Maryland ACP Winners from Mulholland Mohler Residents meeting 2021
Maryellen Woodward

AMERICAN COLLEGE OF PHYSICIANS – MD CHAPTER
MULHOLLAND MOHLER VIRTUAL RESIDENTS MEETING
May 6, 2021
1ST PLACE RESEARCH WINNER
Vinod Solipuram, MD
PROGRAM: St. Agnes Hospital
Co-Author(s) Associates:
Ruoning Ni MD, Roshniben Patel MD, Akhila Mohan MD.
Program Director’s Name: Sapna Kuehl, MD
The effect of JAK inhibitors and methotrexate combination on the risk of malignancy in patients with rheumatoid arthritis: systematic review and meta-analysis of randomized controlled trials
Introduction: Rheumatoid arthritis (RA) is a systemic autoimmune disease. The combination of methotrexate (MTX) and Janus kinase inhibitor (JAKi) therapy is commonly used in the treatment of RA patients who fail to improve with MTX alone. Patients with RA are at increased risk of malignancy; however, it remains unclear whether this combination regimen is associated with a higher risk. A systematic review and meta-analysis of the available randomized controlled trials (RCTs) was done to assess the risk of malignancy in this population.
Methods: PubMed, Cochrane and Embase were thoroughly searched for RCTs in patients with RA receiving JAKi and MTX, from inception of this combination as a mode of therapy to July 2020. The primary endpoints were malignancy events, non-melanomatos skin cancer (NMSC) and malignancy excluding NMSC. The secondary endpoints were serious adverse events (SAE) and death. The risk ratio (RR) and 95% confidence interval (CI) were calculated using the Mantel-Haenszel random-effect method.
Results: 659 publications were screened and 13 RCTs with a total of 6911 patients were included in the analysis. There was no statistically significant difference in the incidence of malignancy (RR = 1.42; 95% CI (0.59, 3.41)), NMSC (RR = 1.44 (0.36, 5.76)) or malignancies excluding NMSC (RR = 1.12 (0.40, 3.13)). No statistically significant difference between the two groups for SAE (RR = 1.15 (0.90, 1.47)) or death (RR = 1.99 (0.75, 5.27)) was found.
Conclusion: The addition of JAKi to MTX is not associated with an increased risk of malignancy when compared to MTX therapy alone. There is no increased risk of SAE or death in patients with RA who are receiving combination JAKi and MTX when compared to MTX alone.

AMERICAN COLLEGE OF PHYSICIANS – MD CHAPTER
MULHOLLAND MOHLER VIRTUAL RESIDENTS MEETING
6 May 2021
3rd PLACE RESEARCH
Zachary Haynes, MD
WALTER REED
Indicate your participation in research process:
I played an integral role in conceiving the research question and defining our initial outcomes of interest and analysis plan. Upon receipt of the finalized data, I assisted with its analysis and the preparation of the abstract and eventual manuscript for presentation/publication.
Co-Author(s) Associates:
Jacob Collen, Ian Stewart
Program Director’s Name: Joshua Hartzell
Obstructive sleep apnea after traumatic injury
Zachary A. Haynes*, Ian J. Stewart and Jacob F. Collen MDa,b
a National Capital Consortium, Bethesda, MD; b Uniformed Services University of the Health Sciences, Bethesda, MD
Purpose: Obstructive sleep apnea has become increasingly prevalent among military members in the past two decades despite being a generally healthy population with fewer traditional risk factors. We sought to determine the incidence and longitudinal predictors of obstructive sleep apnea in a large population of survivors of combat-related traumatic injury and a matched control group.
**Methods:** Retrospective cohort study of military service members deployed to conflict zones from 2002 to 2016 with longitudinal follow-up in the Veterans Affairs and Military Health Systems. Two cohorts of service members were developed: (1) those who sustained combat injuries and (2) matched, non-injured participants. Multivariable analysis, including risk factors and common comorbidities associated with trauma, was performed to control for confounders.

**Results:** 17,570 service members were followed for a median of 8.4 years. After adjustment, traumatic brain injury (HR 1.39, 95% CI 1.20–1.60), post-traumatic stress disorder (HR 1.24, 95% CI 1.05–1.46), depression (HR 1.52, 95% CI 1.30–1.79), anxiety (HR 1.40, 95% CI 1.21–1.62), insomnia (HR 1.71, 95% CI 1.44–2.02), and obesity (HR 2.40, 95% CI 2.09–2.74) were associated with obstructive sleep apnea. While combat injury was associated with obstructive sleep apnea in the univariate analysis (HR 1.25, 95% CI 1.17–1.33), the direction of this association was reversed in the multivariable model (HR 0.74, 95% CI 0.65–0.84). In a nested analysis, this was determined to be due to the effect of mental health diagnoses.

**Conclusions:** The incidence of OSA is higher among injured service members (29.1 per 1000 person years) compared to uninjured service members (23.9 per 1000 person years). This association appears to be driven by traumatic brain injury and the long-term mental health sequelae of injury.

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**MULHOLLAND MOHLER**

**VIRTUAL RESIDENTS MEETING**

6 May 2021

1ST PLACE CLINICAL VIGNETTE

Rawan Amir, MD

Institution: University of Maryland Medical Center & Baltimore VA Medical Center

Co-Author(s) Associates: Drs. Wadea AlKhonazei, Eric McWilliams

Program Director’s Name:

Dr. Susan Wolfsthal

Culture negative late prosthetic valve endocarditis unmasking an unusual diagnosis

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Libman-sacks (LS) endocarditis, also known as marantic endocarditis, is a rare cause of culture-negative endocarditis. It is most commonly associated with malignancies, followed by systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS). LS almost exclusively affects native valves with only one case reporting involvement of a bioprosthetic mitral valve. Herein we report the first case of mechanical valve LS endocarditis, which led to the unmasking of an unusual diagnosis.

A 46-year-old woman with primary infertility, labeled to have rheumatic heart disease, presented with fever and fatigue post mitral and aortic valve replacement. She was hemodynamically stable; physical examination revealed audible opening and closing clicks but was otherwise unremarkable. Labs showed ESR 130 mm/hr and CRP 15.9 mg/L. Transthoracic echocardiogram revealed mobile echo densities on the mitral sewing ring consistent with vegetations. She was hence diagnosed and treated as a case of prosthetic valve endocarditis despite blood cultures revealing no growth. However, failure to respond to treatment prompted further investigations into the causes of non-infective vegetations with a resultant antibody profile consistent with APS. It later became clear she had LS endocarditis associated with undiagnosed APS secondary to SLE.

LS lesions can be found in one out of every ten SLE patients and in nearly one-third of APS patients. It almost exclusively affects native valves with this case being the first to report mechanical valve involvement. LS is usually asymptomatic, yet it may be present with thromboembolic events or symptoms of the underlying condition. In retrospect, our patient had SLE & APS for years, which was missing in several institutions. Although married, her primary infertility prevented the classic symptom of recurrent fetal loss, which may have triggered an earlier diagnosis.

As physicians and caregivers, we are prone to clinical decision-making biases. In this case, premature closure bias occurred several times by assuming her problems were due to complications of valve replacements. With fever presentation, anchoring bias prevented physicians from exploring alternative causes of endocarditis and when multiple cultures were negative, confirmation bias compounded the problem and led to ignoring other possible explanations.

**AMERICAN COLLEGE OF PHYSICIANS – MD CHAPTER**

**MULHOLLAND MOHLER**

**VIRTUAL RESIDENTS MEETING**

6 May 2021

2nd PLACE CLINICAL VIGNETTE

John Preston Claiborne, MD

Institution: University of Maryland Medical Center & Baltimore VA Medical Center

Co-Author(s) Associates: Jonathan Na, MD; Yoon Kook Kim, MD

Program Director’s Name: Susan D. Wolfsthal, MD, FACP

Hemophagocytic lymphohistiocytosis secondary to suspected SARS-CoV-2 infection
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University of Maryland School of Medicine and VA Medical Center, Baltimore, MD

Hemophagocytic lymphohistiocytosis (HLH) is a rare syndrome precipitated by overactivation of macrophages and CD8+ T cells. There are familial and acquired variants of the condition with the latter commonly triggered by viral infections and certain malignancies. Clinically, it is characterized by acute onset of fever, multiorgan failure, hepatosplenomegaly, elevated ferritin and triglycerides, and evidence of hemophagocytosis. With treatment, the overall mortality from HLH is 40–75%

A 24-year-old man with no known past medical history developed headache and fever that progressed over twelve days to abdominal pain, diarrhea, jaundice, oliguria, and dyspnea. His initial symptoms began four days after exposure to an individual with possible SARS-CoV-2. On presentation, examination was significant for temperature of 39.9°C, O₂ saturation of 93% on six liters of O₂ via nasal cannula, scleral icterus, and hepatomegaly. Laboratory evaluation was notable for white blood cell count of 12.2/ mm³, hemoglobin of 13.7 g/dL, platelet count of 55/ mm³, aspartate aminotransferase of 3093 IU/L, alanine aminotransferase of 865 IU/L, INR of 2.6, creatinine of 5.32 mg/dL, ferritin of >50,000 ng/mL, triglyceride level of 1152 mg/dL, and fibrinogen level of 62 mg/dL. A computed tomography (CT) scan of the abdomen revealed hepatosplenomegaly. A bone marrow biopsy showed hemophagocytes. The patient’s HScore was calculated to be 285 points, indicating >99% chance of having HLH.

Investigation of predisposing factors for HLH included the following: 1) viral panel negative but with SARS-CoV-2 antibody positivity; 2) positron emission tomography/CT negative for increased uptake suggesting malignancy; 3) bone marrow biopsy gene analysis negative for lymphoma; and 4) HLH familial gene sequencing panel negative.

The patient required a brief course of intubation and continuous renal replacement therapy for respiratory and renal failure, respectively. HLH was treated with a five-day course of anakinra and intravenous immunoglobulin, followed by eight weeks of dexamethasone and etoposide, and twelve weeks of ruxolitinib with recovery to his baseline level of health, including his renal function.

HLH should be considered in the differential diagnosis of patients with acute onset of multiorgan failure, especially in those with known viral infection, including that by SARS-CoV-2, or known malignancy. After confirmation of HLH, early treatment of the underlying cause and immune activation is paramount to prevent death.

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**MULHOLLAND MOHLER**
**VIRTUAL RESIDENTS MEETING**
**6 May 2021**
**2nd PLACE RESEARCH**
**Abira Usman, MD**
**Sinai Hospital**

**Indicate your participation in research process (4 sentences or less):** Participant selection and consent. Specimen collection and processing in lab. Data input and interpretation. Primary author of abstract.

**Co-Author(s) Associates:**
Kevin Blden MBA, Alastair Cho, Naval Walia MD, Christophe Jerjian MD, Udaya Tantry PhD, Paul A. Gurbel MD

**Program Director’s Name:** Stephanie Sharps, MD

**Metformin use in patients hospitalized with COVID-19**

**Background:** Diabetes Mellitus (DM) is associated with a higher prevalence and increased mortality in patients with COVID-19. Metformin, a first-line glucose-lowering agent for the treatment of Type II DM, has been shown to exert anti-inflammatory and antioxidant effects on endothelial cells. New evidence suggests that metformin reduces mortality in COVID-19 patients, but the exact mechanism and causality remain unclear. Our aim was to assess the effect of metformin on markers of inflammation, oxidative stress and thrombosis and their potential relation to mortality and clinical outcomes.

**Methods:** Medical history, laboratory, and in-hospital clinical outcomes were collected from hospitalized COVID-19 patients with DM, who were metformin treated (n = 34) and metformin naïve (n = 41), and non-DM patients (n = 73) enrolled in the TARGET COVID-Study (NCT#04493307) between June 2020 and February 2021 at Sinai Hospital of Baltimore. Blood and urine samples for biomarker analysis of glycemic control, inflammation, ischemia and oxidative stress were collected within 48 hours of hospital admission. Comparisons between groups were made using ANOVA and unpaired T-Test.

**Findings:** The study population were predominantly minority groups (83%). Hypertension, cardiovascular disease, hyperlipidemia, HbA1c, and glucose were higher in the DM group (p < 0.05). DM patients treated with metformin had a lower intubation rate (5.8% vs. 24.4%, p = 0.03), less days hospitalized (12 ± 14 vs. 18 ± 19, p = 0.13), and lower mortality (8.8% vs. 22.0%, p = 0.12) compared to DM metformin naïve patients and had similar clinical outcomes compared to non-DM patients. By thromboelastography (TEG-6S), platelet-fibrin clot strength (measure of hypercoagulability) was highest in the DM metformin naïve group versus metformin and non-DM
groups [69.6 ± 4.1 vs. 68.6 ± 4.9 and 66.1 ± 6.3 mm, respectively (p < 0.002 for non-DM comparison)]. Metformin treated patients had a lower leukocyte count (8.6 ± 3.8 vs. 10.7 ± 3.8 K/mm3, p < 0.02) and D-dimer levels (1.8 ± 2.1 vs. 3.6 ± 4.5 mg/L, FEU, p < 0.04) compared to DM patients not on metformin. Urinary markers, 11-dehydro- thromboxane, 8-hydroxy-2’-deoxyguanosine and liver-type fatty acid binding were lowest in the DM metformin group and significantly lower than DM metformin naïve group (p < 0.05).

**Interpretations:** Metformin use was associated with improved outcomes, including mortality in patients admitted with COVID-19 and with lower levels of markers of inflammation, oxidative stress, and thrombosis as compared to DM patients not on metformin. Further, focused mechanistic studies are required to support these findings.

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**MULHOLLAND MOHLER**
**VIRTUAL RESIDENTS MEETING**
**6 May 2021**
**3rd PLACE CLINICAL VIGNETTE**
Sanjivani Shrestha, MD
**Institution: MedStar Health Internal Medicine Residency Program**
**Program Director’s Name: Stephanie Detterline, MD, FACP**

**Would you like some iced tea? A case of oxalate nephropathy**
Sanjivani Shrestha and Adam R. Berliner
MedStar Health Internal Medicine, Baltimore, MD

**Introduction:** Oxalic acid is an organic acid found in many foods like spinach, nuts, and tea. Oxalate is excreted by the kidneys, and in excess can lead to renal tubular deposition and acute kidney injury (AKI). We present a case of AKI requiring hemodialysis (HD) due to oxalate nephropathy from copious iced tea ingestion.

**Case presentation:** A 59-year-old man presented to the emergency department with bilateral lower extremity weakness, dry mouth and nausea for one month and decreased urine output for a week. He had a history of coronary artery disease, atrial fibrillation, type 2 diabetes mellitus, stage 3a chronic kidney disease, and laparoscopic sleeve gastrectomy. Examination revealed urinary retention requiring indwelling catheterization. Labs showed hyperkalemia (6.6mEq/L), AKI with BUN 105 mg/dL, creatinine 7.86 mg/dL (baseline creatinine 1.24 one month prior), normal anion gap metabolic acidosis, microscopic hematuria, and proteinuria. Further, labs showed low complement C3 (82 mg/dL), normal C4, negative hepatitis panel, ANA, ANCA, protein electrophoresis, anti-glomerular basement membrane antibody. Renal ultrasound is unremarkable. Differentials for AKI included bladder outlet obstruction, post-infectious glomerulonephritis (dental infection 5 weeks prior), acute tubular necrosis (ATN) or acute interstitial nephritis due to amoxicillin (prescribed after dental infection). Due to worsening renal failure and uremic symptoms despite supportive treatment, kidney biopsy was performed, and patient started on HD. Biopsy results revealed ATN and intra-tubular oxalate concretions consistent with oxalate nephropathy. Subsequent dietary history revealed that after dental infection, patient drank about 2 liters of iced tea daily. He was advised to stop iced tea and required outpatient HD, with eventual return of renal function after 8 weeks allowing liberation from dialysis with a residual serum creatinine of 1.9 mg/dL.

**Conclusion:** Our case highlights the importance of thorough dietary history in cases of AKI. Given the popularity of iced tea, patients and physicians must be aware of the potential for acute oxalate nephropathy.