients. This single-institution retrospective study aims to find if the prevalence of APA in COVID-19 patients has any clinical significance.

Methods: Two cohorts were made based on APA status of the patients (APA positive & APA negative) and were statistically compared. The criteria for the APA positive group include patients with positive titers for lupus anticoagulant or abnormal APA antibodies. A Mann-Whitney U-test for continuous variables or a Fisher's exact test for categorical variables was used to compare prognostic outcomes and laboratory values for the two groups.

Results: No significant difference in demographics was found between the two groups. 39.3% of patients hospitalized with COVID-19 were APA+ and APA positive status is significantly higher in smokers. No statistically significant difference was found in six-month mortality between the two groups. It was statistically found that APA+ patients had a higher nadir of C-reactive protein lab values and a lower nadir of absolute lymphocyte count.

Conclusion: While some laboratory values differ between the two groups, prognostic outcomes of patients were not statistically different between the APA positive and APA negative patients. Currently

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it is unknown if antiphospholipid antibodies have a role in the pathogenicity of COVID-19 and further studies are needed to determine their role in thrombotic events in these patients.

Bictegravir, Emtricitabine & Tenofovir Alafenamide-associated Acute Pancreatitis

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Background: Bictegravir, Emtricitabine & Tenofovir alafenamide (Biktarvy) is now considered as the first line treatment for Human Immunodeficiency virus (HIV).

Case Report: Thirty-six year old male with history of Human Immunodeficiency Virus (HIV) on antiretroviral Bictegravir, Emtricitabine, and Tenofovir alafenamide (Biktarvy) presented to the emergency room complaining of constant sharp epigastric pain for 2 days associated with nausea and one episode of non-bloody vomit. Patient has no history of gallbladder stones, and he drinks alcohol socially. No family history of hypertriglyceridemia. In the emergency room patient was tachycardic at 125 beats/minute, and blood pressure was 110/73 mmHg. Physical examination was remarkable for epigastric tenderness without rigidity. The underlying etiology was believed to be secondary to Biktarvy use since the patient was started 3 months prior to his presentation, Naranjo score is 6. Patient admitted to the regular floor, Biktarvy was discontinued, intravenous lactated ringer started at 150 mL/hour and diet status was nothing by mouth (NPO). Twenty-four hours after admission, patient condition markedly improved and his pain was controlled with intravenous hydromorphone 1 mg as needed. On the fifth day of admission, the patient's abdominal pain completely resolved, and he was able to tolerate regular diet.

Conclusion: Prompt discontinuation of the offending agent is an essential part of treatment plan of acute pancreatitis, as seen in this patient. Healthcare providers should be aware of the unusual adverse event of Bictegravir, Emtricitabine, and Tenofovir alafenamide (Biktarvy) as a potential cause of pancreatitis in patients with Human Immunodeficiency Virus (HIV).

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Vocal Cord Palsy and Neutropenia: Unusual Presentation of B-12 Deficiency in Adult Patient, A Case Report

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Background: Vitamin B12 deficiency commonly causes megaloblastic anemia and rarely pancytopenia. Manifestations of anemia may include gastrointestinal and neurological symptoms which can persist if not treated immediately.

Case Presentation: Patient is a 67-year-old male who presented with severe leukopenia. The lab work was subsequent to a 6-week-course of cefepime for osteomyelitis. On arrival, the patient endorsed pharyngitis, dyspnea, cough productive of clear sputum, and headaches present for 5 days. Initial workup redemonstrated severe leukopenia (WBC: 2.2) with an Absolute Neutrophil Count of 0. The next day, the patient was experiencing dysphagia with thick, white oral secretions that required suctioning and had a strong productive cough. Video swallow study demonstrating severe impairment of pharyngeal swallow with gross aspiration. The patient's blood culture, sputum culture, and RPP all come back within normal limits. On the 6th day of admission, the patient's WBC improved to 10.2 and his Absolute Neutrophil Count was 5.8. He could communicate well, and his dysphagia and dysphonia improved. Repeat Video Swallow Study on day 7 demonstrated only mild oral and pharyngeal phase dysphagia and repeat laryngoscopy revealed normal right vocal cord with persistent left vocal cord paralysis.

Conclusion: B12 deficiency may present in wide different ways. This case highlights the fact that manifestations of vitamin B12 deficiency can be highly variable and underscores the need to keep this disorder on the differential diagnosis in a variety of clinical presentations. Clinicians should be aware of different hematological and neurological presentations.

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Renal Cell Carcinoma Metastasis to the Left Atrium

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Only 13 cases of renal cell carcinoma metastasis to the left atrium (LA) of the heart have been described in literature. Our patient presented with LA metastasis 14 years after a nephrectomy for RCC. Because RCC rarely metastasizes to the heart, its diagnosis is difficult. In addition, affected patients are mostly asymptomatic and can present variably. Our patient had purely neurologic symptoms and none indicating cardiac involvement.

Although unlikely, it is possible that a mass found incidentally in a patient with RCC and metastasis is instead, an atrial myxoma. Our patient's mass had some features of an atrial myxoma (clear definition and pedunculation with a stalk); however, we were unable to confirm this histologically because surgical excision was not performed.

Given the risk of sudden cardiac death, most cardiac masses are removed surgically as soon as possible. For inoperable metastases, molecular targeted therapy is used. Our cardiologists had advised against surgical resection because of a poor prognosis. We prescribed the patient a 10-session regimen of 3-dimensional conformal radiation therapy, axitinib and pembrolizumab. At the 4-month visit, there was substantial improvement in memory recall and the radiotherapy had brought 70% to 75% subjective improvement.

Atrial masses can be detected in patients' years after nephrectomy and may not produce obvious symptoms, so patients with RCC should undergo regular cardiovascular evaluation and investigation of any cardiac mass. If surgery is inadvisable, the patient should be started on immunotherapy, and the cardiac mass should be monitored regularly for structural changes. Given that there is no established algorithm for managing cardiac metastases from RCC, a surgical approach seems most feasible. For inoperable metastases, molecular therapy is an alternative, although further studies are needed to determine efficacy and safety profiles.

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Effect of Antiplatelet Medications on Critically Ill Patients with Pre-existing Atrial Fibrillation

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Introduction: Limited data was found about the usage of antiplatelet medications on patients who previously diagnosed with atrial fibrillation (AF), and were critically ill and admitted to stepdown care unit (SDU) due to other acute conditions. Our goal to clarify the effect of antiplatelet medications on the adverse events (i.e., transfer to intensive care unit (ICU) or death), and the influence of the associated clinical factors.

Method: A retrospective cohort study was conducted on previously diagnosed AF patients, that were admitted to SDU. The exposure was the use of antiplatelet medications, and the primary composite outcome was the transfer to ICU or death.

Results: A total of 1430 patients were included, in which 198 (13.9%) had the primary outcome, the exposed group was less likely to report the outcome than the unexposed group, 10% and 16% respectively (P= 0.001). Univariate logistic regression showed a statistically significant association between the usage of antiplatelet medications and the decreased primary outcome (OR: 0.57, 95% CI:0.41-0.79, P=0.001). The multivariate logistic regression was adjusted for other factors, the association was still statistically significant (OR: 0.50, 95% CI:0.32-0.77, P=0.002), and had less odds to report the main outcome in antiplatelet medications group.

Conclusion: Among the critically ill SDU patients who previously diagnosed with AF, and admitted due to other acute conditions, and who were treated with antiplatelet medications, less likely to be associated with adverse events (transfer to ICU or death) by approximately 50%.

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Lithium-Induced Nephrogenic Diabetes Insipidus Self-Treated With Beer Potomania and Masquerading as Shock: A Case Report

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Introduction: Nephrogenic diabetes insipidus (NDI) is a known adverse effect from lithium use, commonly presenting as polyuria and polydipsia. Patients are often able to drink enough water to keep up with urinary losses. Here we discuss a patient accustomed to drinking 10 beers daily who developed rapid volume depletion, shock, and hypernatremia after his access to oral fluids was disrupted.

Case Description: A 66-year-old male with a past medical history of bipolar disorder and alcohol use disorder presented with altered mental status, ataxia, and severe weight loss. Admission labs were significant for leukocytosis, hyponatremia, lactic acidosis, and acute kidney injury. Despite empiric antibiotics and volume resuscitation for presumed septic shock, on day two, he required pressors for hemodynamic instability and intubation for mental status. Repeat labs revealed hypernatremia and an elevated lithium level. Diagnosis of NDI was confirmed by a high serum and low urine osmolality, without improvement after DDAVP administration. We stopped lithium and initiated hypotonic fluids, amiloride, hydrochlorothiazide, and indomethacin. Gradually the patient's sodium normalized, pressors were weaned off, and he was extubated.

Conclusion: In this case, we describe a delayed presentation of lithium-induced NDI, initially appearing as hypovolemic shock and hyponatremia, then manifesting as persistent hemodynamic instability and hypernatremia on day two. Ad lib fluids and possibly beer potomania enabled self-correction of sodium levels until our patient's oral intake was restricted. Clinicians should include NDI in the differential for patients taking lithium who develop hypotension, hypernatremia, or shock. Rapid identification and treatment may help avoid decompensation.

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Exploring the Accuracy of the Medication Reconciliation Process on the Medical Floor

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Medication reconciliation is an essential step in the admitting process and helps to ensure patients receive the appropriate and best medical care. Sometimes completion of this important task is inaccurate resulting in errors that can carry on during the hospital stay and ultimately to transition care to other settings. As a part of resident driven quality improvement project, we examined the accuracy of the medical reconciliation process for patients admitted to our internal medicine service. The medication list of patients admitted to IMS at the Toledo hospital were audited by medical residents. The initial medication reconciliation was completed by an RN, whereafter the resident uses various means (contacting patient pharmacy or verbal communication with patient) for verification. A medication list was considered accurate if there was a discrepancy in the medication count, route, dose, and/or frequency. During the study period, the medication lists from 94 patients were reviewed on the IMS service. Of those, 52 (53.3%) had at least one discrepancy when reviewed. Of the charts where medication errors were found, 71.3% had three or more discrepancies. The most common type of errors involved incorrect additions or omissions of a prescribed medication (39.8 and 32.7% respectively). Through examination of the medicine reconciliation process we can quantify the errors and begin to take steps to improve the process. Our next focus should be on understanding why medication lists contain erroneous information because of added or missing medications.

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The Importance of Neuro-Imaging in Patients with Symptomatic Presentation of Both Cortical and Subcortical Dementia

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A 45-year-old male presented to the emergency department with a 6 month decline in cognitive function, confusion, gait disturbance, dizziness, and personality change that started after release from immigration jail. His family initially believed that he was acting to get out of jail. However, his symptoms continued to worsen. Upon presentation, he was unaware of place or time, had difficulty answering questions, and could not follow directions. He was hypertensive, complained of nausea with episodes of non-bloody vomiting, and had migraines that would awaken him from sleep. Family history included the death of his father at a young age due to unknown causes, and an unknown mental health disorder in his mother. Negative urine drug screen, blood alcohol level, ammonia levels, and blood culture combined with the progressive nature of his memory loss and cognitive slowing originally led physicians to suspect Early Onset Alzheimer's Disease. However, further neuroimaging was conducted due to unknown family history and possible head trauma while in jail. Imaging included a head CT that revealed nonspecific white matter hypodensities in the high frontal lobes. Carotid ultrasound revealed no significant plaque buildup. Brain MRI revealed innumerable scattered punctate foci raising suspicion for subcortical vascular dementia. Binswanger Disease and Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL) are both forms of subcortical vascular dementia that are being explored as causes for this patient's decline.

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Are Three Better than Two? – Incidental Finding of Incomplete Cor Triatrium Dextrum during 2nd Trimester of Pregnancy

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Background: Cor triatriatum sinistrum is a type of congenital heart defect that occurs due to the left atrium being divided into two chambers by a fibromuscular septum. An even rarer subsection of this is cor triatriatum dextrum, in which the fibromuscular septum divides the right atrium.

Case Presentation: We present a patient with intermittent palpitations, chest pressure, and lightheadedness without syncope related to her cor triatriatum dextrum exacerbated by her pregnancy status. Without any prior history of congenital heart defects or pertinent family history, this seemingly health female prior to her pregnancy likely revealed and exacerbated her symptoms and lead to the diagnosis.

Conclusion: Treatment in the setting of an asymptomatic presentation of a pregnant patient with history of cor triatriatum remains unclear. Many physicians elect close follow up to monitor for development of symptoms. In symptomatic cases, rate control, thromboembolic prophylaxis, and hemodynamic stabilization are mainstays of treatment. This unique presentation in a rare patient population furthers literature and gives a perspective on pregnancy and structural heart disease like cor triatriatum.

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Who Left the Dog Out (of the History)? - Capnocytophage Canimorus Baceteremia Induced Sepsis

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Capnocytophage canimorsus is a gram-negative rod bacterium that composes the microbial biome in the oral cavity of some canines and felines. It is mostly seen in patients with underlying disorder such as asplenia, general alcohol abuse, and cirrhosis. It can lead to multiple complications for patients that include meningitis, endocarditis, and sepsis. The history and the broad differential are important details for clinicians because of its slow growing nature during blood culturing. Broad-spectrum antibiotics and life support are considered the mainstays of treatment for a patient presenting with unknown sepsis that may be caused by C. canimorsus. The authors present the risk factors, clinical picture, and treatment for the encounter of a patient with sepsis secondary to C. canimorsus.

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Antioxidant Therapy Restores Hepatic Metabolic Enzymes Altered by Exposure to Microcystin-LR in a Murine Model of Non-Alcoholic Fatty Liver Disease

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Introduction: We have shown that exposure to the environmental liver toxin Microcystin-LR (MC-LR) in the setting of pre-existing Non-alcoholic Fatty Liver Disease (NAFLD) induces significant hepatotoxicity and oxidative stress. Therefore, we hypothesized if targeted antioxidant therapy would improve MC-LR metabolism and reduce hepatic injury.

Methods: Six-week-old C57Bl/6J mice fed with choline-deficient high fat diet with 0.1% methionine to induce NAFLD were gavaged with 100 µg/kg MC-LR/24 hrs for 15 days. Antioxidants included augmentation of the glutathione detoxification pathway with N-acetylcysteine (NAC) given at 40 mM in drinking water; and interruption of specific Src kinase-mediated oxidant signaling pathways with a novel peptide (pNaKtide) at 25 mg/kg injected intraperitonially once a week.

Results: Histologic analysis revealed significant increase in hepatic inflammation with MC-LR exposure which was attenuated in both antioxidant treatment groups. 8-OHDG levels in urine and protein carbonylation in liver, both markers of oxidative stress, were significantly downregulated upon antioxidant treatment after MC-LR exposure. Analysis of key drug transporters as well as Phase I & II enzymes using quantitative PCR revealed that exposure to MC-LR significantly upregulated expression of the drug transporter Abcb1a; Cyp3a11, Phase I enzyme belonging to the Cytochrome P450 family whereas Phase II enzymes, Pkm (Pyruvate kinase, muscle), Pklr (Pyruvate kinase, liver, and RBC) and Gad1 (Glutamic acid decarboxylase) were significantly downregulated. Antioxidant therapy with both pNaKtide and NAC significantly attenuated these changes and restored microcystin detoxification.

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Conclusion: These results suggest that NAFLD significantly alters the metabolism of MC-LR, and this can be reversed with targeted antioxidant treatment.

Hepatitis C Screening in Pregnancy: A Single Center Quality Improvement Experience

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Background: Hepatitis C infection is a preventable but serious illness with more than half the patients developing chronic infection if infected. According to CDC, an estimated 57,500 acute Hepatitis C occurred in United States in 2019. National data revealed increase in reported cases of HCV infection every year from 2009 to 2017. Among these patients, highest rates of incidence in people aged 20-39 years. CDC recommends Hepatitis C screening for everyone at least once in their lifetime and for all pregnant women during each pregnancy regardless of risk factors. We conducted a quality improvement project in our hospital regarding Hepatitis C screening among pregnant women. Our objective was to assess compliance with CDC guideline recommendation regarding Hepatitis C screening in pregnant women and suggest ways to improve it.

Methods: We gathered data of all the pregnant women who presented to the hospital for delivery from September 2020 to May 2021 which were a total of 2735 patients, among these 63 patients were screened for Hepatitis C. We reached out to all our obstetrics and gynecology providers through emails prompting them to screen patients for Hepatitis C during their pregnancy episode. We also educated patients on importance of Hepatitis C screening and effects of acute HCV infection on both child and mother encouraging them to ask providers for screening test if they are not offered one. Printed handouts regarding Hepatitis C screening were distributed among the patients. Then we ran another data analysis report in Epic for all pregnant patients June 2021 to March 2022 which showed 3161 patients presented to hospital for delivery and among them 121 were screened for Hepatitis C.

Results: A chi-square analysis was performed which showed chi-square statistic (x2) 11.271 with a p value of 0.001 indicating significant results. Overall, 65% increase in screening for Hepatitis C among pregnant women presenting to the hospital was observed after implementing Hepatitis C screening protocol.

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Conclusion: Hepatitis C screening is recommended in all pregnant women during their pregnancy episode. We requested our Epic IT team to introduce an EPIC Hard Stop protocol for Hepatitis C when pregnant women present for their initial visit and recommended Hepatitis C screening to be made a part of Obstretical triage order panel. We also encouraged all providers to refer all Hepatitis C positive patients to GI to establish care for Hepatitis C treatment.

Mantle Cell Lymphoma With GI Involvement Presenting as Bilateral Eyelid Swelling

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Introduction: Mantle cell lymphoma (MCL) is a subtype of non-Hodgkin lymphoma accounting for about 5% of non-Hodgkin lymphomas. Usual presentation is with lymphocytosis or widespread lymphadenopathy, extranodal manifestations involving bone marrow and GI tract are also common. We describe a case of MCL presenting as bilateral eyelid swelling.

Case Presentation: An 80-year old Caucasian male presented to his ophthalmologist for swelling of his bilateral lower lids for the past few months. He denied any visual disturbance or any other associated symptoms. His past medical history was significant for hypertension, cholecystectomy and cataracts surgery. He worked as a farmer, with occupational exposure to glyphosate-based insecticides, and smoked a pack of cigarettes per day for 20 years. Physical exam was significant only for bilateral lower eyelid swelling (Figure 1A). Lab work was unremarkable. The ophthalmologist suspected amyloidosis, and a biopsy was sent to diagnose the underlying etiology. He then immediately referred the patient to Hemeoncology as biopsy had revealed MCL. GI was consulted, EGD revealed normal esophageal mucosa. Mild erythema in the gastric body/antrum, status post biopsy (Figure 1B). Colonoscopy revealed colonic mucosa to be unremarkable with no evidence of inflammation or ulceration or masses. Biopsy of gastric mucosa (Figure 1C) showed an atypical lymphoid infiltrate in both gastric and duodenal mucosa composed of small lymphocytes positive for CD20, CD5, cyclin D1 and negative for CD3, CD10. There was no evidence of H. pylori. Bone marrow biopsy was also positive for MCL. PET scan showed increased activity in the skin of the nose, enlarged lymph nodes in the mediastinum and inguinal region. It was determined to be stage IV mantle cell lymphoma. Patient was then referred to Radiation Oncology for evaluation of involved site radiation therapy (ISRT) of the eyelids and then targeted therapy with Calquence rather than chemotherapy, given his age.

Discussion: Romaguera et al. described that 88% of patients with MCL have lower GI tract involvement, and 43% of patients with MCL have upper GI tract involvement. Similar studies have since reaffirmed this association, leading to the recommendation that all patients with a new diagnosis of

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MCL undergo further intestinal workup. Eyelid swelling or mass is a rare presentation of MCL and a high degree of suspicion is required for diagnosis of MCL with this rare presentation.

Nosocomial vs Healthcare Associated vs Community Acquired SBP – A Systematic Review and Meta-Analysis

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Introduction: Spontaneous bacterial peritonitis (SBP) is a common complication in decompensated liver cirrhosis. SBP is defined as ascitic fluid polymorphonuclear cell count > 250/mm3. Community acquired SBP (CA-SBP) occurs within 48 hours of admission to the hospital. Healthcare associated SBP (HA-SBP) is defined as SBP occurring in patients who were hospitalized in the preceding 90 days to months. Nosocomial SBP (N-NBP) occurs more than 48- 72 hours after hospital admission.

Methods: We conducted a systematic review and meta-analysis on the studies that compared N-SBP, HA-SBP and CA-SBP. We performed a comprehensive database search in PubMed, Embase and Web of Science from inception through May 18, 2022. Randomized controlled trials, prospective and retrospective cohort studies and case series were included. Number of N-SBP, HA-SBP and CA-SBP episodes, ascitic fluid culture results and previous SBP episode data was gathered. The primary outcome was mortality rate in all types of SBP. The secondary outcome was resistance to third generation cephalosporins. The random effects model was used to calculate the risk ratios (RR), mean differences (MD) and confidence intervals (CI). A p value <0.05 was considered statistically significant. Heterogeneity was assessed using the Higgins I2 index.

Results: Fourteen retrospective and prospective cohort studies comprising a total of 2302 SBP episodes were included. The mortality rate was statistically significantly higher in N-SBP compared to HA-SBP (RR 1.84, p<0.0001, CI 1.43- 2.37, I2=0%) and CA-SBP (RR 1.69, p<0.00001, CI 1.4-1.98, I2= 33%), but not statistically significant between HA-SBP and CA-SBP (RR=1.40, p=0.34, CI=0.71-2.76, I2=53%). Resistance to third generation cephalosporins was statistically significantly higher in N-SBP

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compared to HA-SBP (RR=2.02, p=0.003, CI 1.26-3.22, I2=54%), CA-SBP (RR=3.96, p<0.00001, CI=2.50-3.60, I2=52%) and between HA-SBP and CA-SBP (RR=2.25,p=0.002, CI=1.33-3.81, I2=0%).

Conclusion: A lower threshold to start broad spectrum antibiotics with targeted therapy guided through culture data should be undertaken for appropriate treatment of SBP and to improve mortality in N-SBP and HA-SBP.

Sarcoidosis and increased risk of Colorectal cancer: A systematic review and Meta-analysis

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Introduction: Sarcoidosis is a chronic inflammatory condition that appears to be associated with increased risk of malignancies. The aim of this study is to evaluate the correlation between sarcoidosis and the risk of colorectal cancer.

Methods: We performed a comprehensive search in the databases of PubMed/MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials from inception through October 7, 2020. From each study, we collected the number of sarcoidosis patients with and without colorectal cancer. The primary outcome was the occurrence of colorectal carcinoma in both groups. The random-effects model was used to calculate the risk ratios (RR), mean differences (MD), and confidence intervals (CI). A p value <0.05 was considered statistically significant.

Results: A total of nine cohort studies involving 26347 patients were included in the meta-analysis. Incidence of colon cancer was significantly higher in patients with sarcoidosis in comparison to the control group (RR 1.36, 95% CI 1.17-1.57, p <0.0001). The incidence of rectal cancer was also significantly higher in patients with sarcoidosis compared to the control group (RR 1.23, 95% CI 1.01-1.5, p 0.03)

Conclusion: Our meta-analysis demonstrated that patients with sarcoidosis appear to be at significantly increased risk of colorectal cancer compared to the general population. This may worsen the prognosis in these patients even though sarcoidosis usually has a benign course. The chronic inflammatory nature of the disease as well as the immunosuppressive medications used in the management of sarcoidosis can play a role.

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Do Patients with Scleroderma Benefit from Surgical Treatment for Gastroesophageal Reflux?

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Introduction: Gastroesophageal reflux (GERD) is common in patients with scleroderma that may be complicated by esophagitis, strictures, and Barret's esophagus. Anti-reflux medications are still considered the first line treatment of GERD in SSc patients. Surgical treatment is usually preserved for reluctant cases. We conducted this meta-analysis to assess for the benefit of surgery in treating GERD in SSc patients.

Methods: A comprehensive literature search of PubMed, Embase, and Web of Science databases was conducted through June 01, 2022. We included all studies that assessed for the outcomes of surgical treatment of GERD in SSc patients. We calculated pooled odds ratios (OR) for the outcomes that were reported in ≥3 studies using a random-effects model.

Results: A total of 142 patients with SSc who underwent surgical treatment of GERD were included in nine studies. Persistence of dysphagia and acid reflux symptoms were used to assess for the outcomes of surgery as they were reported in ≥3 studies. Our meta-analysis showed that there is about 61.5% decrease in dysphagia after surgery with an OR of 0.385 (0.250, 0.541). Our study also showed a 26% decrease in acid reflux symptoms after surgery with an OR of 0.741 (0.484, 0.897)

Conclusion: The treatment of refractory GERD in patients with SSc remains challenging. Our study showed that surgery has been associated with lower rates of dysphagia and acid reflux. However, further studies should be conducted to assess for the definitive indications, and the adverse outcomes of surgery in SSc patients.

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Predictors of Remission in Rheumatoid Arthritis Patients Treated with Biologics: A Systematic Review and Meta-Analysis

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Introduction: Biologics have emerged as an effective treatment of rheumatoid arthritis (RA). However, there is a significant proportion of patients who fail to respond to biologics. Identifying the predictors that affect the response to biologics remains challenging.

Methods: A comprehensive literature search of PubMed, Embase, and Web of Science databases was conducted through May 01, 2022. We included all studies that used a multivariate model to assess for the predictors of remission in RA patients treated with biologics. We calculated pooled odds ratios (OR) with 95% confidence intervals (CI) for risk factors reported in ≥3 studies using a random-effects model.

Results: A total of 16,934 patients with RA who were treated with biologics were included in twenty-one studies. Our study showed that old age (OR 0.98 (0.97, 0.99), P <0.00001), female gender (OR 0.66 (0.56, 0.77), P <0.00001), smoking history (OR 0.86 (0.75, 0.99), P 0.04), obesity (OR 0.95 (0.91, 0.99), P 0.02), poor functional status (OR 0.62 (0.48, 1.27), P < 0.00001), high disease activity (OR 0.90 (0.85, 0.96), P 0.0005), and elevated ESR (OR 0.99 (0.98, 1.00), P 0.009) were poor predictors of remission. While positive Anti-citrullinated Protein Antibodies (OR 2.52 (1.53, 4.12), P 0.0003) was associated with high remission rate.

Conclusion: Old age, female gender, obesity, smoking history, poor functional status, high disease activity, and elevated ESR at the time of diagnosis have been associated with poor response to biologics. Our findings could help establish a risk stratification model for predicting the remission rate in RA patients receiving biologics.

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Clinically Significant Gastrointestinal Bleeding Using Proton Pump Inhibitors or Histamine Type-2 Receptor Antagonists in Patients Intubated for Over 48 Hours: A Systematic Review and Meta-Analysis

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Introduction: The use of stress ulcer prophylaxis (SUP) is routine in the intensive care unit (ICU) to prevent serious deleterious effects of gastrointestinal bleeding (GIB). Aim of our investigation was to perform a literature review and meta-analysis to compare the effectiveness of proton pump inhibitors (PPIs) to histamine type-2 receptor antagonists (H2RAs) in a selective high risk patient population that has been mechanically ventilated for over 48 hours.

Methods: Comprehensive search of published studies indexed in PubMed/MEDLINE, EMBASE, and the Cochrane Central Register of Controlled Trials to obtain randomized controlled trials (RCTs) that evaluated the use of PPIs and H2RAs in patients intubated for >48 hours. Primary outcome was the occurrence of clinically significant or overt GIB (CS/O-GIB). Secondary outcomes were occurrence of ventilator associated pneumonia (VAP), ICU mortality, and ICU length of stay (LOS).

Results: Seven RCTs involving 27905 patients that were mechanically ventilated for >48 hours were including in the meta-analysis. Rate of CS/O-GIB was significantly lower in patients receiving PPIs compared to H2RAs while intubated (1.6% vs. 2.5%, RR 0.59, 95% CI 0.45-0.79, P = 0.0003, I2= 31%). There was no significant difference between the two groups in-terms of rate of VAP, ICU morality, and ICU LOS.

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Conclusion: This meta-analysis demonstrates that PPIs in patients mechanically ventilated for over 48 hours are more effective in preventing CS/O-GIB when compared to H2RAs, without leading to a significant increase in the rate of VAP.

Inhaled Pulmonary Vasodilators in COVID-19 Infection: A Systematic Review and Meta-Analysis

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Introduction: Inhaled pulmonary vasodilators (IPVD) have been previously studied in patients with non-coronavirus disease-19 (COVID-19) related acute respiratory distress syndrome (ARDS). The use of IPVD have been shown to increase PaO2/FiO2 (P/F) ratios in ARDS patients. However, the role of IPVD in COVID-19 ARDS is still unclear. Therefore, we performed this meta-analysis to evaluate the role of IPVD in COVID-19 patients.

Methods: Comprehensive literature search of PubMed, Embase, Web of Science and Cochrane Library databases from inception through April 22, 2022 was performed. The single arm studies and case series were combined for a 1-arm meta-analysis, and the 2-arm studies were combined for a 2-arm meta-analysis. Primary outcomes for the 1-arm and 2-arm meta-analyses were change in pre- and post-IPVD P/F ratios and mortality, respectively.

Results: 13 single arm retrospective studies and 5 case series involving 613 patients were included in the 1-arm meta-analysis. 3 studies involving 640 patients were included in the 2-arm meta-analysis. The pre-IPVD P/F ratios were significantly lower compared to post-IPVD, but there was no significant difference between pre- and post-IPVD PEEP and lung compliance. The mortality rates, need for endotracheal intubation, and hospital LOS were similar between the IPVD and standard therapy groups.

Conclusion: Although IPVD may improve oxygenation, our investigation showed no benefits in terms of mortality compared to standard therapy alone. However, randomized controlled trials are warranted to validate our findings.

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Pulse versus Non-pulse Steroid Regimens in Patients with Coronavirus Disease 2019: A Systematic Review and Meta-Analysis

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Introduction: Systemic steroids are associated with reduced mortality in hypoxic patients with COVID-19. However, there is no consensus on the doses of steroid therapy in these patients. Several studies showed that pulse dose steroids (PDS) could reduce the progression of COVID-19 pneumonia. However, data regarding the role of PDS in COVID-19 is still unclear. Therefore, we performed this meta-analysis to evaluate the role of PDS in COVID-19 patients compared to non-pulse steroids (NPDS).

Methods: Comprehensive literature search of PubMed, Embase, Cochrane Library, and Web of Science databases from inception through February 10, 2022 was performed for all published studies comparing PDS to NPDS therapy to manage hypoxic patients with COVID-19. Primary outcome was mortality. Secondary outcomes were the need for endotracheal intubation, hospital length of stay (LOS), and adverse events in the form of superimposed infections.

Results: A total of ten observational studies involving 3065 patients (1289 patients received PDS and 1776 received NPDS) were included. The mortality rate was similar between PDS and NPDS groups (RR 1.23, 95% CI 0.92-1.65, P=0.16). There were no differences in the need for endotracheal intubation (RR 0.71, 95% CI 0.37-1.137, P=0.31), LOS (MD 1.93 days; 95% CI -1.46, 5.33; P=0.26), or adverse events (RR 0.93, 95% CI 0.56-1.57, P = 0.80) between the two groups.

Conclusion: Compared to NPDS, PDS was associated with similar mortality rates, need for endotracheal intubation, LOS, and adverse events. Given the observational nature of the included studies, randomized controlled trials are warranted to validate our findings.

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Utility of Midodrine During the Recovery Phase of Shock: A Systematic Review and Meta-Analysis

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Introduction: The use of midodrine is becoming common in the intensive care unit (ICU), but the data remains unclear. Therefore, we performed a meta-analysis of available randomized controlled trials (RCTs) to evaluate the efficacy and safety of using midodrine in conjunction with intravenous vasopressors (IVVs).

Methods: Comprehensive literature search of PubMed, Embase, Web of Science, and Cochrane Library databases from inception through April 07, 2022, for all published studies investigating the use of midodrine in the ICU in patients requiring IVV. Our primary outcome was the total duration of IVVs use. Secondary outcomes were IVV weaning time, ICU LOS, hospital LOS, and adverse events.

Results: 5 RCTs involving 346 patients (175 patients received midodrine plus IVVs and 171 received standard care with only IVVs or IVVs plus placebo) were included. There was no significant difference in total duration of IVV use, IVV weaning time, ICU LOS, hospital LOS, or adverse events between the two groups.

Conclusion: The addition of midodrine was not associated with a shorter duration of IVV use or quicker weaning of IVVs. Midodrine use also did not significantly reduce ICU and hospital LOS.

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Heerfordt-Waldenstrom Syndrome: A Case Report

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Background: Heerfordt-Waldenstrom Syndrome(HWS) is a variant of sarcoidosis, which presents with swelling of the Parotid or salivary glands, facial nerve paralysis and anterior uveitis. The incidence is rare, with only 6% of sarcoidosis patients having parotid gland enlargement, and 5% of patients with cranial nerve palsy.

Case Presentation: A 44-year-old woman with non-significant past medical history presented to the emergency department with several weeks of low back and flank pain. She was also complaining of weakness, weight loss, voice hoarseness and worsening shortness of breath. Six months prior to her presentation, she was diagnosed with a left sided facial nerve palsy. Examination revealed bilateral parotid gland enlargement, left ptosis, left facial drooping and cervical, axillary and femoral lymphadenopathy. Workup for malignancy was negative. Tests for syphilis, acid-fast bacilli and fungal infection were negative. ACE levels found to be increased. CT neck and chest revealed extensive lymphadenopathy, multiple lung nodules and infiltrative densities replacing bilateral parotid glands. Lymph node biopsy confirmed revealed necrotizing granulomas, confirming diagnosis. Patient was initiated on Solumedrol 125mg bid, after which she endorsed improvement in voice hoarseness, shortness of breath and pain. She was transitioned to prednisone 60mg daily and azathioprine 50mg daily at discharge and will follow up with rheumatology and pulmonology for further management.

Discussion/Conclusion: Heerfordt-Waldenstrom syndrome should be considered in the differential for new onset facial nerve palsy without a clear source. When only two of the symptoms are present, it is considered incomplete HWS.

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Applications of Inhalational Nitrous Oxide in Patients as an Alternative to Traditional Narcotics and Sedation Agents in the Emergency Department

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This is the case of a 76-year-old woman who received nitrous oxide as analgesia for a shoulder reduction in the emergency department (ED). The goal of discussing this case is to emphasize the accessibility, efficacy, and safety of using nitrous oxide as a sedation agent in place of narcotics in the ED. From 4/11/22-6/15/22, nitrous oxide has been used as an analgesic at two of ProMedica Toledo's Hospital emergency departments 50 times for a variety of encounters ranging from laceration to open limb fracture repair. This effort is in support of the ProMedica Toledo's PAIN (Prescribing Alternatives Instead of Narcotics) program with an overarching goal to reduce opioid use in the ED. Nitrous oxide can be used for analgesia, pain management, and anxiolysis. It is a colorless, odorless gas that has rapid onset of 1-2 minutes and a short duration of 3-5 minutes. Nitrous has minimal effects on respiration and hemodynamics and has a minimal side effect profile compared to other sedatives. Nitrous is easy to administer, thus there are a wide variety of indications such as being used as an adjunct in fracture reduction, cardioversion, or foreign body removal. The opioid epidemic is an ever present and growing issue in the United States and any effort to curb narcotic use is imperative to prioritize. It is the responsibility of caregivers to learn and understand the indications and contraindications of the use of nitrous oxide as an analgesic. This is a meaningful step in working to curb the opioid epidemic and optimizing patient care in the acute setting.

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Assessing Resident Confidence in Placing a Central Venous Catheter Before and After a Simulation-Based Training Course

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Introduction: Central venous catheters (CVCs) are an advantageous device used to deliver necessary treatment for patients with extended hospital stays. The ability to properly place a central line is an essential skill for resident trainees and physicians to be able to successfully complete. The goal of our study was to assess the confidence of residents in placing a central line before and after a simulation-based training.

Methods: This study was conducted with residents and fellows at the University of Toledo Medical Center across five different specialties in June of 2021. A voluntary survey was administered before and after a central line simulation-based training, measuring confidence through a series of 16 Likert scale questions with the answer options of: 1 = strongly disagree, 2 = disagree, 3 = undecided, 4 = agree, 5 = strongly agree. Results: Sixteen residents completed both the pre- and post-survey and 45 total residents completed the training, yielding a 35.6% response rate. Of all 16 Likert scale statements proposed on both the pre- and post-surveys, mean confidence increased significantly ($P<0.05$) across all statements. This includes confidence in the objectives of conducting, discussing, and teaching the procedure.

Conclusion: Central venous catheter simulation-based training significantly improved resident confidence in procedural proficiency. Simulation-based training is an effective method for teaching procedural skills and education to trainees, thus ultimately improving patient care.

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Efficacy and Safety of Carotid Endarterectomy Versus Carotid Artery Stenting in Asymptomatic Severe Carotid Stenosis: A Systematic Review and Meta-Analysis

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Background: Severe carotid stenosis (CS) is defined as 70-99% blockage of the carotid artery. In patients with severe CS, both carotid endarterectomy (CEA) and carotid artery stenting (CAS) carry procedural risks, however they can restore patency and significantly reduce long-term stroke risk. Most studies compare outcomes between procedures in symptomatic patients; however, there is limited data comparing CEA to CAS in asymptomatic severe CS.

Methods: We performed a literature search using PubMed, Embase, and Cochrane Library from inception through September 2021 to investigate the efficacy and safety of CAS compared to CEA in patients with asymptomatic severe CS. The primary outcome was all-cause mortality and secondary outcomes were stroke, MI, and stroke post 30-day follow up.

Results: 4 randomized controlled trials involving 6442 patients were included in this meta-analysis. There is no difference in the primary outcome of all-cause mortality between CEA and CAS. Compared to CAS, CEA has significantly lower rate of stroke [RR 1.56; CI 1.13, 2.15; P = 0.006]. Alternatively, CAS has significantly lower rate of MI [RR 0.49; CI 0.27, 0.91; P = 0.02]. There is no significant difference in risk of stroke post 30-day follow up.

Conclusion: Based on our results, there is lower risk of stroke with CEA and lower risk of MI with CAS, however no difference in all-cause mortality or stroke post 30-day follow-up. Further trials with large sample sizes are needed to confirm our findings.

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Efficacy and Safety of Dual Antiplatelet Therapy Versus Direct Oral Anticoagulant Following Left Atrial Appendage Closure: A Systematic Review and Meta-Analysis

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Background: Percutaneous left atrial appendage occlusion (LAAO) offers a nonpharmacologic strategy for stroke prevention in patients with atrial fibrillation, however it carries the risk of device thrombosis. Current guidelines recommend oral anticoagulant for 45 days, followed by dual antiplatelet therapy (DAPT) for 6 months. However, given the high bleeding risk in this population, studies have been done comparing DAPT to direct oral anticoagulants (DOAC) following LAAO.

Methods: We performed a literature search using PubMed, Embase, and Cochrane Library from inception through February 2022 to investigate the efficacy and safety of DAPT compared to DOAC in patients following LAAO. The primary outcome was all-cause mortality and secondary outcomes were ischemic stroke, device related thrombosis, and major bleeding.

Results: A total of three studies including 400 patients (150 patients received DOAC and 250 received DAPT) were included. All-cause mortality was significantly higher in the DAPT group compared to the DOAC group (RR 2.29, 95% CI 1.31-4.01, P=0.004). The rates of DRT (RR 4.82, 95% CI 0.60-38.89, P=0.14), ischemic stroke (RR 1.23, 95% CI 0.38-4.05, P=0.73), and major bleeding (RR 1.34, 95% CI 0.50-3.65, P=0.56) were numerically lower in the DOAC group compared to DAPT group, although the differences did not reach statistical significance.

Conclusion: Our study demonstrated the superiority of DOACs vs. DAPT following LAAO in terms of all-cause mortality. DOACs had lower DRT, ischemic stroke, and major bleeding trends compared to

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DAPTs but the differences were not statistically significant. Large-scale trials comparing DOAC and DAPT are necessary to validate our findings.

Ventricular Fibrillation Arrest after Blunt Chest Trauma in a 33-year-old Male, Commotio Cords?

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Background: Commotio cordis is an event in which a blunt, non-penetrating blow to the chest occurs. This triggers a life-threatening arrhythmia and often sudden death. This phenomenon is predominately seen in young, male athletes. We present a case in which ventricular fibrillation occurs in an older male athlete after blunt trauma.

Case Presentation: A patient with no known medical history was brought to the emergency department after being found unconscious secondary to ventricular fibrillation after a soccer ball kick to the chest. He was subsequently resuscitated on the soccer field. The patient was admitted to the hospital. Initial lab workup was significant for elevated troponin and lactate, which returned to normal levels. An echocardiogram showed global left ventricular systolic dysfunction with an estimated ejection fraction of 45–50%. Coronary angiography demonstrated nonobstructive coronary arteries. The patient was diagnosed with commotio cordis and discharged from the hospital in stable condition. Follow-up investigations included an echocardiogram which continued to demonstrate low ejection fraction and event monitor demonstrating frequent polymorphic ventricular tachycardia with periods of asystole.

Conclusion: This case is unique in that blunt trauma to the chest from a soccer ball immediately triggered ventricular fibrillation in a patient with a possible cardiomyopathy. It is possible that the blunt trauma caused primary commotio cordis that led to cardiomyopathy in a previously healthy man, or that an underlying cardiomyopathy made it more likely for this to occur. Increased awareness and prevention efforts of blunt chest trauma are required to reduce the associated life-threatening arrhythmias.

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Imipramine, Ulcerative Colitis and Linear Iga Bullous Dermatosis - A Curious Triad

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Introduction: Linear IgA bullous dermatosis (LABD) is a rare autoimmune subepithelial vesiculobullous phenomenon caused by IgA antibodies against skin or mucosal basement membrane antigens. Though most commonly idiopathic, known causes include medications and gastrointestinal diseases. We present a case of LABD associated with ulcerative colitis which was temporally associated with initiation of imipramine.

Case: 18 year old male presented to the ED for evaluation of a painful, blistering rash that began on his neck and spread over 24 hours. Patient had been started on Imipramine 2 weeks prior for nocturnal enuresis. On examination, the patient had diffuse annular arrangement of tender vesicles and bullae which progressively worsened to fluid-filled blisters on his extremities. Punch biopsies showed subepidermal blistering dermatosis with papillary dermal neutrophils compatible with dermatitis herpetiformis. The patient began to experience bloody stools, and colonoscopy revealed active ulcerative colitis. Subsequent immunofluorescence studies on the skin biopsy showed continuous strong IgA linear deposition along the basement membrane consistent with linear IgA bullous dermatosis.

Discussion: In this patient, the presentation of LABD could be a drug-induced dermatitis or an associated finding of ulcerative colitis; however, both are rare. It has been theorized that the pathogenesis of rheumatological conditions involves exposure to a trigger in a susceptible individual. The temporal association of the imipramine initiation suggests that the medication may have acted as the trigger for LABD development during this initial flare of UC. We therefore propose imipramine as a potential causative agent for the development of LABD in patients with IBD.

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Worsening Pericardial Effusion Despite Intensive Hemodialysis

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End-stage renal disease affects over 500,000 people living in the United States. Complications of end-stage renal disease can include pericarditis and pericardial effusion. Treatment for renal disease is dialysis, and the most common type of dialysis is hemodialysis. Some patients are able to successfully complete peritoneal dialysis at home, which is more convenient. However, patient compliance plays an important role in making sure peritoneal dialysis remains a successful treatment. Hemodialysis is associated with an increased risk of bleeding compared to peritoneal dialysis. In our case presentation, we discuss a 31 year old male developing a hemorrhagic pericardial effusion after undergoing an emergent transition from peritoneal dialysis to hemodialysis with heparin administration in the setting of worsening uremia during two separate hospital admissions less than one month apart. The patient had a pericardial effusion of 2.4 cm without tamponade physiology during his first admission, and upon the second admission the effusion grew to 5.75 cm with tamponade physiology. He had the fluid drained and showed significant clinical improvement. We will further discuss how urgent transition from peritoneal dialysis to hemodialysis with heparin use can worsen a hemorrhagic pericardial effusion.

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Mesenteric Mesothelial Cyst a Relatively Rare Complication of Peritoneal Dialysis and Intra-Abdominal Surgical Sequel, Case Presentation

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Introduction: Mesenteric mesothelial cysts are relatively rare intra-abdominal lesions that are often asymptomatic and can be multiple and variable in sizes even in the same individual. They are often identified incidentally on radiological studies for intra-abdominal symptoms. Some can be infected and show various inflammatory changes. We present a case of a patient with multiple cysts in which simultaneous sampling of different lesions yielded a sterile result and heavy growth of MRSA pointing to need for multiple sampling.

Case Presentation: A 33-year-old African American male with past medical history of ESRD post renal transplant currently on hemodialysis. Presented with shortness of breath, cough, mild abdominal discomfort. He reported missing last two hemodialysis session, vitals on presentation were only remarkable for hypertension (SBP156) and pulse of 102, on physical exam a positive JVD and HJR was noted with normal first and second heart sounds, S4 gallop noted. Abdomen was distended and a palpable mass in the epigastrium. Lab work was remarkable for Hgb 7.1, normal WBC, elevated procalcitonin, Cr of 10.88 and BUN of 50. Abdominal ultrasound showed 4 complex cystic lesions with loculation and septation of varying degrees, two in midline (epigastric) with one measuring 10.5 X 8.6X 9.2and another 2 in the left flank with largest measuring 15.4X 5.4 x 5.0. Bilateral atrophic native kidneys and transplanted kidney were noted. Aspiration of the midline epigastric lesion yielded 40cc of blood-tinged material with 257962 RBC, 318 nucleated cells, 20% lymphocytes, 28% neutrophils and mesothelial cells and core biopsy was unsuccessful while left upper quadrant cyst yielded 300cc of amber fluid with >25 WBC, many gram positive and heavy growth of MRSA. Intravenous Vancomycin was given with significant improvement of the culprit lesions on repeat CT abdomen. Abdominal ultrasound Abdominal CT.

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Discussion: Mesenteric mesothelial cysts can be located anywhere in the abdomen. They may result from trauma, lymphatic malformation or infection. Rare complications may include infection, obstruction, rupture or torsion. Presenting symptoms include abdominal pain, heaviness and other nonspecific symptoms. The cysts can be single, multiple, simple, loculated or septated and complex in character with varying sizes and can contain serous, bloody and chylous and infected materials. The exact etiology has never been fully elucidated but lymphatic drainage failure and inflammatory processes have been postulated. Imaging modalities include ultrasonography, computed tomographic studies and magnetic resonance imaging. Diagnostic aspiration studies help in tailoring treatment and while surgery is felt to be the gold standard for treatment, care must be exercised to avoid other organ perforation that may occur with adherent tissues. In this case, we believe that the cysts were complications of previous peritoneal dialysis treatments and peritonitis and recommend synchronous sampling of multiple cysts since benign and infected cysts can coexist.

Efficacy and Safety of Intravascular Lithotripsy in the Treatment of Calcified Peripheral Artery Disease: A Systematic Review and Meta-Analysis

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Introduction: Intravascular lithotripsy (IVL) is a novel endovascular calcified peripheral artery disease (PAD) therapy technique. Data regarding IVL clinical utility for PAD remain sparse. We aimed to evaluate the safety and efficacy of IVL in managing calcified PAD.

Methods: A comprehensive literature search (PubMed and Embase) through November 2020. Studies evaluating the clinical outcomes of IVL use in the management of calcified PAD. Primary outcomes: IVL delivery success rate, pooled mean of acute lumen gain, minimal lumen diameter (MLD), and residual stenosis. Secondary outcomes: 30- day major adverse effects (MAEs), (dissection, perforation, thrombus formation, and distal embolization rates).Meta-analyses were conducted using a random-effect model.

Results: 7 studies (503 patients; 605 lesions). IVL success rate=99.6% (95% CI: 0.991-1.002). Pooled mean acute lumen gain=2.745 mm (95% CI: 1.826-3.664). Minimal diameter (MLD)= 4.017 (95% CI: 2.910-5.123). Mean residual stenosis (MRS) = 21.737 mm (95% CI: 17.749-25.724).30-day MAE rate=0.018 (95% CI: -0.002-0.038), including dissection rate = 0.03 (95% CI: -0.003-0.047) and perforation rate = 0.004 (95% CI: -0.001-0.009). No studies reported embolization or thrombus formation.

Conclusion: IVL is an effective and safe technique in managing calcified PAD, achieving significant improvement of acute lumen gain and low 30-day MAEs. However, further studies with large sample sizes are needed to determine the long-term efficacy and safety of IVL in PAD.

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Steroid-unresponsive Immune-mediated Hepatitis Induced by Durvalumab: A Case Report

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Introduction: Lung cancer is the leading cause of cancer death in the United States. Durvalumab is a monoclonal antibody against programmed cell death ligand (PD-L1) and CD80 used for the treatment of stage III non-small cell lung cancer. Immune-mediated hepatitis is a common side effect of durvalumab, which is reported in 12% of patients. However, most durvalumab-induced hepatitis is mild and progression to severe (grade 4) immune-mediated hepatitis is rare and seen in only 0.4% of patients. Of these patients, only 1.7% required corticosteroids, and mycophenolate was required in 0.1%. We report a case of grade 4 immune-mediated hepatitis induced by durvalumab, which was unresponsive to high-dose corticosteroids and needed treatment with mycophenolate.

Case Presentation: A 78-year-old female with a history of lung adenocarcinoma presented with abnormal liver function tests on routine screening after two cycles of durvalumab. The patient reported jaundice, pale stools, dark-colored urine, and pruritus. On admission, her vitals were normal. Initial labs revealed a significant elevation in total bilirubin, alkaline phosphatase, alanine aminotransferase, and aspartate aminotransferase. She was started on high-dose steroids for grade 4 immune-mediated hepatitis. Initially, she showed temporary improvement on steroids but declined on day 2 of admission with an increase in total bilirubin and alkaline phosphatase. Mycophenolate was added on day 4, and magnetic resonance cholangiopancreatography was done and ruled out obstruction. The administration of mycophenolate provided a gradual improvement of hepatitis. However, on day 6, a sharp decline in her pulmonary function prompted a transfer to the intensive care unit (ICU) for acute respiratory failure, which was likely secondary to immunotherapy. On day 9, the patient elected to withdraw her treatment and be admitted to hospice.

Conclusion: We describe a rare case of steroid-unresponsive severe immune-mediated hepatitis induced by durvalumab. As the use of durvalumab is rising following FDA approval, physician cognizance of immune-mediated hepatitis induced by durvalumab is important. This requires careful monitoring of liver function tests in cancer patients on immune checkpoint inhibitors such as durvalumab, and demonstration of acute liver injury should be evaluated and managed promptly.

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Steroid-unresponsive Immune-mediated Hepatitis Induced by Durvalumab: A Case Report

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Introduction: Lung cancer is the leading cause of cancer death in the United States. Durvalumab is a monoclonal antibody against programmed cell death ligand (PD-L1) and CD80 used for the treatment of stage III non-small cell lung cancer. Immune-mediated hepatitis is a common side effect of durvalumab, which is reported in 12% of patients. However, most durvalumab-induced hepatitis is mild and progression to severe (grade 4) immune-mediated hepatitis is rare and seen in only 0.4% of patients. Of these patients, only 1.7% required corticosteroids, and mycophenolate was required in 0.1%. We report a case of grade 4 immune-mediated hepatitis induced by durvalumab, which was unresponsive to high-dose corticosteroids and needed treatment with mycophenolate.

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Conclusion: We describe a rare case of steroid-unresponsive severe immune-mediated hepatitis induced by durvalumab. As the use of durvalumab is rising following FDA approval, physician cognizance of immune-mediated hepatitis induced by durvalumab is important. This requires careful monitoring of liver function tests in cancer patients on immune checkpoint inhibitors such as durvalumab, and demonstration of acute liver injury should be evaluated and managed promptly.

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Racial Differences in Hypercholesterolemia Prevalence: A Cross-sectional Study Using 2017-2018 National Health and Nutrition Examination Survey Data

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Introduction: African Americans (AA) have a 20% higher risk of CVD death than Whites. Treating hypercholesterolemia (HCL) is paramount in CVD primary prevention. Some evidence showed that AA have a lower risk of HCL compared to whites.

Methods: A cross-sectional study using the 2017-18 National Health and Nutrition Examination Survey data. Logistic regression analysis was used to compare the prevalence of diagnosed HCL in AA and whites aged 18-80 years old. Serum total cholesterol (TC) and high-density lipoprotein (HDL) levels were compared by multiple linear regression.

Results: Among 2549 participants, 51.7% were females, and 63.4% were white. The mean (SD) age was 51.6 (19.1) years. AA had a 24 % reduced risk of HCL diagnosis than whites after adjusting for age, Body Mass Index (BMI), diabetes, hypertension, and smoking; OR [95%CI]= 0.767 [0.621, 0.923]. There was no difference in TC level ($p=0.7242$), while HDL was higher among AA ($p<0.0001$, $\beta=3.83$), adjusting for age, gender, BMI, smoking, diabetes, education level, and use of cholesterol medications.

Conclusion: Consistent with some evidence, AA had a lower prevalence of HCL diagnosis and higher HDL levels.

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The Rate of Adverse Events of Sodium-Glucose Cotransporter 2 Inhibitors: A Meta-Analysis of Randomized Clinical Trials

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Introduction: Sodium-glucose cotransporter 2 (SGLT2) inhibitors have proven cardiovascular benefits in diabetics and in patients with heart failure in the presence or absence of diabetes. We sought to assess the rate of adverse events with the use of SGLT2 inhibitors compared to placebo.

Methods: We included all randomized, double-blinded, placebo-controlled trials of SGLT2 inhibitors regardless of the indication. Data were pooled using the Mantel-Haenszel random-effects model to calculate the relative risk (RR) and 95% confidence interval (CI).

Results: We included a total of 62 trial comprising 95,594 patients (55,739 patients in the SGLT2 arm and 39,855 patients in the placebo arm). Compared to placebo, use of SGLT2 inhibitors was associated with a statistically significant increased rate of overall infections (9.6% vs. 5.7%, RR: 1.28, 95% CI: 1.18 - 1.40), and diabetic ketoacidosis (0.2% vs. 0.08%, RR: 2.7, 95% CI: 1.62 - 4.50). The increased rate of overall infections was primarily driven by higher rates of genital infections (3.6% vs. 0.7%, RR: 3.23, 95% CI: 2.73 - 3.82). The rates of hypoglycemia, bone fracture and amputation were not significantly different between both treatment arms (10.0% vs. 7.3%, RR: 1.06, 95% CI: 0.98 - 1.14), (3.6% vs. 3.6%, RR: 1.02, 95% CI: 0.94 - 1.10), and (1.5% vs. 1.3%, RR: 1.09, 95% CI: 0.94 - 1.27), respectively.

Conclusion: SGLT2 inhibitors increase the risk of diabetic ketoacidosis and genital infections. The overall rate of diabetic ketoacidosis was, however, low.

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Knowledge, Attitude and Practices of Women Towards Breast Cancer in Arbaji Village, Gezira State, Sudan

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Introduction: Breast cancer is a worldwide disease resulting in many deaths. Although breast cancer incidence is lower in Sub-Saharan African countries than in developed countries, African women are more likely be diagnosed at later stages and are more likely to die from it. This is due to the lack of awareness, and accessibility to screening methods. The aim was to assess the knowledge, attitude, and practice towards early breast cancer detection tools.

Material and Methods: This community-based cross-sectional study was conducted in Arbaji village, Sudan. The sample included 80 women aged between 15-90 years, samples were taken from females above 15 who came to the rural hospital's outpatient. Data were collected using a self-administrative questionnaire (34 Questions) and analyzed using SPSS.

Results: About (20%) of the participant had family history of Breast cancer. The knowledge of Breast Cancer was (90%), while knowledge of Self-examination and Clinical breast examination was (43% and 81%) respectively, while less than (8.8 %) heard about Mammography. Regarding the practice, only (16.3%) practice Breast Self-examination, and none of them ever had a mammography. (5%) discovered an abnormality on Breast self-examination, all of them went to the doctor.

Conclusion: Rural women have poor knowledge about breast cancer early detection tools, Breast self-examination is hardly practiced, though the willing to learn is high. It is important to increase awareness about Breast Cancer early detection methods in the community through health education campaigns and screening programs. This would have an overall positive impact on reducing the disease burden.

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Full Thickness Versus Circular Peroral Myotomy in the Treatment of Esophageal Achalasia: A Systematic Review and Meta-Analysis

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Introduction: Peroral endoscopic myotomy (POEM) is an effective procedure that is used to treat esophageal achalasia. Early studies recommended a circular myotomy where the circular muscle layer is cut with preservation of the longitudinal layer. Recent studies have investigated full thickness myotomy as a possible alternative.

Methods: We performed a comprehensive search in the databases of PubMed/MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials from inception through April 20th, 2022. We considered only randomized controlled trials. The primary outcome was clinical success. The secondary outcomes were the occurrence of subcutaneous emphysema and post-procedure reflux symptoms. The random-effects model was used to calculate the risk ratios (RR), mean differences (MD), and confidence intervals (CI). A p value <0.05 was considered statistically significant.

Results: Six randomized controlled trials involving 774 patients were included in the meta-analysis. The rate of clinical success was not statistically different between the two groups (RR 1.02, 95% CI 0.98-1.06, p = 0.45, I2 = 0%) (Figure 1a). The rate of subcutaneous emphysema was significantly lower in the full thickness group (RR 0.62, 95% CI 0.43-0.89, p = 0.01, I2 = 0%) (Figure 1b). The rate of post-procedure reflux symptoms was not statistically different between the two groups (RR 1.10, 95% CI 0.60-2.02, p = 0.75, I2 = 22%).

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Discussion: Our meta-analysis demonstrated that clinical success and the post-procedure reflux symptoms were both not statistically different between full thickness and circular PEOM. However, subcutaneous emphysema was significantly lower in the full thickness myotomy group.

The Role of Tranexamic Acid Use in Reducing Mortality in Acute Upper GI Bleeding: A Systemic Review and Meta-analysis

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Introduction: Tranexamic acid (TXA) prevents fibrinolysis and is utilized in surgical setting to prevent trauma bleeding. The use of TXA in acute UGIB has been evaluated in numerous studies but without conclusive evidence on its mortality benefits.

Methods: We performed a comprehensive search of the databases: PubMed/MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials from inception through May 15th, 2022. We considered only randomized controlled trials. The primary outcome was the all-cause of mortality rate. The secondary outcomes were the refractory bleeding and the need of endoscopic intervention. The random-effects model was used to calculate the risk ratios (RR) and 95% confidence intervals (CI). A p value <0.05 was considered statistically significant.

Results: Twelve randomized controlled trials involving 14,100 patients were included in the meta-analysis. The mortality rate which was significantly lower in patients who received TXA (4.6% vs 5.3%, RR 0.73, 95% CI 0.58-0.93, p=0.01, I2 = 17%) (Figure 1a). The rate of refractory bleeding was also lower in the same group (10.6% vs 21.1%, RR 0.57, 95% CI 0.37-0.87, p =0.009, I2 = 43%) (Figure 1b). There was no statistical difference in the rate of requiring endoscopic intervention (40.3% vs 42.5%, RR 0.95, 95% CI 0.75-1.20, p =0.67, I2 =23%) (Figure 1c).

Discussion: Our meta-analysis demonstrated that the all-cause mortality rate was significantly lower in the patients with acute UGIB who received TXA. Moreover, the rate of refractory UGIB was lower in patients who were given TXA. TXA maybe utilized clinically in patients presenting with UGIB.

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A case of Extra Mammary Paget's disease in a Geriatric Patient

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Background: Paget's disease is a rare form of adenocarcinoma of the breast. It involves apocrine gland-bearing skin that presents as a slowly expanding well-defined patch. It presents as an erythematous plaque on apocrine gland bearing areas including vulva, perineum, perianal region, scrotum, and penis. EMPD is a marginated plaque resembling Paget's disease and is very rare. We present a case with biopsy-proven EMPD in the left inguinal area which is an unusual area.

Case Report: A 67-year-old male with a history of renal cell cancer status post left nephrectomy, diabetes, HTN and COPD presented with complaint of fatigue and 40 Ibs weight loss in 2 months. On physical examination, a suspicious erythematous plaque on his left inguinal region is noted. According to the patient, this lesion was present for several months and had recently increased in size. Skin biopsy was done that suggested invasive adenocarcinoma with pagetoid epidermal involvement of peripheral and deep margins. Surgery was consulted and a wide local excision of the left groin with sentinel lymph node biopsy was performed. The biopsy was positive for malignant cells. The patient is diagnosed with cutaneous invasive adenocarcinoma. Based on Ohara et al, his staging was pT1N1M0, stage IIIa. The patient underwent lymph node dissection. He was referred to medical oncology for discussion of the benefits and risks of systemic chemotherapy. Underlying malignancy was ruled out based on whole-body enhanced CT and colonoscopy. Since the patient was cancer free pathologically, it was recommended that he undergo routine follow-up every 6 months for 5 years postoperatively for surveillance.

Conclusion: EMPD is considered an adenocarcinoma originating from the skin or skin appendages in areas with apocrine glands. The primary location is the vulvar area, followed by the perianal region, scrotum, penis and axillae. Commonly confined to the epidermis, EMPD can be invasive, associated with contiguous extension or upward pagetoid spread of underlying malignancy or with distant synchronous malignancy. Because of its association with other cancers, formal evaluation is warranted. Surgical excision remains the mainstay of treatment. Conventional chemotherapies have been used for the treatment in patients with distant metastases, but the efficacy is not satisfactory, and the prognosis for such patients is poor.

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Typical Imaging Findings Of TB in an Old Patient with IPF

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Introduction: The diagnosis of pulmonary TB should be suspected in patients with relevant clinical manifestations and epidemiologic factors, history of TB infection, known or possible TB exposure, past or present residence in or travel to an endemic area. Older patients aged 65 years or more had fewer "classical" clinical and radiological presentations of TB. Idiopathic pulmonary fibrosis (IPF) is a progressive fibrotic lung disease without a clear etiology. TB in IPF subjects has also been shown to be difficult to diagnose and the typical locations of reactivated PTB has been shown to be significantly less often involved in the IPF group. We present a geriatric patient with IPF which had delay in diagnosis of TB due to atypical imaging findings for TB.

Case Report: A 76-year-old southeast Asian male, immigrated to the USA more than 20 years ago with PMH of IPF presented with SOB, cough, fever and weight loss. At the first office visit, xray was obtained which showed left upper lobe infiltrate. The patient started on antibiotic for community acquired pneumonia, symptoms did not improve and at the second office visit, chest CT scan obtained which showed consolidation in left upper lobe, treatment continued for CAP. After the 3rd visit the patient admitted to the hospital, chest CT scan again showed consolidation concerning for pneumonia and evidence of usual interstitial pneumonia suggestive of IPF. Treatment continued for CAP. He was discharged and readmitted to another hospital due to the worsening of his symptoms, persistent cough and episode of hemoptysis. Bronchoscopy and BAL were done. AFB culture was positive x3 for Mycobacterium tuberculosis complex and MTB PCR was detected. The patient was started on the four drug TB regimen.

Conclusion: The global population is ageing quickly and our understanding of age-related changes in the immune system suggest that the elderly will have less immunological protection from active TB. TB in the elderly presents with fewer of the classical symptoms of TB and less specific radiological changes than in younger patients. The atypical manifestation of pulmonary TB is also common in patients with IPF. Anchoring bias may lead to delay in TB diagnosis, especially with atypical clinical presentations and imaging findings for TB.

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A Case of Acute Myopericarditis in a Patient with Human Metapneumovirus (hMPV) Respiratory Infection

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Human metapneumovirus (hMPV), a relatively newly isolated virus, has emerged as one of the most common pathogens implicated in respiratory tract infections worldwide. Although very rare, myocarditis has also been associated with this viral infection. A 36-year-old male with type 2 diabetes and essential hypertension presented to the emergency room with one-day chest pain and persistent cough for 3 weeks. His chest pain was pleuritic, alleviated by sitting up. He was hemodynamically stable and physical examination was unremarkable except for lower extremity edema. Troponin and EKG were unremarkable. BNP was elevated at 308 pg/mL, and D-dimer was high at 0.8 mcg/mL. ESR and CRP were both elevated at 16 mm/hr and 79.6 mg/L respectively. CT angiography of the chest revealed tree-in-bud like opacities in the left upper lobe and ground-glass opacities in the right lung. TTE revealed diffuse global hypokinesis and an ejection fraction of 30-35%. Cardiac MRI showed diffuse hypokinesia and myopericarditis. Infectious workup was only positive for hMPV on respiratory pathogen panel (RPP). The patient was diagnosed with hMPV pneumonia, complicated by acute myopericarditis and new onset systolic heart failure. He was treated with ibuprofen and colchicine, and guideline-directed medical therapy for systolic heart failure. With the rising popularity of RPP tests in recent years, the increasing detection of hMPV infections will shed more light on its association with myopericarditis. hMPV is ubiquitous and this case highlights the importance of recognizing the cardiovascular effect of the virus, especially in patients with respiratory tract infection symptoms.

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The Efficacy of Cardiac Myosin Inhibitors Versus Placebo in Patients with Symptomatic Hypertrophic Cardiomyopathy

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Introduction: Given the interplay between hypertrophic cardiomyopathy, elevated resting LVOT gradients (≥ 50 mm Hg) and heart failure and cardiovascular death, cardiac myosin inhibitors have recently emerged as a promising novel therapy to improve HCM-related outcomes by regulating myocardial relaxation and contractility, and thereby reducing intracavitary gradients.

Methods: We performed a literature search using PubMed, Embase, and Cochrane Library from inception through May 2022 to assess the impact of novel cardiac myosin inhibitors (Mavacamten and Aficamten) on LVOT gradient and functional capacity in patients with symptomatic hypertrophic cardiomyopathy. The co-primary outcomes were mean percent change from baseline in resting LVOT gradient, Valsalva LVOT gradient, and NYHA Class Improvement ≥ 1. Secondary outcomes included mean percent change from baseline NT ProBNP, Troponin I, and LVEF.

Results: 4 studies (all randomized-control trials, including 3 Mavacamten-focused and 1 Aficamten-focused trials) involving 463 patients were included in the meta-analysis. Compared to patients receiving placebo, the cardiac myosin inhibitor group demonstrated statistically significant differences in percent change in mean resting LVOT gradient (MD -62.48, CI -65.44, -59.51, p <0.00001), Valsalva LVOT gradient (MD -54.21, CI -66.05, -42.36, p <0.00001), and mean percentage in NYHA Class Improvement ≥ 1 (OR 3.43, CI 1.90, 6.20, p <0.0001). Regarding secondary outcomes, the intervention group demonstrated statistically significant reductions in meant percent change from baseline in NT-proBNP (MD -69.41, CI-87.06, -51.75, p < 0.00001), Troponin I (MD, -44.19, CI -50.59, -37.78, p < 0.00001), and LVEF (MD -6.31, CI -10.35, -2.27, p = 0.002).

Conclusion: The use of cardiac myosin inhibitors in patients with symptomatic hypertrophic cardiomyopathy may confer both clinical and symptomatic benefits, at the possible expense of LV ejection fraction. Further trials with large sample sizes are needed to confirm our findings.

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The Impact of Sacubitril / Valsartan Versus ACE/ARB Therapy on Functional Capacity in Heart Failure with Preserved Ejection Fraction

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Background: The availability of pharmacological therapies producing a symptomatic benefit on patients with heart failure with preserved ejection fraction remains limited. Given prior evidence suggesting the efficacy of Angiotensin Receptor Neprilysin Inhibitors (ARNIs) in reducing cardiovascular mortality and CHF-related hospitalizations, as well as noted correlation between subjective, patient-oriented measures and objective outcomes (for example, medication compliance derived from perceived symptomatic benefit), we sought to investigate the effect of ARNIs on exercise capacity in a patient-defined manner.

Methods: We performed a literature search using PubMed, Embase, and Cochrane Library from inception through May 2022 to assess the impact of Sacubitril/Valsartan versus ACE/ARB therapy on physical activity tolerance in patients with heart failure with preserved ejection fraction. The co-primary outcomes were mean percent change in NYHA Class Improvement ≥ 1 from baseline and mean change in KCCQ-CSS scores from baseline.

Results: 2 studies (both randomized control trials) involving 7394 patients were included in the meta-analysis. Compared to patients receiving ACE/ARB therapy, the ARNI group showed no statistically significant difference in either mean percent change in NYHA Class Improvement ≥ 1 from baseline (OR 1.10, CI 0.88, 1.37, p =0.40) or mean change in KCCQ-CSS scores from baseline (MD 0.25, CI -1.22, 1.72, p =0.74).

Conclusion: The use of ARNI compared to ACE/ARBs confers no statistically significant improvement in functional capacity in patients with heart failure with preserved ejection fraction. Further trials with large sample sizes are needed to confirm our findings.

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The Impact of Sacubitril / Valsartan Versus ACE/ARB Therapy on Functional Capacity in Heart Failure with Reduced Ejection Fraction

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Introduction: Angiotensin Receptor Neprilysin Inhibitors (ARNI) have emerged as a promising pharmacological therapy with heart failure-related hospitalization and mortality benefits in patients with heart failure with reduced ejection fraction. Given the correlation between subjective, patient-oriented measures and objective outcomes (for example, perceived symptomatic benefits promoting medication compliance), we sought to investigate the effect of ARNIs on exercise capacity in a patient-defined manner.

Methods: We performed a literature search using PubMed, Embase, and Cochrane Library from inception through May 2022 to assess the impact of Sacubitril/Valsartan versus ACE therapy on physical activity tolerance in patients with heart failure with reduced ejection fraction. The co-primary outcomes were change from baseline mean KCCQ-23 scores and the 6-minute walk test (6MWT).

Results: 2 studies (both randomized control trials) involving 8539 patients were included in the meta-analysis. Compared to patients receiving ACE therapy, the ARNI group showed no statistically significant difference in either change from mean baseline KCCQ-23 scores (MD 4.23, CI, -0.88, 0.93, p =0.10) or the 6MWT (MD 2.09, CI -11.60, 15.79, p = 0.76).

Conclusion: The use of ARNI compared to standard ACE therapy confers no statistically significant improvement in functional capacity in patients with heart failure with reduced ejection fraction. Further trials with large sample sizes are needed to confirm our findings.

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Efficacy and Safety of Insulin Icodec Versus Glargine U100- A meta-analysis of randomized controlled trials

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Background: Insulin Icodec is a once-weekly basal ultra-long-acting insulin that is currently in development.

Methods: We conducted a meta-analysis of randomized controlled trials that investigated the efficacy and safety of insulin icodec compared to glargine U100. From each clinical trial, we collected the number of patients who received icodec insulin and glargine U100. The primary outcome was change in hemoglobin A1C (HBA1C) from baseline. Secondary outcomes included percent of time in range (TIR) of blood glucose (3.9-10.0 mmol/L or 70-180 mg/dL) measured via continuous glucose monitoring during weeks 15 and 16 as well as occurrence of hypoglycemic episodes during treatment. The random-effects model was used to calculate the risk ratios (RR), mean differences (MD), and confidence intervals (CI). A p-value <0.05 was considered statistically significant.

Results: Three randomized controlled trials involving 552 patients with type 2 diabetes were included in the meta-analysis. The difference in change in HBA1C between the icodec and glargine U100 groups was not statistically significant (Standard difference in means: -0.068, 95% CI: -0.388, 0.253, P-value=0.679, I2=67%). Furthermore, TIR percentage was comparable between the two groups (RR: 1.04, 95% CI: 0.898, 1.206: P-value=0.593, I2=0%). However, treatment with icodec was associated with lower risk of combined level 2 (< 3 mmol/L or < 54 mg/dL) and 3 (severe) hypoglycemia (RR: 0.69, 95% CI: 0.674, 0.713: P-value <0.05, I2=99.9%)

Conclusion: Our meta-analysis demonstrated that in comparison to once daily insulin glargine U100, once weekly treatment with insulin icodec had similar glucose lowering efficacy but a better safety profile.

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Characterization of the Novel IQGAP1-Adrenergic Receptor Pathway in Lung Cancer

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Lung cancer is the leading cause of cancer death for both men and women making up almost a quarter of all cancer-related death in the United States. The IQ-motif containing Ras GTPase-activating-like (IQGAP1) protein is a ubiquitously expressed protein in humans. IQGAP1 is a signaling scaffold involved in regulating various cellular functions ranging from organization of the actin cytoskeleton, transcription, and cellular adhesion to regulating the cell cycle and secretion. Chronic activation or inhibition of IQGAP1 both leads to a myriad of diseases, including cancer and diabetes. We employ a pharmacogenetic approach to define mechanisms of IQGAP1 in such diseases and identify potential therapeutics. Our studies revealed that yeast cells lacking IQGAP1, the homolog of human IQGAP1, had diminished cell growth when treated with norepinephrine (NE), suggesting that NE works through IQGAP1. The Alpha-2A-Adrenergic receptor (α-2ADR) is a known target of NE that we recently found differentially expressed in various lung cancer cell lines and interacts with IQGAP1. To begin characterizing this pathway, we determined dose effect of NE on proliferation of human lung cancer cells and identified an optimal dose (IC50) of NE. Next, we evaluated the effect of that dose on the gene expression levels of the two proteins and a downstream transcription factor, Nuclear Respiratory Factor 1 (NRF1), comparing response of lung cancer cells with normal lung epithelia by qRT-PCR. Our results showed that while NE significantly downregulated the α -2ADR mRNA in normal cells, it caused a slight increase in some cancer cells. Our ongoing research will examine the effect of NE on protein levels and localizations in lung cancer and IQGAP1 mutant cells, as well as on the activity of signaling components downstream of IQGAP1. Our findings have significance in precision medicine.

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Characterization of the Novel IQGAP1-Adrenergic Receptor Pathway in Lung Cancer

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Lung cancer is the leading cause of cancer death for both men and women making up almost a quarter of all cancer-related death in the United States. The IQ-motif containing Ras GTPase-activating-like (IQGAP1) protein is a ubiquitously expressed protein in humans. IQGAP1 is a signaling scaffold involved in regulating various cellular functions ranging from organization of the actin cytoskeleton, transcription, and cellular adhesion to regulating the cell cycle and secretion. Chronic activation or inhibition of IQGAP1 both leads to a myriad of diseases, including cancer and diabetes. We employ a pharmacogenetic approach to define mechanisms of IQGAP1 in such diseases and identify potential therapeutics. Our studies revealed that yeast cells lacking IQGAP1, the homolog of human IQGAP1, had diminished cell growth when treated with norepinephrine (NE), suggesting that NE works through IQGAP1. The Alpha-2A-Adrenergic receptor (α-2ADR) is a known target of NE that we recently found differentially expressed in various lung cancer cell lines and interacts with IQGAP1. To begin characterizing this pathway, we determined dose effect of NE on proliferation of human lung cancer cells and identified an optimal dose (IC50) of NE. Next, we evaluated the effect of that dose on the gene expression levels of the two proteins and a downstream transcription factor, Nuclear Respiratory Factor 1 (NRF1), comparing response of lung cancer cells with normal lung epithelia by qRT-PCR. Our results showed that while NE significantly downregulated the α -2ADR mRNA in normal cells, it caused a slight increase in some cancer cells. Our ongoing research will examine the effect of NE on protein levels and localizations in lung cancer and IQGAP1 mutant cells, as well as on the activity of signaling components downstream of IQGAP1. Our findings have significance in precision medicine.

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Hepatic Arterial Infusion Chemotherapy versus Trans-arterial Chemoembolization in Unresectable Hepatocellular Carcinoma: A Systematic Review and Meta-Analysis

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Introduction: Trans-arterial chemoembolization (TACE) has been one of the standard options for patients with unresectable hepatocellular carcinoma (HCC). Recent studies have shown that liver arterial infusion chemotherapy (HAIC) has favorable outcomes in these patients, but its use has been limited due to the need for technical expertise. In this systematic review and meta-analysis, we compared the efficacy and safety of HAIC vs. TACE for unresectable HCC.

Methods: We performed a comprehensive literature search of PubMed, Embase, and Cochrane databases through January 12, 2022, for all peer-reviewed studies that compared the outcomes of HAIC vs. TACE in patients with large, unresectable HCC. Our primary outcomes were the objective response rate (ORR), disease control rate (DCR), and progressive disease (PD). The secondary outcomes were overall survival (OS), progression-free survival (PFS), and grade ≥3 adverse events (AEs). Pooled risk ratio (RR) and hazard ratio (HR) with the corresponding 95% confidence intervals (CIs) were obtained by the Mantel-Haenszel method within a random-effect model. Heterogeneity was assessed using the Higgins I2 index.

Results: Six studies (one randomized controlled trial [RCT], two non-randomized trials, and three retrospective cohort studies) were eligible for final analysis. A total of 899 patients were included for the final evaluation. HAIC was associated with significantly higher ORR (RR 2.70, 95% CI 2.06-3.55, P<0.001, I2=10.1%) and DCR (RR 1.42, 95% CI 1.19-1.70, P<0.001, I2=54.5%) and substantially reduced PD (RR 0.55, 95% CI 0.40-0.75, P<0.001, I2=56.6%) compared to TACE. The median OS was significantly longer in the HAIC group, ranging from 11.4 to 23.1 months vs. TACE, ranging from 4 to 16.1 months (HR 0.49, 95% CI 0.28-0.85, P=0.01 I2=84.7%). The median PFS was significantly longer in the HAIC group, ranging from 5.5 to 9.6 months, vs. TACE, ranging from 1.5 to 5.4 months (HR 0.45, 95% CI 0.26-0.79, P=0.001, I2=84.6%). Notably, the incidence of grade≥3 AEs was lower in the HAIC group than in TACE (RR 0.61, 95% CI 0.47-0.80, P<0.001, I2=16.4%).

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Conclusion: Compared to TACE, HAIC significantly improved ORR, DCR, and OS in unresectable HCC with a significantly better safety profile. However, our meta-analysis is hampered by the limited number of studies. Future large-scale multicenter RCTs are warranted to further evaluate the outcomes of HAIC vs. TACE in the management of unresectable HCC.

Probing Dynamics of 14-3-3: A Potential Remedy for Pancreatic Cancer

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Introduction: Pancreatic cancer is the third-most-common cause of cancer-related deaths in the U.S. Drug development for pancreatic cancer has greatly advanced over the past decade. However, chemoresistance exacerbates challenges in improving the efficacy of the current treatment regimens. 14-3-3 is a small, homo-dimeric, regulatory protein, mostly expressed in epithelial cells. It promotes cancer metastasis, confers resistance to anticancer drugs and radiation, and increases cell cycle arrest upon DNA damage. Overexpression of 14-3-3 is correlated with a poor survival rate among pancreatic cancer patients. 14-3-3, therefore, is a potential anticancer target for the treatment of pancreatic cancer. It belongs to the 14-3-3-protein family with other six isoforms involved in diverse cellular pathways. The discovery and development of 14-3-3-isoform-selective inhibitors are indispensable because of the pan-inhibitory nature of currently available inhibitors of 14-3-3 isoforms.

Methods: Molecular Dynamics Simulation and Biological Small-angle X-ray scattering were used to study protein dynamics of 14-3-3- isoforms.

Results: We found potential differences in conformational states between 14-3-3-isoforms when unbound by a ligand and similarities in bound states. Unbound 14-3-3 displayed unique, wide-open conformation i.e. significant flexibility, in comparison to other unbound isoforms. Principal Component Analysis captured a highly, flexible loop region between Helices 3 and 4 which could play an important role in regulating the open-close conformational change in 14-3-3-isoforms.

Conclusion: Our study revealed that the dynamics are not conserved among 14-3-3 isoforms and this promising finding could lead to the development and discovery of 14-3-3-isoform-selective inhibitors for pancreatic cancer.

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The Dominant Negative IQGAP1(IR-WW) Domain as a Potential Therapy in Brain Cancer

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Glioblastoma is a lethal brain tumor that currently has no effective treatment due to a lack of therapeutic targets. IQGAP1 is an oncoprotein that normally acts as a signaling scaffold that regulates diverse cellular functions which underlie cell dynamics, architecture, and proliferation. Genetic mutant analysis in breast cancer cells has shown that the various domains of IQGAP1 have distinct effects on cell proliferation. IQGAP1 is localized to the centrosome, and phosphorylation-cycling of IQGAP1 is important for its subcellular localization as well as its nucleocytoplasmic shuttling that regulates its role in cytokinesis. Research in our lab showed that expression of the dominant- negative (unphosphorylated) IQGAP1IR-WW fragment arrests cytokinesis and can serve as basis for potential future therapy in cancer. Our experiment tested this hypothesis in brain cancer cell lines.

Preliminary results showed that the overexpression of IQGAP1IR-WW in glioblastoma cells decreased cell proliferation and led to multinucleated cells. These results are consistent with our previous findings in cervical cancer cells and present IQGAP1 as a clinical target in oncology.

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Predictors of 6-Month Mortality in Hospitalized COVID-19 Patients, A Single-Institution Study

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Background: Much of the data relating to post-acute COVID-19 infection morbidity and mortality risk is ninety-day data; however, less is known about longer term outcomes of mortality.

Objectives: Our objective is to determine predictors of 6-month mortality on admission in hospitalized COVID-19 patients.

Methods: This is a single-institution, retrospective study. We included patients hospitalized with COVID-19 from University of Toledo Medical Center in Toledo, Ohio who were admitted within the timeframe of March 20,2020 to June 30, 2021. Two groups were created based on the mortality outcome at 6 months from COVID-19 positive testing: survivors and non-survivors. The clinical variables or outcomes and laboratory values were compared using non-parametric methods due to the small sample size and non-normality of the data. Either the Mann-Whitney U-test for continuous variables or the Fisher's exact test for categorical variables was used for statistical analysis.

Results: Lactate dehydrogenase (LDH) (p=0.032) and D-dimer levels (p=0.019) were significantly higher in non-survivors on admission than in survivors. Demographic factors, comorbid conditions, and other laboratory data did not differ significantly between survivors and non-survivors.

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Conclusion: Increased LDH and D-dimer levels on admission were found to predict 6-month mortality in hospitalized COVID-19 patients.

Immune Checkpoint Inhibitor Induced Hepatitis Injury: Risk Factors, Outcomes, and Impact on Survival

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Purpose: Immune checkpoint inhibitors (ICIs) are associated with a unique set of immune-related adverse events (irAEs). Few studies have evaluated risk factors and outcomes of patients who develop ICI-induced hepatitis (ICIH).

Methods: We utilized an institutional database of patients with advanced cancers treated with ICI to identify patients with ICIH. irAEs were graded using the Common Terminology Criteria for Adverse Events v4. Overall survival (OS) was calculated from the date of ICI to death from any cause or the date of the last follow-up. OS with 95% confidence intervals were estimated using the Kaplan–Meier method and stratified by occurrence of ICIH.

Results: We identified 1,096 patients treated with ICI . The most common ICIs were PD1/L1 (n=774) and CTLA-4 inhibitors (n=195). ICIH occurred among 64 (6%) patients: severity was < grade 3 in 30 and ≥ grade 3 in 24 patients (3.1% overall). Median time to ICIH was 63 days. ICIH was more frequent in women (p=0.038), in patients treated with combination ICIs (p<0.001), and when given as first line therapy (p=0.018). Occurrence of ICIH was associated with significantly longer OS, median 37.0 months (95% CI 21.4, NR) compared to 11.3 months (95% CI 10, 13, p<0.001); there was no difference in OS between patients with ≥ grade 3 ICIH vs grade 1-2.

Conclusion: Female sex, combination immunotherapy, and first line of immunotherapy were associated with ICIH. Patients with ICIH had improved clinical survival compared to those that did not develop ICIH.

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The Effects of the Chemotherapy Drug Cisplatin on Cell Migration

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Cell migration is an essential function of all living cells. In mammalian cells, cell migration plays a crucial role such as promoting organ development, sperm and egg motility, and wound healing. However, in cancer, cell migration promotes metastasis, which is the primary cause of cancer patient mortality. The mechanisms that underlie cell promotion are emerging. Our research displayed that the scaffold oncoprotein IQGAP1 normally regulates cell migration by controlling kidney epithelial cell adhesion. Thirty percent of cancer patients treated with chemotherapy develop acute kidney injury, but the mechanism underlying this fatal condition is unknown. We hypothesized that chemotherapy drugs displace IQGAP1 from cell junctions and increase cell migration and dissociation of renal cells. Using wound healing assays and the model Madin-Darby Canine kidney cells (MDCK), we evaluated the effects of the standard-of-care chemotherapy drug cisplatin on cell migration.

Our results illustrated that cisplatin significantly inhibited cell migration. These results are also consistent with our findings that cisplatin inhibits cell proliferation. Furthermore, cisplatin leads to treatment-resistant kidney cell injury. Therefore, this data paves the way for our ongoing studies on the role of IQGAP1 as a target of cisplatin.

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Immunotherapeutic Interventions in Carcinoid Tumors

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Introduction: Management of carcinoid tumors consists of pharmacological treatment and surgical resection. Pharmacologic treatments have side effects and are often limited in their scope. Though surgical intervention can be curative, carcinoid tumors are asymptomatic and are not detected until they metastasize. Immunotherapy has the potential to overcome the limitations both surgical and pharmacologic options face. Active and passive immunotherapeutic options for treatment of carcinoid tumors are summarized here.

Methods: A PubMed search was conducted yielding studies focused on carcinoid tumor characteristics, standards of care, and immunotherapeutic approaches. Carcinoid tumor immunotherapy clinical trial results and other relevant data was extracted from each study.

Results: The search yielded 16 studies encompassing 6 immunotherapies. Two studies reported overall response rates (ORR) to combined ipilimumab-nivolumab as 25% and 26%. ORR to pembrolizumab monotherapy was reported by two studies as 3.7% and 12%. Pembrolizumab combined with lanreotide produced stable disease in 40% of patients. Spartalizumab ORR was 7.4%. Lu-Dotatate ORR was 14.7% with 65.2% progression-free survival after 20 months. Tidutamab achieved stable disease in 27% of patients. AdVince was tumoricidal to 100% of resected metastatic carcinoid tumor cells and delayed subcutaneous carcinoid tumor growth in mice.

Conclusion: All immunotherapeutic agents achieved significant antitumor activity defined by their respective studies, with the exception of spartalizumab. However, immunotherapy demonstrated limited benefit as a monotherapy to carcinoid tumor management. Treatment related-adverse events may require future monitoring and evaluation. Further investigation is warranted to assess immunotherapy efficacy as an adjunct to chemotherapy and surgical resection.

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Glioblastoma in Pregnant Patient with Pathologic and Exogenous Sex Hormone Exposure and Family History of High-Grade Glioma

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Introduction: Glioblastoma (GBM) incidence is higher in males, suggesting sex hormones may influence GBM tumorigenesis. Patients with GBM and altered sex hormone states could offer insight into a relationship between the two. Most GBMs arise sporadically, but reports describing familial GBM suggest genetic predispositions exist. However, no existing reports examine GBM development in the context of both supraphysiologic sex hormone states and familial predisposition.

Methods: We present a case of GBM in a pregnant patient with a family history of GBM, detail the patient's clinical presentation, and review the literature describing relationships among sex hormones, genetics, and glioblastoma.

Results: A 35-year-old female with polycystic ovary syndrome and undergoing in-vitro fertilization (IVF) treatment presented with seizure and headache. Imaging revealed a right frontal brain mass. The patient underwent a right frontal craniotomy with maximal surgical debulking of the mass. She was discharged after 4 days and later underwent dilation and curettage and began Stupp protocol. Molecular and histopathological analysis of the resected tumor supported a diagnosis of IDH-wild type GBM. Her family history was significant for GBM. Current literature indicates testosterone promotes GBM cell proliferation, while estrogen and progesterone effects vary with receptor subtype and hormone concentration, respectively.

Conclusion: Sex hormones and genetics likely exert influence on GBM development and progression that may compound with concurrence. Here we describe a case of GBM in a young patient with a family

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history of glioma and atypical sex hormone exposure due to endocrine disorder and pregnancy assisted by exogenous IVF hormone administration.

Natural killer cells: a review of biology, therapeutic potential and challenges in treatment of solid tumors

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Natural killer (NK) cells lead immune surveillance against cancer and early elimination of small tumors. Owing to their ability to engage tumor targets without the need of specific antigen, the therapeutic potential of NK cells has been extensively explored in hematological malignancies. In solid tumors, however, their role in the clinical arena remains poorly exploited despite a broad accumulation of preclinical data. We will review our current knowledge of NK cells' biology, and highlight the challenges facing NK cell antitumor strategies in solid tumors. We then summarize the abundant preclinical attempts at overcoming these challenges, present past and ongoing clinical trial data and finally discuss the potential impact of novel insights on the development of NK cell-based therapies.

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NF1 in Solid Tumors: The Unknown Soldier of Tumor Suppressor Genes

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Many of the altered properties of cancer cells are attributed to inactivation of normal cellular regulatory genes that suppress uncontrolled proliferation, evasion of apoptosis, metastasis and tumorigenesis. Loss of tumor suppressor genes (TSG) is crucial for cancer development, along with gain-of-function alterations in proto-oncogenes. NF1 is a TSG well-known in association with Neurofibromatosis type 1 (NF1) syndrome. However, the role of NF1 mutation in cancer has not been extensively studied, unlike other TSGs such as retinoblastoma (Rb), p53, Adenomatous Polyposis Coli (APC), or Phosphatase and Tensin Homolog (PTEN). Here we will discuss the molecular role of NF1 in cancer development and cancer-related cellular signaling. We also review studies that have assessed the prevalence of NF1 mutations and loss-of-function across different solid tumors, and focus on their role in mediating malignant transformation, and modulating response to therapy. This sheds light on the challenges that have hindered a better understanding of NF1's role in cancer development, and discusses the prospect of NF1 as a biomarker for targeted therapies.

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A patient with Factor V Leiden mutation who developed a Pulmonary Embolism and Deep Vein Thrombosis post Covid

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Introduction: A well-known sequelae of infection with Covid-19 is coagulopathy, which presents as a prothrombotic state in the acute and chronic phases of infection. Current literature outlines the incidence of Covid coagulopathy in patients without a previous history of hypercoagulability, however few sources have examined the consequences of Covid coagulopathy in patients with existing prothrombotic states. We present a case of a patient with a known hypercoagulable condition presenting with covid coagulopathy.

Case Presentation: A 53-year-old male with a past medical history of Factor V Leiden mutation on warfarin, atrial fibrillation, and Covid pneumonia complicated by hypoxic respiratory failure 6 weeks ago presented to the emergency department at the University of Toledo with a chief complaint of bilateral arm pain of 2 days duration, along with redness and swelling of his arms. Patient reportedly had a supratherapeutic INR of 8.8 two days prior to presentation, and became subtherapeutic after vitamin K administration, with an INR of 1.64 one day prior to presentation. In the ED, physical exam was notable for diminished pulses in the upper extremities. CT of the upper extremities was negative for arterial occlusion, but CTA chest did reveal a pulmonary embolism. Patient had recurrent pain in the arms, and on day 3 of admission, ultrasound of the upper extremities revealed bilateral deep venous thromboses.

Conclusion: Patients with known thrombophilic disorders are at risk for covid coagulopathy. Closer monitoring of anticoagulation therapies is warranted for these patients who contract Covid-19 to minimize the risk of thromboembolic events.

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Daptomycin Associated Rhabdomyolysis with Concurrent Use of Atorvastatin

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Introduction: Daptomycin is the only lipopeptide drug approved for clinical use. Daptomycin also associated with increase level of creatinine kinase.

Case Report: 74-years-old Caucasian female with body mass index of 41.16 kg/m2 and past medical history of hyperlipidemia on atorvastatin instructed by the infectious disease clinic to go to the emergency room due elevated kidney function and liver enzymes. One month prior to her presentation, patient was admitted to the hospital after she was found to have right multi-lobule psoas abscess and iliacus muscle abscess. At that time, she was started on intravenous (IV) Vancomycin 1000 mg daily. In the 17th day follow up with infectious disease clinic, she was found to have acute kidney injury secondary to IV vancomycin with increase of creatinine at 1.89 mg/dL. IV vancomycin discontinued then she was started on daptomycin infusion of 3690 mg daily. Fourteen days after initiating daptomycin infusion, blood work up show worsen creatinine level at 2.18 mg/dL. Further blood work up revealed elevated aspartate aminotransferase (AST) at 1200 U/L, elevated alanine aminotransferase at 325 U/L, elevated creatinine kinase (CK) total at 38,390 U/L and elevated myoglobin at 28,663 ng/mL. Patient diagnosed with rhabdomyolysis secondary to daptomycin, Naranjo score is 6. Daptomycin and atorvastatin were discontinued, and normal saline infusion started with rate of 200 mL/hr. Patient total stay of admission was 5 days and blood work up show marked improvement.

Conclusion: Daptomycin associated rhabdomyolysis is a rare and concerning side effect that require prompt discontinuation of the antibiotic.

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Bleeding Risk with Dual Antiplatelet Therapy and Gastrostomy Tube Placement: A Systematic Review and Network Meta-Analysis

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Background/Objective: Gastrostomy tube (G tube) is a commonly performed procedure for nutritional support. Current guidelines recommend discontinuation of dual antiplatelet therapy (DAPT) prior to G tube placement to reduce bleeding risk. We aim to compare bleeding risk in single, dual and no antiplatelet therapy during G tube placement.

Methods: The following databases were searched: PubMed, Embase, Cochrane, and Web of Sciences to include comparative studies evaluating single antiplatelet (aspirin, clopidogrel), dual antiplatelet (DAPT, aspirin and clopidogrel), and no antiplatelet therapy. Direct as well as network meta-analyses comparing these arms were performed using random effects model. Risk Differences (RD) with confidence intervals were calculated.

Results: A total of 12 studies with 8471 patients were included in the final analysis. On direct meta-analysis, there was no significant difference noted between DAPT compared to Aspirin (RD 0.001 95% CI -0.012–0.014, p = 0.87), Clopidogrel (RD 0.001 95% CI -0.009–0.010, p = 0.92) or no antiplatelet group (RD 0.007 95% CI -0.011–0.026, p = 0.44). These results were consistent on network meta-analysis and no difference was noted in bleeding rates when comparing DAPT with Aspirin (RD 0.001,95% CI -0.007–0.01, p = 0.76), Clopidogrel (RD 0.001,95% CI -0.01–0.011, p = 0.90) and no antiplatelet group (RD 0.002,95% CI -0.007–0.012, p = 0.62).

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Conclusion: There is no significant difference in bleeding risk between DAPT, single antiplatelet or no antiplatelet therapy. G tube placement can be safely performed while being on DAPT with no additional bleeding risk.

Efficacy and Safety of EUS-directed Transgastric ERCP (EDGE) vs Laparoscopic-Assisted ERCP: A Systematic Review and Meta-Analysis

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Background: The altered anatomy in Roux-en-Y gastric bypass (RYGB) makes conventional Endoscopic retrograde cholangiopancreatography (ERCP) a technically challenging procedure. EUS-directed Transgastric ERCP (EDGE) and Laparoscopic-Assisted ERCP (LA-ERCP) are alternative modalities used with comparable efficacy and adverse events in such patients. We conducted a meta-analysis comparing EDGE and LA-ERCP to assess the efficacy and safety in patients with RYGB.

Methods: We conducted a comprehensive literature search from inception through July 7th, 2022 on MEDLINE, EMBASE, Cochrane Register of Controlled Trials, and Web of Science database using the core concepts of "EDGE" and "LA-ERCP". We excluded case reports, case series (<10 patients) and review articles. Relative risk (RR) was calculated when comparing dichotomous variables while mean difference (MD) was calculated for continuous outcomes. A 95% confidence interval (CI) and p-values (<0.05 considered significant) were also generated.

Results: The search strategy yielded a total of 55 articles. We finalized 4 studies with total 192 patients (75 EDGE and 117 LA-ERCP). The rates of technical success were not significantly different for LA-ERCP and EDGE (RR= 0.994, CI: 0.939 – 1.051, P= 0.830, I2= 0%) Similarly, no difference in adverse events were noted between the two groups (RR= 1.216, CI: 0.561-2.634, P= 0.620, I2= 10.67%). Shorter procedure time was noted for EDGE compared to LA-ERCP group (MD= 91.53 mins, CI: 69.911 – 113.157, P<0.001 I2= 8.32%).

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Conclusion: EDGE and LA-ERCP are comparable in terms of efficacy and safety. In addition, EDGE has overall lower procedural time. Our study suggests EDGE should be considered as a first-line therapy if expertise available.

Fresh vs Frozen vs Lyophilized Fecal Microbiota transplant for Recurrent Clostridium Difficile Infection: A Systematic Review and Network Meta-analysis

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Introduction: Clostridium Difficile Infection (CDI) is a significant source of morbidity and mortality which is on the rise. Fecal Microbiota Transplantation (FMT) is an alternative therapy to antibiotics with a high success rate and low relapse rate. Current data regarding the efficacy of the types of FMT used, namely Fresh, Frozen and Lyophilized is conflicting. Our review attempts to consolidate this data and highlight the most efficacious treatment currently available.

Methods: PubMed/Medline, Embase, Web of Science Core Collection, and Cochrane Central Register of Controlled Trials, were systematically searched from inception through May 3, 2022. Studies in which patients undergoing any form of FMT who had failed antibiotic treatment previously were included. Both pairwise (direct) and network (direct + indirect) meta-analysis was performed using Random effects model and DerSimonian Laird approach. Risk difference with (RD) with 95% confidence interval (CI) were calculated.

Results: A total of 8 studies including 4 RCTs and 4 cohort studies were included with a total of 616 patients. Fresh FMT was determined to be most successful with 93% efficacy 0.956 95 % CI (0.913 – 0.999) followed by Frozen with 88 % efficacy 0.902 95 % CI (0.857 – 0.947) and Lyophilized with 83% efficacy 0.828 95 % CI (0.745 – 0.910) . When compared to Fresh group, lower recovery rate was noted with both Frozen group (RD -0.06 95% CI -0.11-0.00, p=0.05) and Lyophilized group (RD -0.16 95% CI -0.27--0.05, p= 0.01). The direct meta-analysis showed no statistically significant difference between fresh vs frozen group. (RD -0.051 95% CI -0.116-0.014, p=0.178) as shown in Figure 2A. No

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significant differences were noted in Frozen vs Lyophilized group as shown in Figure 2B. (RD -0.061 95% CI -0.038-0.160, p=0.617). On network meta-analysis, when compared to Fresh group, lower recovery rate was noted with both Frozen group (RD -0.06 95% CI -0.11-0.00, p=0.05) and Lyophilized group (RD -0.16 95% CI -0.27--0.05, p= 0.01).

Conclusion: Our review shows Fresh FMT to be more efficacious compared to other forms of FMT i.e. Frozen and Lyophilized techniques. Clinicians should strive to use Fresh FMT, if possible, when dealing with recurrent CDI.

Myasthenic Crisis-Induced Takotsubo Cardiomyopathy: What to Know

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Myasthenia gravis (MG) is an autoimmune disorder in which antibodies are formed against post-synaptic nicotinic acetylcholine receptors that leads to impeded muscle contraction, and commonly affects the oculomotor muscles. MG can be complicated by myasthenic crisis (MC), a life-threatening exacerbation of myasthenic weakness that can lead to respiratory depression and possibly even death. Takotsubo cardiomyopathy (TTC) is a dilated cardiomyopathy that can mimic a myocardial infarction and causes reversible systolic dysfunction By themselves, MC has a mortality of 4% and TTC is approximately 2.4%. A review of 32 known cases of MC-associated TTC revealed a mortality of 15.6%, suggesting an unfortunate synergistic effect that significantly increases mortality. Here, we review the current cases and clinical patterns of 32 known cases of MC-associated TTC.

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Urban-rural Disparities in Trends of Pulmonary Hypertension-Related Mortality in the United States, 2004-2019

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Introduction: Despite medical advances that have extended life expectancy in pulmonary hypertension (PH) patients over the past few decades, mortality has continued to be high within the United States. Yet, there is a paucity of research regarding rural-urban disparities associated with PH mortality, with trends only being reported prior to 2011.

Methods: We extracted PH-related urban-rural deaths from 2004 to 2019 from the Centers for Disease Control and Prevention Wide-Ranging OnLine Data for Epidemiologic Research (CDC WONDER). Crude and age-adjusted mortality rates (CMR and AAMR) per 100,000 people were calculated. Associated average percentage changes (APC) were computed using Joinpoint trend analysis software and reported as average annual percent changes (AAPCs).

Results: A total of 353, 916 pulmonary hypertension-related deaths occurred in the study population within the US between 2004 and 2019. The AAMR for overall PH increased from 8.19 in 2004 to 11.63 in 2019. Rural counties had an overall significantly higher AAMR than urban counties, (rural: 10.75 [95% CI, 10.67 to 10.84] versus (urban: 9.70 [95% CI, 9.66 to 9.74].

Conclusion: Overall, our results indicate a gap in PH-associated healthcare services among those living in rural counties as compared to those living in urban counties within the US.

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Do Zinc Supplements Reduce Mortality in Patients with COVID-19? A Systematic Review and Meta-Analysis

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Introduction: Zinc is a trace element that has major role in human immune system. This study aims to assess the clinical benefits of zinc supplements on all-cause mortality in patients with COVID-19.

Method: PubMed/MEDLINE, EMBASE, and Cochrane databases were searched for studies that evaluated the clinical efficacy of zinc supplements in patients diagnosed with COVID-19. The outcome was all-cause mortality rate. Pooled relative risk (RR) and corresponding 95% confidence intervals (ICs) were calculated and combined using a random-effects model.

Results: A total of 6 studies (3 randomized clinical trials and 3 retrospective observational studies) that included 1,670 patients with COVID-19 (855 received zinc supplements vs. 812 received standard of care without zinc) were included in our systematic review. Our meta-analysis showed that there is statistically significant difference in all-cause mortality rate between the two groups favoring zinc supplements (RR 0.66; 95%CI 0.54 - 0.81; P <0.0001)

Conclusion: Our study demonstrated that zinc supplements in addition to standard of care can reduce all-cause mortality in patients with COVID-19.

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Successful Administration of the Influenza Vaccine after Prior Serum Sickness in an HIV-Positive Patient

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Serum sickness is a type III hypersensitivity reaction to an antigen, leading to accumulation of immune complexes, inflammation, and vasculitis; causing symptoms like fever, rash, abdominal pain, and arthralgia (1). Serum sickness reactions to vaccination have previously been described (2-6), and are treated with steroids and removal of the offending agent (1). However, successful desensitization has been previously described (7). We present a case of successful re-administration of the influenza vaccine in an HIV+ patient, with previous history of serum sickness secondary to influenza vaccination. A 48-year-old male with uncontrolled HIV was admitted in October 2017 due to rash after receiving the influenza vaccine. The rash started on his arm and spread medially; and was associated with joint swelling and extremity pain. The patient was admitted and treated with prednisone, which resolved his serum sickness. At the time of presentation, the patient's last CD4 count was 4, and a viral load was 177,000. HIV genotype revealed M184V and K65R mutations. In July 2018, the patient established care for uncontrolled HIV. He was prescribed lamivudine-zidovudine, dolutegravir, and darunavir-cobicistat. Adherence to therapy resulted in CD4 count of 223 and an undetectable viral load in September 2021. In November 2021, he successfully received the inactivated influenza vaccine, without resultant serum sickness. In this case, after immune reconstitution, the patient was able to tolerate the influenza vaccine. Serum sickness reaction to influenza vaccination has not previously been described in HIV+ patients but may be an important consideration prior to vaccination in immunocompromised individuals.

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Daptomycin Induced Rhabdomyolysis and Subsequent Compartment Syndrome: A Case Report

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Introduction: Rhabdomyolysis is an infrequent complication of Daptomycin, but progression to compartment syndrome has not previously been reported in published literature. We present a case of a 56-year-old who developed compartment syndrome after daptomycin treatment for a S. aureus infection of a penile implant.

Case Presentation: The patient presented to the emergency department complaining of bilateral upper extremity pain and swelling for several hours. The patient was 5 days into a 4-week course of daptomycin prescribed to him from another healthcare facility to treat an S. aureus infection of a penile implant complicated by bacteraemia. The patient complained of arm swelling and pain that developed several days prior to presentation. Physical examination revealed significant swelling and allodynia of the bilateral forearms. Laboratory evaluation revealed markedly increased creatine phosphokinase (CPK) and D-dimer levels, indicating severe rhabdomyolysis. During his admission, his forearm pain worsened, and he was diagnosed with bilateral forearm compartment syndrome. Emergent fasciotomies of bilateral forearms were completed and resolved the compartment syndrome. He subsequently recovered with minimal clinical sequela.

Discussion: While compartment syndrome occurs secondarily to fractures in 75% of cases, it can also be a sequelae of soft tissue injuries, poor positioning during surgery, burns, vascular injuries, infections, and medication. Prescribing physicians should be cognizant of the possibility of compartment syndrome in patients with severe rhabdomyolysis secondary to daptomycin so that intracompartmental pressures can be obtained and surgical management quickly initiated.

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An Alprostadil Intracavernosal Injection Leading to a Psoas Muscle Abscess

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Introduction: Alprostadil is a synthetic prostaglandin E1 that can be self-administered via intracavernosal injection as a vasodilatory treatment for erectile dysfunction. The psoas muscle has close anatomical relationships such as to the ureters and renal pelvises, and is vulnerable to infection from regional structures. Lumbar artery derivatives supply the muscle. Primary psoas abscess is often associated with trauma, while Crohn's disease is linked to secondary abscess.

Case Presentation: A 59-year-old male presented with a three-week history of fevers, chills, and body aches. Eight months prior, the patient had undergone laparoscopic prostatectomy with bilateral pelvic lymph node dissection and nerve sparing as prostate cancer therapy. Since, the patient had reported stress incontinence with heavy lifting but denied hematuria, dysuria, flank pain, or testicular pain. The patient was diagnosed with erectile dysfunction related to prostatectomy and received intracavernosal alprostadil and combination treatment with sildenafil six months. Imaging revealed a loculated, peripherally-enhancing fluid collection in the hemipelvis along the inferior margin of the right psoas muscle. Blood and urine cultures were negative. An abscess aspirate sample revealed methicillin-sensitive Staphylococcus aureus. The patient was treated with cefazolin 2g IV every eight hours for six weeks.

Discussion: The case offers an example of intracavernosal injection of alprostadil precipitating psoas muscle abscess, as opposed to more common cavernous or penile abscesses. Psoas abscess can arise from contiguous spread from adjacent structures or by the hematogenous route from a distant site. This case highlights the importance of considering intracavernosal injections as potential local introduction mechanisms for psoas infection.

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Fatal central pontine myelinolysis in a patient with uncontrolled HIV and normal sodium levels

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Introduction: Central pontine myelinolysis (CPM) is a demyelinating process of the pons and CNS. While the etiology of CPM remains unclear, the condition is often associated with iatrogenic rapid correction of hyponatremia. CPM is characterized by a breakdown in the blood-brain-barrier triggered by osmotic stress related to electrolyte imbalances. While HIV affects the nervous system in up to 90% of patients, CPM remains rare.

Case Presentation: A 41-year-old HIV-positive female was admitted for generalized weakness and altered mental status. She was noncompliant with antiretroviral therapy and initial CD4 count was 34. Initial assessment revealed hypertension, anemia, and elevated creatinine. Sodium was 138 mmol/L on admission. MRI on hospital day 3 showed several foci of abnormality in the bilateral caudate nuclei, thalami, basal ganglia, and the pons suggestive of CPM with extrapontine involvement. Lumbar puncture revealed elevated protein with normal cell count, negative culture and meningitis panel. The patient was started on dolutegravir with renally-dosed tenofovir and lamivudine. The patient remained obtunded for her ICU stay. She expired three days later.

Discussion: This case offers an example of CPM in the setting of HIV without sodium imbalance. It is important to consider an osmotic demyelinating process in the differential for neurologic symptoms of HIV and to investigate alternative etiologies of CPM in the absence of electrolyte abnormalities. Treatment of CPM with normal electrolytes includes addressing underlying causes that could precipitate metabolic derangement or increased permeability of the blood-brain barrier; this means management of underlying HIV even in a previously asymptomatic patient.

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Impact of a Dedicated Outpatient Parenteral Antibiotic Therapy Clinic on Patient Outcomes

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Introduction: Outpatient parenteral antibiotic therapy (OPAT) can provide substantial benefits to both patients and the healthcare system. However, OPAT is also associated with risks that can end up harming patients, such as increasing the risk of rehospitalization and adverse events. We developed a predictive model of 30-day readmission among patients discharged on OPAT by using patient populations before and after the establishment of a dedicated OPAT clinic.

Methods: A retrospective cohort study was conducted by using medical records. Logistic regression was applied to determine the association between readmission and visit to OPAT clinics while also examining covariates including sex, comorbidities, pathogen, and planned length of therapy. We hypothesized that at least one visit to the OPAT clinic would reduce the risk for readmission within 30 days.

Results: Among 368 patients, 240 (65.2%) received outpatient follow-up care at the OPAT clinic. 88 (23.9%) were readmitted within 30 days. A multivariate logistic regression model indicated that an OPAT clinic visit was associated with a reduced risk of readmission compared to those that did not visit an OPAT clinic (odds ratio of 0.45 [95% confidence interval 0.27 – 0.78]) after adjusting for covariates that were selected using outcomes of univariate analyses.

Conclusion: The predictive model for readmission developed in this study can be utilized to establish interventions to prevent readmission for OPAT patients. Future studies will have to continue examining the association between OPAT clinic visits and readmission along with other predictors to further improve the outcomes of OPAT patients.

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A Pathway of Distinction in Global Health – A Professional Development Model to Prepare Medical Students as Future Global Health Leaders

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Background: Medical student evaluation and assessment both within the medical school institution and at the national licensing level continues to evolve. The first step of the United States Medical Licensing Examination will become a pass-fail examination in January 2022, and medical schools are adapting assessment tools to evaluate the potential of their learners. Students likewise wish to differentiate themselves among their peers as future clinicians and explore career opportunities earlier in training, particularly topics outside of the traditional undergraduate medical education curriculum. The University of Toledo College of Medicine and Life Sciences (UTCOMLS) launched a Professional Development Initiative to optimize student wellness and personal identify formation. This initiative examined strategies for the creation of pathways of distinction within the longitudinal curriculum. We present the initial plans for a Pathway of Distinction in Global Health at UTCOMLS.

Methods: The UTCOMLS convened a Global Health Curriculum Working Group to develop a course for pre-clinical medical students and to design a distinction track in Global Health. The initial Pathway of Distinction in Global Health at the UTCOMLS consists of three foundational requirements for medical students.

- Completion of a "Global Health and Human Rights" course, a once-weekly one-hour seminar convened over 32 weeks throughout the first and second-year of medical school;
- Completion of a fourth-year Global Health elective at an approved affiliate partner site at UTCOMLS;
- Completion of a capstone experience in Global Health. Medical students that complete all three requirements will be awarded a "Distinction in Global Health" upon graduation. Students will

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also be counseled regarding post-graduation residency programs and career opportunities with an emphasis in global health.

Results: An initial cohort of 22 first- and second-year medical students has enrolled in our Global Health and Human Rights course, with the intention of proceeding in the Distinction Track in Global Health. This builds on a tradition of sending between 15-20 students yearly to our eleven international partner sites in China, Jordan, Lebanon, India, Ethiopia, the Philippines, Nepal, and Pakistan. Our next phase is to develop a database of capstone opportunities and to identify advisors with whom students can collaborate as they complete their capstone projects.

Discussion: The Pathway of Distinction in Global Health offers an opportunity for medical students to distinguish themselves as future global health professionals. As the assessment and evaluation of medical students evolves, universities should consider formal pathways to cultivate the career prospects of their students most committed to global health.

Early Infectious Diseases Consultation and Procalcitonin-Guided Therapy Limits Unnecessary Antibiotic Use in COVID-19

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Background: Antibiotic stewardship has been a central challenge of the COVID-19 pandemic. Empiric antibiotic therapy is offered in 56.6%-74.6% of inpatients with COVID-19, with microbiologically confirmed bacterial pneumonia reported in only 3.5%-16% of cases. Procalcitonin (PCT) as a biomarker for bacterial infection is of interest in improving antibiotic use. PCT-guided antibiotic stewardship initiatives have demonstrated reduction in the use of antibiotics in the COVID-19 pandemic. An Infectious Diseases (ID) consultation was obtained on most patients at our institution throughout the COVID-19 pandemic. We report a significant reduction in antibiotic use among COVID-19 patients in the setting of near-universal ID consultation in COVID-19 patients.

Methods: We evaluated the records of 1346 patients with COVID-19 from March 2020 – May 2021 at four hospitals with ID consultant availability. We assessed the inclusion of an ID consultant, antibiotic indication, initiation and discontinuation, PCT levels, radiologic images, and changes to therapy decisions. A chi-square test of independence and simple logistic regression were conducted to determine whether an association exists between the PCT level and the decision to discontinue antibiotics.

Results: Of 1346 patients with a confirmed COVID-19 diagnosis, 64.6% (870/1346) received antibiotics on admission. The most common diagnosis associated with initial antibiotic administration was bacterial pneumonia (692/870, 79.5%). An ID consultation was obtained on 97.8% (677/692) of the patients that received antibiotics for suspected bacterial pneumonia. In 48.1% (326/677) of these patients, antibiotics were discontinued within the first 48 hours of the ID consultation. A statistically significant difference was noted between the PCT level and continuation of antibiotics ($X2= 67.02$, $p < .01$). The odds of discontinuing antibiotics for the upper (PCT > 0.51) and middle (PCT = 0.26-0.50) groups were 0.22 and 0.37, respectively, when compared to the lower (PCT ≤ 0.25) group.

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Conclusion: Early consultation of an ID specialist and evaluation of PCT levels leads to significant reductions in inappropriate antibiotic use. PCT may be a useful adjunct in assisting with the decision to discontinue antibiotics.

Protease-Inhibitor Binding Reveals Conformational Transition Mechanism

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Human Immunodeficiency Virus Type-1 (HIV-1) protease is a flexible dimeric protein required for post-translational activation of the HIV Gag-ProPol polypeptide. In clinic, protease inhibitors are commonplace in the multi-drug regimens used by physicians to combat drug-resistant HIV strains with an unfortunate exchange for greater patient toxicity. To confront HIV-1 protease drug resistance, Ghosh and colleagues developed protease inhibitors modeled after FDA approved HIV-1 protease inhibitor, Darunavir. These new inhibitors, Inhibitor 3 (In3) and Inhibitor 4 (In4), differ from each other by a single atom; an oxygen in In3 instead of a carbon in In4. Surprisingly, In4 exhibited a >1,000-fold drop in enzymatic inhibition, and >500-fold loss in antiviral capacity compared to In3. We investigated the mechanism behind this reduction in affinity utilizing Molecular Dynamics (MD) simulations. We found that In3 locks the protease in the closed conformation while In4 does not. The Apo-protease simulations suggested Asp29 is part of a residue triad which plays a critical “switch” role in the protease conformational transition. The formation of an Asp29-Arg87 salt bridge contributed to the closed conformation’s stability, which was further enhanced by the hydrogen bond between the oxygen of In3 and the main chain nitrogen atom of Asp29, which was abrogated in In4 binding. Additionally, arginine stacking between Arg87 and Arg8 of the opposite chain stabilized the protease open conformation. These observations explain the tremendous drop in affinity of In4 compared to In3 and reveal the mechanism of HIV-1 protease conformational changes that are being validated by mutagenesis and Bio-SAXS in-vitro.

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Protease-Inhibitor Binding Reveals Conformational Transition Mechanism

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Cellulosimicrobium Bacteremia in a Patient With Small Cell Lung Cancer: Emergence of a New Gram-Positive Branching Rod

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A 64-year-old male with a history of esophageal adenocarcinoma, placement of a spinal stimulator, cervical and lumbar fusions, and stage IV small cell lung cancer on palliative chemotherapy with carboplatin and etoposide, presented to the hospital with neutropenic fever. He reported intermittent fevers prior to admission and had episodic fevers with a Tmax = 38.2° throughout his hospitalization. Ocular examination revealed no evidence of endophthalmitis or keratitis. Oral examination revealed no tongue ulcers, and an abdominal examination revealed no tenderness. He was empirically placed on cefepime and vancomycin. Chest x-ray revealed multifocal pneumonia. His neutropenia recovered on hospital day 2, but his fevers persisted and were attributed to pneumonia and possible bacteremia. On hospital day 3, initial blood cultures revealed a branching gram-positive rod. The initial suspicion for a causative agent was Nocardia or Actinomyces; vancomycin was discontinued and intravenous trimethoprim-sulfamethoxazole and meropenem were initiated. The blood cultures were identified as Cellulosimicrobium species on hospital day 11; his meropenem was discontinued and vancomycin was initiated. A transthoracic echocardiogram did not reveal endocarditis, and the patient was discharged on hospital day 24 and completed a 14-day total course of vancomycin. Cellulosimicrobium spp. is an emerging pathogen that has been described as an opportunistic infection in immunocompromised hosts. This case highlights Cellulosimicrobium spp. as an opportunistic pathogen, especially in immunocompromised individuals as a source of secondary bacteremia. It emphasizes that Cellulosimicrobium spp. should be considered in a differential diagnosis as it is an emerging pathogen with increasing prevalence.

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CMV transverse myelitis in Unmanaged HIV Infection

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Introduction: Acute transverse myelitis (ATM) is an inflammatory spinal cord injury that may be an isolated process or caused by a secondary disease (1). Symptoms include lower limb weakness, urinary incontinence, numbness, or paresthesia. Prior to the availability of antiretroviral therapy (ART), ATM was seen in patients with primary HIV infection due to opportunistic infections (2). We present a case of ATM attributed to cytomegalovirus secondary to uncontrolled HIV.

Case Presentation: A 33-year-old HIV-positive male presented with lower extremity weakness and bipedal paresthesia. He had been diagnosed with HIV in 2017 but had never initiated ART due to financial constraints. His initial CD4 count was 7 cells/mm3 and his viral load was 208,000 copies/mL. A viral meningitis panel detected herpes simplex virus 1 (HSV-1), cytomegalovirus (CMV), and varicella zoster virus (VZV). A cytomegalovirus DNA quantitative PCR revealed 6,381,260 IU/mL. Treatment was initiated with valganciclovir 900 mg oral twice daily for 14 days for induction therapy, bictegravir-emtricitabine-tenofovir alafenamide one tablet daily, and sulfamethoxazole-trimethoprim one tablet oral daily. His weakness and strength improved. Unfortunately, this patient was subsequently lost to follow up and the outcome is unknown.

Discussion: With developments in management of HIV with ART, opportunistic infections are seen less often. Our patient underscores that advanced presentations can still occur and are often secondary to gaps in education and accessibility. This case highlights the necessity for comprehensive patient education and the importance of adhering to ART regimens to maintain a high CD4+ count and prevent progression of the disease.

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Streptococcal Pneumoniae Mycotic Aneurysm: A Rare Case of Disseminated Pneumococcal Disease in an Immunocompetent Host

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Introduction: Mycotic abdominal aortic aneurysm (MAAA) is a rare infection of the aortic wall that may progress to aortic rupture. The most common infecting organisms are Staphylococcus and Salmonella species. Clinical characteristics are diverse and depend on the source of the infection. We present a case of mycotic AAA caused by Streptococcus pneumoniae without an apparent source of infection.

Case Presentation: A man in his sixties presented to the hospital with a three-day history of low back pain, chills, and rigors. CT revealed a ruptured AAA measuring 5.3 cm with stranding and multiple prominent adjacent lymph nodes. MRI lumbar spine showed prevertebral edema. AAA repair was performed with a rifampin-soaked tube. Cultures taken from the aneurysm revealed S. pneumoniae. He was treated with intravenous beta-lactam therapy for six weeks, followed by one year of amoxicillin for suppression. Pneumococcal vaccine was recommended to prevent future infections.

Discussion: S. pneumoniae makes up approximately 8% of all bacterial abdominal aortic aneurysms. Common symptoms include abdominal and back pain, pulsating mass, fever, and sepsis. Diagnosis is suggested by findings of lymphadenopathy on imaging and confirmed with positive surgical cultures. The use of antimicrobial therapy and surgery are essential for management. Pneumococcal vaccination is underutilized as defense against invasive disease. Disseminated pneumococcal disease in an immunocompetent host is a rare phenomenon in recent years due to vaccination, with review of the literature revealing only one similar reported case. Our case highlights the importance of vaccinations in preventing disseminated infection in even the healthiest of patients.

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Herpes Simplex Virus-1 Encephalitis Secondary to Whole Brain Radiation Therapy

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Background: Encephalitis is inflammation of the brain parenchyma with associated neurological dysfunction. Herpes simplex virus-1 (HSV-1) encephalitis (HSE) is the most common cause of encephalitis. HSV-1 characteristically remains dormant in the trigeminal ganglion and reactivates during states of immunosuppression, including stress, cancer or chemotherapy. There have been few reported cases of HSE following whole brain radiation therapy (WBRT) for treating intracranial tumors. Importantly, reported HSE cases following WBRT demonstrate an atypical presentation of encephalitis. We report a case of HSE following WBRT to treat brain metastases of renal cell carcinoma.

Case Presentation: A 67-year-old female patient who recently underwent WBRT to treat brain metastases from renal cell carcinoma presented with an elevated temperature, weakness and altered mental status. The patient was admitted, and baseline CT imaging did not demonstrate any acute abnormalities. The next day the patient's neurological status declined substantially, prompting MR imaging that revealed lesions in the temporal lobes, encompassing the amygdala and hippocampus bilaterally. Extra limbic lesions were also demonstrated. Empirical intravenous acyclovir was initiated upon suspicion of possible HSE. Later imaging revealed cerebellar folia enhancement, suggesting probable leptomeningeal carcinomatosis. CSF PCR was positive for HSV-1, confirming the diagnosis of HSE. The patient's condition significantly improved and ultimately returned to baseline.

Conclusion: We present a case of HSE following WBRT. HSE must be promptly treated to avoid catastrophic outcomes. However, rapid treatment may be difficult due to a delay in diagnosis, which is difficult due to the atypical presentation of HSE secondary to WBRT.

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MC1R Deficiency Enhances Th1 Response and Impairs Regulatory T Cell Homeostasis In Nephrotoxic Serum Nephritis

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Background: The melanocortin neuropeptides, represented by adrenocorticotropic hormone, have recently emerged as a novel therapeutic choice for treating refractory glomerular diseases. As a key cognate receptor of the melanocortin hormone system, melanocortin 1 receptor (MC1R) plays a pivotal role in regulating immune response and inflammation, and has become a novel therapeutic target for a number of diseases. However, its role in the pathogenesis of immune-mediated glomerular disease remains unknown.

Methods: Wild-type (WT) mice and the recessive yellow mice (e/e) with the naturally occurring loss-of-function null mutation of MC1R received injection of the rabbit anti-mouse nephrotoxic serum (NTS) to develop the NTS nephritis and were examined 2 weeks later.

Results: The e/e mice developed more severe crescentic glomerulonephritis than WT mice, marked by aggravated proteinuria, kidney dysfunction, and renal lesions like glomerular hypercellularity, crescent formation, and renal inflammation and fibrosis. The exacerbated NTS nephritis in e/e mice was associated with greater levels of autologous IgG2c and IgG3 either deposited in glomeruli or in sera. In addition, profiling of signature cytokines of Th immunity revealed that e/e mice with NTS nephritis exhibited higher renal expression of IFN-γ, and an increasing trend in renal expression of TNF-α, as compared with WT mice, consistent with a reinforced Th1 immune response. Moreover, shown by immunohistochemistry staining, the number of FoxP3+ regulatory T cells in the NTS nephritic kidneys was diminished in e/e mice, as compared with WT mice. Mechanistically, MC1R was evidently detected in diverse renal leukocytes prepared from the diseased WT mice, including T lymphocytes, suggesting that T cells may be direct effector cells of the melanocortin hormones via MC1R signaling.

Conclusion: MC1R-mediated melanocortinergic signaling represses Th1 immune response and is required for regulatory T cell homeostasis in murine models of NTS nephritis, resulting in renal protection in experimental crescentic glomerulonephritis.

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Negative Modulation of B Cell Activation by MC1R Signaling Protects Against Membranous Nephropathy

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Background: The pituitary neuropeptide melanocortins, represented by ACTH, have recently emerged as a novel therapeutic modality for membranous nephropathy (MN). However, the mechanism of action remains elusive.

Methods: Passive Heymann nephritis (PHN), a model of MN, was induced in wild-type (WT) rats and melanocortin 1 receptor (MC1R) knockout (KO) rats generated by using the CRISPR/Cas9 technology, followed by treatment with various melanocortin agents, including the Repository Corticotropin Injection, the non-steroidogenic pan-MCR agonist NDP-MSH, and the selective MC1R agonist MS05. Some rats received adoptive transfer of syngeneic bone marrow-derived cells (BMDC) beforehand. Kidney function and injuries were evaluated.

Results: MC1R KO exacerbated proteinuria, podocyte injury and glomerulopathy, associated with enhanced glomerular deposition of autologous IgG and the C5b-9 complement complex, denoting a sensitized autologous humoral immune response. Melanocortin therapy ameliorated PHN in WT rats, coinciding with diminished glomerular deposition of autologous IgG and C5b-9. The beneficial efficacy of melanocortin therapy was blunted in KO rats but was restored by adoptive transfer of syngeneic BMDC derived from WT rats. Mechanistically, MC1R was evidently expressed in B lymphocytes, and negatively associated with B cell activation as revealed by gene set enrichment analysis. MC1R agonism triggered MITF induction in activated B cells in a cAMP-dependent mode, and repressed the expression of IRF4, resulting in suppressed plasma cell differentiation and IgG production.

Conclusion: MC1R signaling plays a key role in negative modulation of B cell activation and suppresses humoral immune response in PHN, representing a novel therapeutic target for MN.

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Pharmacological Melanocortin 5 Receptor Activation Attenuates Glomerular Injury and Proteinuria in Rats with Puromycin Aminonucleoside Nephrosis

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Background: Clinical evidence indicates that the melanocortin peptide ACTH is effective in inducing remission of nephrotic glomerulopathies like minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS), including those resistant to steroids. This suggests that a steroid-independent melancortinergic mechanism may contribute. However, the type of melanocortin receptor (MCR) that conveys this beneficial effect as well as the underlying mechanisms remain controversial. Burgeoning evidence suggests that MC5R is expressed in glomeruli and may be involved in glomerular pathobiology. This study aims to test the effectiveness of a novel highly selective MC5R agonist (MC5R-A) in puromycin aminonucleoside (PAN) nephrosis.

Methods: Rats were injured with a tail vein injection of PAN, and 5 days later, were randomized to daily MC5RA or vehicle treatment.

Results: Upon PAN injury, rats developed evident proteinuria on day 5, denoting an established nephrotic glomerulopathy. Following vehicle treatment, proteinuria continued to persist on day 14 with prominent histologic signs of podocytopathy, marked by ultrastructural glomerular lesions, including extensive podocyte foot process effacement. Concomitantly, there was loss of podocyte homeostatic markers, such as synaptopodin and podocin, and de novo expression of the podocyte injury marker desmin. Treatment with MC5R-A attenuated urine protein excretion and mitigated the loss of podocyte marker proteins, resulting in improved podocyte ultrastructural changes. In vitro in cultured podocytes, MC5R-A prevented the PAN-induced disruption of actin cytoskeleton integrity and apoptosis. MC5R-A treatment in PAN-injured podocytes also reinstated inhibitory phosphorylation and thus averted hyperactivity of GSK3β, a convergent point of multiple podocytopathic pathways.

Conclusion: Collectively, pharmacologic activation of MC5R by using the highly selective small-molecule agonist is likely a promising therapeutic strategy to improve proteinuria and glomerular injury in protenuric nephropathies.

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Oxalate Diet Induced Chronic Kidney Disease in Dahl-Salt-Sensitive Rats Induces Uremic Cardiomyopathy

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Background: Patients with chronic kidney disease (CKD) often develop "uremic" cardiomyopathy characterized by left ventricular hypertrophy and cardiac remodeling, causing high morbidity and mortality. Increased levels of dietary oxalate, a renally-eliminated terminal toxic metabolite, can lead to CKD. Dahl-salt-sensitive rats (SS) are mainstay models of hypertensive renal disease; however, characterization of other diet-induced CKD models with uremic cardiomyopathy would allow for comparative studies.

Objective/Hypothesis: Our objective was to characterize a clinically relevant diet-induced rodent model of uremic cardiomyopathy. We hypothesized that SS rats fed a high oxalate diet will develop cardiac dysfunction compared to SS rats fed a normal chow diet.

Methods/Results: Ten-week-old male SS rats were fed either 0.2% salt normal chow (SS-NC) or 0.2% salt and 0.67% sodium oxalate (SS-OX) for five weeks (n=6-8/group). SS-OX rats demonstrated increased 24-hour urinary protein excretion (97% vs SS-NC, $p<0.01$), plasma Cystatin C (135% vs SS-NC, $p<0.01$), and hypertension (23% increase in systolic blood pressure vs. SS-NC, $p<0.05$). Renin-angiotensin-aldosterone-system profile demonstrated significant ($p<0.05$) increases in circulating plasma angiotensin (128% vs SS-NC), angiotensin I (56% vs SS-NC), and suppression of aldosterone (-54% vs SS-NC). SS-OX also displayed increased cardiac tissue fibrosis (188% vs. SS-NC, $p<0.05$) and inflammation (75% vs. SS-NC, $p<0.0001$). Echocardiography of SS-OX rats showed increased posterior wall thickness (128% vs. SS-NC, $p<0.01$), increased septal wall thickness (113% vs. SS-NC, $p<0.05$), indicating left ventricular hypertrophy.

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Conclusion: Oxalate diet induces significant renin-angiotensin-aldosterone-system activation, hypertension, cardiac fibrosis, inflammation, left ventricular remodeling, introducing a novel diet-induced model to study the cardiovascular complications of CKD.

Computational and Experimental Analysis Reveals the Arachidonic Acid Metabolite 20-Hydroxyeicosatetraenoic Acid is a Novel Ligand of the Na/K-ATPase

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Objective: We sought to determine the ability of 20-HETE to bind with the NKA relative to other known NKA ligands using a computational molecular modeling approach. We further sought to test the ability of 20-HETE to stimulate NKA mediated signaling in renal proximal tubule cells.

Methods: Computational molecular modeling to investigate the interaction of 20-HETE and NKA was performed using Maestro software analysis (Schrodinger 2021-2). In vitro experiments of NKA signaling were performed with both 20-HETE and its stable analog, 5,14-20-HEDE, in renal LLC-PK1 proximal tubule cells.

Results: First, we performed induced fit docking to predict the binding free energy of both 20-HETE and its stable analog, 5,14-20-HEDE, in comparison with the well-established cardiotonic steroid NKA ligand telocinobufagin. This docking analysis predicted that 20-HETE and 5,14-20-HEDE interact with the NKA with similar binding free energy as cardiotonic steroids (Predicted binding free energies: telocinobufagin =-9.2; 20-HETE= -8.5 and 5,14-20-HEDE = -8.18). Further this computational modeling demonstrated that all of these molecules interact in the same binding pockets of the NKA. Next, our in-vitro experiments showed that 20-HETE and its analog 5,14-20-HEDE increased MAPK activation in a dose dependent manner from 10 nM to 10 uM in LLC-PK1 cell lines. This MAPK activation was significantly reduced after pretreatment with pNaKtide, a specific inhibitor of the NKA-Src signaling complex (1uM pNaKtide, 30 minutes).

Conclusion: The result of these study suggests that 20-HETE interacts with NKA in similar manner as cardiotonic steroids and is capable of inducing NKA signaling in renal proximal tubules.

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A Case Series of Potential Cyanotoxin Exposure

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Introduction: Harmful algal blooms (HABs) are increasing in prevalence and severity globally and locally in the Great Lakes region. HABs have the potential to produce serious adverse human health effects due to the production of cyanotoxins from cyanobacteria. Common routs of exposure include recreational exposure (swimming, skiing, and boating), ingestion, and aerosolization of contaminated water sources. Cyanotoxins have been shown to adversely effect several major organ systems contributing to hepatotoxicity, gastrointestinal distress, and pulmonary inflammation.

Methods: We present three pediatric case-reports that coincided with HAB exposure with a focus on presentation of illness, diagnostic work-up, and treatment of HAB-related illnesses.

Results: Potential cyanotoxin exposure occurred while swimming in the Maumee River and Maumee State Park in Northwest OH during the summer months which coincide with peak HAB activity. Primary symptoms included generalized macular rash, fever, vomiting, diarrhea, and severe respiratory distress. Significant labs included leukocytosis and elevated C-reactive protein. All patients ultimately recovered with supportive care.

Conclusion: Symptoms following potential cyanotoxin exposure coincide with multiple disease states representing an urgent need to develop specific diagnostic tests of exposure.

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Disruption of CD40 Results in Significantly Attenuated Renal Inflammation Following Glycerol-Induced Acute Kidney Injury

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Introduction: We have shown that disruption of the prominent pro-inflammatory receptor CD40 attenuates renal tubular atrophy and tubular cell death following high salt diet in our CD40 knockout (KO) model in addition to significantly reduced renal fibrosis following experimentally induced ischemic renal injury. We have also demonstrated significantly reduced pro-inflammatory and pro-fibrotic signaling in human CD40 KO renal proximal tubule epithelial cells. We performed the following study to test the hypothesis that disruption of CD40 significantly attenuates acute kidney injury (AKI).

Methods: Age matched (8-week-old) C57/BL6 wild-type and C57/BL6 CD40 KO male mice (n=8) were administered glycerol (7.5 ml/kg in 50% glycerol) to induce AKI. After 24h, animals were euthanized and kidneys were assessed for evidence of renal injury.

Results: Renal expression of CD40 was increased in the proximal tubules of wild-type mice in response to AKI. CD40 KO mice demonstrated reduced renal inflammation compared with wild-type mice following AKI. In addition, CD40 KO mice demonstrated significantly attenuated renal cortex gene expression of inflammatory markers IL1β, TGFβ1, and the fibrosis marker Col3a1 following AKI compared to wild-type (all $p<0.05$).

Conclusion: Disruption of CD40 results in significant attenuation of renal inflammation following experimentally induced AKI. Our results indicate that disruption of CD40 signaling may be a promising therapeutic target for the treatment of AKI.

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Pleural plasmacytomas in a Patient with Multiple Myeloma Relapse

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Introduction: Pleural plasmacytoma in the setting of relapsed multiple myeloma (MM) is a rare yet serious condition, less than 10 cases have been reported in the literature.

Case Report: A 66-year-old woman with history of IgA lambda MM diagnosed 10 years ago. She remained in remission for about 9 years. She presented with dyspnea on exertion with decrease breathing sound in the right side of the chest. CXR showed moderate right side pleural effusion and PET/CT scan revealed multiple lytic lesions and PET-avid foci in the skeleton and pleural soft tissue lesions. Thoracoscopy with pleural mass biopsy confirmed the diagnosis of extramedullary plasmacytomas in the setting of multiple myeloma relapse. The patient was started on pomalidomide, bortezomib, and dexamethasone.

Discussion: Pleural plasmacytomas are extremely rare and account for around 3-6% of extramedullary disease in MM patients. FDG-PET/CT allows the examination of the whole body in a single and faster study, and can help identify active disease in patients with relapsed or refractory MM. Pulmonary nodules or pleural lesions can be diagnosed by performing a transbronchial biopsy, CT-guided needle biopsy, or a surgical biopsy through open thoracotomy, medical thoracoscopy (MT) or video-assisted thoracoscopic surgery (VATS). MT has excellent accuracy and is less invasive, thus has increasingly been used. The treatment of solitary extramedullary plasmacytomas, including pleural plasmacytomas, is with radiation. The treatment of extramedullary plasmacytomas in the setting of MM relapse is a multimodal approach using different strategies, such as advanced radiotherapy techniques, immunomodulatory agents and proteasome inhibitors.

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Spontaneous Second Intercostal Artery Bleeding Complicated with Massive Hemothorax after Lower Limb Angioplasty Procedure

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Introduction: This is an extremely rare case of left massive hemothorax secondary to a spontaneous rupture of an intercostal artery. Presenting with a combination of hypovolemic and obstructive shock.

Case: A 42-year-old male with PMHx of polysubstance, and Buerger's disease presented with right lower limb ischemia. Patient underwent RLE angiogram and balloon angioplasty. Intraoperatively, he received 11,000 unit of heparin. In the PACU, he became unresponsive and went into a severe shock state, intubated and resuscitated with IV fluid and vasopressors. Examination showed absence breath sounds in the left lung. CTA chest showed large left hemothorax with linear contrast extending from the posterior second intercostal artery compatible with acute hemorrhage with right mediastinal shift. Massive transfusion protocol was initiated. Angiogram showed bleeding from the Lf posterior 2nd intercostal artery. Transthoracic arterial coil embolization was performed and successfully stopped the bleeding. Two left-sided chest tubes were placed and 1 L of frank blood was drained. Next day, his vitals were stable, and was extubated to room air.

Discussion: Spontaneous intercostal artery bleeding is extremely rare and reported in patients with underlying disorders, such as neurofibromatosis type 1, SLE, coarctation of aorta, Kawasaki disease, or Ehler-Danlos. High blood pressure or physical can trigger intercostal artery bleeding. We believe that our patient is the first reported case of spontaneous second intercostal artery bleeding in absence of underlying disorders. Being fully anticoagulated with high-dose heparin during the angioplasty and being agitated with forceful movement directly after weaning off the sedation might have caused the spontaneous rupture.

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Streptococcus intermedius - An Uncommon Cause of Severe Pulmonary Infections in Immunocompetent Patients

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Streptococcus intermedius is a Gram-positive, facultative anaerobe that is considered a rare cause of severe pulmonary infections in immunocompetent patients.

- Case1: A 69-year-old woman with PMHx of T2DM, and chronic dysphagia presented with worsening shortness of breath for one-week, high WBC, and CT chest showed left large, loculated pleural effusion with LLL consolidation.
- Case2: A 51-year-old woman with PMHx ADHD, depression, anxiety, and RA presented with pleuritic right-sided chest pain for 2 days, hypotension, tachycardia, high WBC, CT chest of the showed large right sided loculated hydropneumothorax with multiple consolidative opacities in right lung.

For both cases pleural fluid analysis was consistent with empyema, culture was positive for Streptococcus intermedius. Chest tubes were placed. Both patients responded to a combination of medical and surgical treatment and were discharged from the hospital in a stable condition.

Discussion: Streptococcus intermedius is commonly identified in abscesses of brain or liver. However, it is important causative agent of severe respiratory infections, including necrotizing pneumonia, lung abscesses, and empyema. S.intermedius is the causative of about 13-44% of pulmonary abscesses and/or cases of empyema, and accounts for around 2-5% of cases of bacterial pneumonia. Aspiration of oral secretion is the main risk factor. S. intermedius is generally susceptible to beta-lactam agents, including penicillins and cephalosporins, though some cases of resistance have been reported. In patients who are allergic or resistant to beta-lactam antibiotics, vancomycin may be considered an appropriate alternative. The duration of antibiotic therapy may vary from 2 to 4 weeks.

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Pulse Versus Nonpulse Steroid Regimens in Patients with Coronavirus Disease 2019: A Systematic Review and Meta-Analysis

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Background: Systemic steroids are associated with reduced mortality in hypoxic patients with COVID-19. However, there is no consensus on the doses of steroid therapy in these patients. Several studies showed that pulse dose steroids (PDS) could reduce the progression of COVID-19 pneumonia. However, data regarding the role of PDS in COVID-19 is still unclear. Therefore, we performed this meta-analysis to evaluate the role of PDS in COVID-19 patients compared to non-pulse steroids (NPDS).

Methods: Comprehensive literature search of PubMed, Embase, and Cochrane Library databases from inception through December 01, 2021 was performed for all published studies comparing PDS to NPDS therapy to manage hypoxic patients with COVID-19. Primary outcome was mortality. Secondary outcomes were the need for endotracheal intubation, hospital length of stay (LOS), and adverse events in the form of superimposed infections.

Results: A total of nine observational studies involving 2632 patients (1080 patients received PDS and 1552 received NPDS) were included. The mortality rate was similar between PDS and NPDS groups (RR 1.19, 95% CI 0.86-1.65, P=0.28). There were no differences in the need for endotracheal intubation (RR 0.71, 95% CI 0.37-1.137, P=0.31), LOS (MD 1.93 days; 95% CI -1.46, 5.33; P=0.26), or adverse events (RR 0.93, 95% CI 0.56-1.57, P = 0.80) between the two groups.

Conclusion: Compared to NPDS, PDS was associated with similar mortality rates, need for endotracheal intubation, LOS, and adverse events. Given the observational nature of the included studies, randomized controlled trials are warranted to validate our findings.

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Pembrolizumab-induced Pneumonitis

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Introduction: Pembrolizumab is a monoclonal antibody targeting the anti-programmed death protein 1, which is present on the surface of T and B cells. Here we present a case of a 47-year-old female with diagnosed with triple negative left sided invasive ductal carcinoma stage IIIC treated with several round of chemotherapy which included Pembrolizumab. The patient subsequently developed worsening respiratory functions requiring oxygen and eventually lead to intubation with ICU admission. After extensive workup the patient was diagnosed with Pembrolizumab-induced pneumonitis.

Methods: EMR records were gathered from hospital visits. Patient was physically seen throughout her hospital course. Images were gathered with patient consent from EMR.

Results: Following intubation the patient was transferred to a university-based hospital where she was treated with 500mg of prednisone for three days as well as ventilator support. Gradual improvement led to extubation with continued improvement in oxygen requirement.

Conclusion: Pembrolizumab induced pneumonitis is a rare but life-threatening complication.

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Reversal of Spironolactone-Induced Gynecomastia: A Review and Case Report of Spironolactone-Induced Gynecomastia

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Introduction: Gynecomastia, an enlargement of male breast tissue is a common, asymptomatic condition that increases with aging and obesity; however, the condition can be detrimental to one's mental health. Medications account for approximately 20-25% of the new cases of gynecomastia in adults, and the anti-hypertensive agent spironolactone. Eplerenone, a more selective aldosterone inhibitor compared to spironolactone, is cited as an alternative that can reverse spironolactone-induced gynecomastia in patients with hyperaldosteronism and cirrhosis. Therefore, we have reviewed the recent literature to assess the reports relating spironolactone-induced gynecomastia reversal after discontinuation of spironolactone and replacement with eplerenone, and we present a case of spironolactone-induced gynecomastia.

Methods: The PubMed database was queried to identify all original articles on this topic from January 1, 2005 through August 1, 2022 based on the search term "gynecomastia, spironolactone, eplerenone." A manual search of the works cited included original articles.

Results: The search yielded 42 articles. In total, 4 articles were included in the final review with a total of 204 patients. Systematic or meta-analytic reviews were excluded. All included studies demonstrated resolution of gynecomastia with discontinuation of spironolactone or replacement with eplerenone.

Conclusion: Based on the results of this review, it is clear that there is a significant gap in the literature pertaining to the importance of identifying and treating gynecomastia, and reversing spironolactone-induced gynecomastia in patients with heart failure and cirrhosis. Future studies should aim to investigate the therapeutic benefits of discontinuing spironolactone in medication-induced gynecomastia or replacing treatment with eplerenone.

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Use of Internal Standards to Develop Improved Methylation Detection in cfDNA

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Detection of aberrant levels and patterns of methylation in circulating free genomic DNA (cfDNA) may be useful in predicting the presence of malignancy in a particular tissue or in monitoring known malignancies for recurrence or treatment resistance. The goal of this study is to develop methods to improve accurate and sensitive detection of methylation in cfDNA utilizing synthetic spike-in internal standards (IS) that enable target- and assay-specific limits of detection and control for technical error. Initial testing of an off-the-shelf IS yielded promising results but, technical error increased as methylation increased, likely due to suboptimal IS design and experimental conditions. Next, a mixture of optimized IS for five targets known to be altered in cancer, SOX2, CDO1, TAC1, SOX17, and HOXA7, was created. Each IS was designed to be spiked into DNA, bisulfite-treated and measured in either hybrid capture or amplicon-based next generation sequencing libraries. Sequence changes (either A>T or T>A to avoid changes caused by bisulfite treatment) were introduced approximately every 50 bp to allow the IS to be distinguished from endogenous DNA. IS were cloned into plasmids, linearized, quantified and combined to create the IS mix. This IS mixture will be combined with a set of reference human genomic DNA samples obtained from the National Institute of Standards and Technology known to have differing levels of methylation such that the ratio of IS mixture:genomic DNA varies. These will be bisulfite-treated, used to prepare amplicon libraries and sequenced. Methylation, technical error and limit of detection will be assessed.

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Hyperpigmentation in Systemic Sclerosis

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Introduction: Systemic sclerosis (SSc) is a chronic multisystem autoimmune disorder that is associated with skin pigmentation disorders and vasculopathy. There seems to be a common origin to the development of vasculopathy and pigmentation disorders in SSc. A unique interplay exists between the potent vasoconstrictor peptide endothelin-1 and melanin synthesis. In this abstract, we present a case of diffuse hyperpigmentation and its relationship with recurring digital ulcers and severe Raynaud's in an SSc patient.

Methods: EMR records were gathered from the patients EMR and outpatient visits with patient consent. Images of the patient were taken with patient consent. The patient was physically seen throughout her hospital stay.

Results: Hyperpigmentation, particularly diffuse hyperpigmentation, has previously been linked to increase incidence of digital ulcers in SSc patients. Endothelin-1 has been established as a key mediator of vasculopathy in systemic sclerosis patients by acting as a potent vasoconstrictor and by inducing differentiation of fibroblasts, ultimately leading to fibrosis. The clinical manifestation of this in SSc patients is microvascular disease. It is hypothesized that increased endothelin-1 in SSc patients play a role in increased melanin synthesis in these patients. This is a lesser known feature of SSc, and both patients and healthcare providers should be educated of this association.

Conclusion: Hyperpigmentation is a rare feature of SSc, but when present, may indicate that the patient is more likely to develop future digital ulcers. This is a feature of SSc that should not be overlooked as it can potentially lead to earlier management of disease.

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Working To Understand Familial Lung Cancer And Its Genetic Underpinnings

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The primary focus of our research is to identify hereditary genetic variants that may predispose to lung cancer. In this study we processed blood and buccal swab samples collected from affected and unaffected members of families with statistically significant enrichment for lung cancer. DNA extracted will be sequenced and analyzed for variants associated with lung cancer risk. Blood or buccal swab samples were collected from individuals within lung cancer families. Samples were stored at -80 °C until sample processing. Specimen samples were processed using the Qiagen FlexiGene® DNA Kit or Gentra® Puregene® Buccal Cell kit. Purity was assessed through NanoDrop 2000 Spectrophotometry. A260/A280 spectrophotometry readings were obtained for DNA specimens from blood (N=59, mean=1.87, standard deviation 0.046) and buccal swabs (N=3, mean=1.94, standard deviation=0.08). Mean DNA yield for blood samples was 301 µg and for buccal swabs was 8.86 µg. The A260/A280 ratio assessed DNA purity, with a ratio of 1.8-2.0 generally accepted as optimal. Our average sample purity fell within this optimal quality range. The DNA yield required for genomic sequencing is 3 µg, so for blood specimens we have, on average, one hundred times more yield than is necessary, so excess DNA can be stored for future use. Meeting the quantity and quality standards, the DNA samples were shipped to the NIH Intramural Sequencing Center (NISC) for PCR-free whole genome sequencing. DNA variants identified through sequencing will be studied for association with hereditary lung cancer risk.

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Iatrogenic Horner's Syndrome Due to Chest Tube Compression during Decortication

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Background: Horner's syndrome is a condition classically presenting with unilateral ptosis, miosis, and facial anhidrosis resulting from disruption of sympathetic innervation. This may occur due to insults to the sympathetic chain in the head, neck, and thoracic cavity. We present an iatrogenic cause of Horner's syndrome due to compressive injury to the sympathetic chain by chest tube placement during decortication surgery.

Case Presentation: A 24-year-old woman with alcohol use disorder presented to the emergency department with chest pain and cough with heavy sputum production. Chest CT revealed a large left-sided pleural based opacity later confirmed to be empyema positive for Strep Constellatus by fluid culture. Despite seven days of chest tube drainage, antibiotics, and a 4-day course of intrapleural tPA and deoxyribonuclease, her left-sided fibrous lung entrapment failed to resolve and she underwent left thoracotomy with complete decortication. On postoperative day one, the patient was found to have unequal pupils and drooping of the left eye lid. Further examination revealed both pupils were reactive to light, however left pupil was sluggish. She denied any associated symptoms such as lacrimation, conjunctivitis, double-vision, facial droop. She was diagnosed with iatrogenic Horner's syndrome. The chest tube was withdrawn by two centimeters. She was initiated on oral prednisone 60 mg daily for 5 days. Significant improvement in symptoms was noted on day 5 from treatment initiation.

Discussion: Peripheral Horner's syndrome is rare complication that can occur with intrathoracic surgeries and chest tube placement. It is critical to recognize its symptoms and primary cause early in the postoperative course to initiate the proper intervention and to best counsel patients on the disease course.

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Fatal Case of Invasive Pulmonary Aspergillosis Post COVID-19 Pneumonia Due to Aspergillus Niger

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Introduction: Invasive pulmonary aspergillosis (IPA) including aspergillus tracheobronchitis mostly affects immunocompromised patients such as transplant or cancer patients. However, as the coronavirus disease 2019 (COVID-19) pandemic has developed, IPA has been increasingly reported in patients with severe COVID-19. The prevalence of COVID-19 associated pulmonary aspergillosis (CAPA) ranged from 0 to 33%. Most cases of CAPA reported in the literature are caused by Aspergillus fumigatus. However, only few cases of Aspergillus niger are reported in the literature. Herein, we describe a fatal case of CAPA caused by Aspergillus niger.

Case Presentation: 69 year old female with a history of diabetes mellitus type II was initially hospitalized for COVID-19 pneumonia that was treated with Remdesivir and Dexamethasone and later discharged to rehabilitation facility on two liters/minute of oxygen. Two weeks later, she presented with worsening shortness of breath, hemoptysis, and increased oxygen requirement. On admission, laboratory tests showed white blood cell count of 23.6/mm3, elevated C-reactive protein at 22.4 mg/L, and elevated procalcitonin at 0.42 ng/mL. Computed tomography (CT) of the chest showed diffuse ground glass infiltrates from prior COVID-19 pneumonia and a new cavitary lesion in the left upper lobe (Figure 1A). Patient was initially started on empiric antibiotics for suspected necrotizing pneumonia. Bronchoscopy revealed diffuse plaques overlaying the upper airway, trachea and all the major bronchi (Figure 1B) and bronchoalveolar lavage (BAL) cultures grew Aspergillus niger which was also detected in the endobronchial biopsies that were obtained. (1, 3)-β-D-glucan was 60 pg/mL and Aspergillus galactomannan antigen was detected on both serum and BAL. Voriconazole therapy was started after bronchoscopy. Despite the antifungal therapy, patient's clinical condition continued to decline, she was transferred to the intensive care unit where she was intubated and placed on mechanical ventilation for hypoxemic respiratory failure. Unfortunately, she developed multiorgan failure and expired on the same day.

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Discussion: Aspergillus fumigatus is the most isolated Aspergillus species in patients with CAPA. However, other species such as Aspergillus niger can be detected, as in our case. The possible etiology for CAPA may include host immune dysregulation due to T-cell perturbations, lymphopenia, and utilization of glucocorticoids. Given the overlap between the clinical features of COVID-19 and pulmonary aspergillosis, early diagnosis is challenging, in fact, often diagnosed post-mortem. Our case highlights the importance of including pulmonary aspergillosis in the differential diagnosis of COVID-19 patients presenting with relapsing respiratory failure and/or cavitary lesion.

Rare Case of Mantle Cell Lymphoma Presented as Malignant Pleural Effusion and Pleural Nodules

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Introduction: Mantle cell lymphoma is a relatively uncommon type of B cell non-Hodgkin lymphomas (NHL), it comprises about 7 percent of adult NHL in the United States and Europe with an incidence of approximately 4 to 8 cases per million persons per year. Most patients have advanced stage disease at diagnosis, presenting with lymphadenopathy, with only 25 percent present as extranodal disease such as gastrointestinal tract, breast, and orbit. Pleural involvement reported only in about one percent of cases.

Case Presentation: 53 year old male with past medical history of obesity and hypertension presented to the hospital with two weeks history of flank pain and shortness of breath. Chest X-ray revealed left sided pleural efusion. Computed tomography (CT) of the chest confirmed the efusion and also showed nodular pleural thickening. Computed tomography (CT) of the abdomen and pelvis showed left renal mass and multiple soft tissue masses with one measuring up to 4.5 cm on the right flank. Pleural fluid that was obtained by thoracentesis was noted to be bloody and exudative (LDH: 750 Units/L, Protein 4.7 g/dL, Glucose 12 mg/dL, Lymphocytes 70%). The cytology result of the pleural fluid was consistent with lymphoma. Medical thoracoscopy was done which demonstrated pleural nodularity and adhesions. Multiple pleural biopsies were obtained. Neoplastic cells obtained from the pleural biopsies stained positively for CD20, CD5, and CD10, cyclin D1 and SOX11. Cytogenetic FISH evaluation completed on the pleural fluid revealed an IgH/CCND1 variant translocation, and TP53. Simultaneously, the neoplastic cells identified within the biopsies taken from the left renal mass and right flank soft tissue mass were similar in histomorphology to the neoplasm identified in the pleural samples. Cerebrospinal fluid flow cytometry was consistent with central nervous system involvement. All the immunophenotypic and cytogenetic findings were consistent with a mantle cell lymphoma. Treatment plan included Cytarabine, Methotrexate, and CAR T-Cell therapy.

Discussion: Although pleural involvement is not uncommon in many types of lymphoma, it is rarely reported to be involved in mantle cell lymphoma which is on its own considered a rare form of B-cell non-Hodgkin lymphomas (NHL). We report a case of advanced stage lymphoma presented with malignant pleural efusion and direct involvement of the pleural space. The main treatment modality

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consist of combination chemotherapy plus immunotherapy (ie, chemoimmunotherapy) with or without high dose therapy and hematopoietic cell transplantation (HCT).

