

The Department of Internal Medicine Brody School of Medicine East Carolina University

Presents the

34th Annual Yash P. Kataria Internal Medicine Research Day March 18, 2020



34th Annual Yash P. Kataria Internal Medicine Research Day 2020

Wednesday, March 18th, 2020 10:00 AM – 4:00 PM East Carolina Heart Institute

Paul Bolin, Jr., MD

Professor and Chair Department of Internal Medicine

Research Day Advisory Committee Badih Kabchi, MD, Co-Chair Arjun Mohan, MD Co-Chair Cindy Kukoly Cathy Munson

"The glory of medicine is that it is constantly moving forward, that there is always more to learn. The ills of today do not cloud the horizon of tomorrow, but act as a spur to greater effort."

> William James Mayo Founder, Mayo Clínic



Department of Internal Medicine

34th Annual Yash P. Kataria Internal Medicine Research Day

Wednesday, March 18th, 2020

9:30am	Refreshments- ECHI Atrium & Conference Room	Poster Presentations available for viewing				
9:55am	Welcome – ECHI Auditorium	Paul Bolin, Jr., MD, Chair Department of Internal Medicine				
	Administrative Comments – ECHI Auditorium	Arjun Mohan, MD & Badih Kabchi, MD Co-Chairs Research Committee				
	First Oral Session, ECHI Moderator: Ogugua Ndili					
10:00am OP 1	CIRCULATING TUMOR DNA: A BIOMARKER FOR IMMUNOTHERAPY RESPONSE IN ADVANCED LUNG CANCER	<u>E Appah,</u> M Yogarajah, P Walker, M Muzaffar.				
10:15am OP2	RACIAL VARIATION IN MOLECULAR PROFILE OF ADVANCED GASTROINTESTINAL CANCERS	<u>S Macherla</u> , S Nandimandalam, S Jayananda, E Appah, A Bulumulle, S Baig, A Patel, S Polsani, M Muzaffar				
10:30am OP3	FACTORS INFLUENCING INPATIENT COLONOSCOPY BOWEL PREPARATION QUALITY	<u>S Poola.</u> N Jampala , E Ali				
10:45 am OP4	APOPTOSIS IN ALVEOLAR MACROPHAGES AND GRANULOMAS: A POSSIBLE ROLE OF OXIDIZED PHOSPHOLIPIDS IN SARCOIDOSIS	<u>E Soliman</u> , AEM Elhassanny, A Malur, K Kew, ON Obi, MJ Thomassen				
11:00 am	Keynote Address: ECHI	Auditorium				
	"How to Sugged in Clinical Desear	ah in the 21st Contum"				
	"How to Succeed in Clinical Research	-				
	Marc A. Judson, I					
	Professor of Medicino Chief, Division of Pulmonary and					
	Chief, Division of Pulmonary and Critical Care Department of Medicine Albany Medical College					
12:00pm	ECHI Conference I	Room				
	Lunch followed l					
	Poster Session (12:00 –	-1:45pm)				

Second Oral Session, ECHI Auditorium Moderator: Yuxuan Mao, MD

1:45pm	OP5	HIGH UTILIZATION RATE OF IMPLANTABLE CARDIOVERTER DEFIBRILLATORS AMONG VICTIMS OF OUT OF HOSPITAL PREMATURE NATURAL DEATH IN A LARGE RURAL COMMUNITY	<u>O Eboh.</u> V Okunrintemi, O Derbal, Y Mao, SM Hill, E Lee, A Naniwadekar, I Pursell, S Sears, J Mounsey
2:00pm	OP6	USE OF A TRAINED CANINE TO DETECT CLOSTRIDIOIDES DIFFICILE IN THE HOSPITAL ENVIRONMENT.	<u>R Harrison,</u> K Pittman, L Pittman, P Cook.
2:15pm	OP7	INFLUENZA VACCINATION RATES: DID WE DO BETTER?	<u>S Poola,</u> M Freiberg, R Kilgore, J Chu, A Laughman, R Narayan, M Turner
2:30pm	OP8	THE BURDEN OF HYPONATREMIA AND HYPERCALCEMIA ON HOSPITALIZATIONS AND MORTALITY IN LUNG CANCER PATIENTS IN THE UNITED STATES: AN ANALYSIS OF NATIONWIDE INPATIENT DATABASE	S Kamboj, V Kumar, W Acker, S Mazurkivich, C R Subramanian, M Muzaffar
2:45pm	OP9	THE SIX-MINUTE WALK TEST AFTER CRITICAL ILLNESS: A SYSTEMATIC REVIEW AND META-ANALYSIS	<u>SR Nalamalapu,</u> S Parry, K Nunna, A Rabiee, L Friedman
3:00pm	OP10	TREATMENT DELAYS WITH PEMBROLIZUMAB BASED REGIMENS AND SURVIVAL OUTCOMES IN ADVANCED NON SMALL CELL CANCER	<u>A Bulumulle,</u> K Sehgal, H Brody, R Gill, S Macherla, A Qilleri, D McDonald, C Cherry, M Shea, M Huberman, P VanderLaan, G Weiss, P Walker, D Costa, D Rangachari, M Muzaffar.
3:15pm	OP11	THE REAL-WORLD INCIDENCE OF IMMUNOTHERAPY- RELATED THYROID DYSFUNCTIN: A RETROSPECTIVE ANALYSIS OF A SINGLE CENTER'S EXPERIENCE OVER FIVE YEARS	<u>H Brody</u> , A Bulumulle, S Macherla, J Rahim, P Namireddy
3:30pm	OP12	ETHNIC MINORITIES EXPERIENCE INFREQUENT BIOLOGIC SWITCH DESPITE ACTIVE RHEUMATOID ARTHRITIS DISEASE	<u>EL Treadwell</u> , G Kerr
3:45pm		<i>Closing Remarks and Award I</i> Paul Bolin, Jr., MD, Chair, Department Yash P. Kataria, MD – Founder of the R	of Internal Medicine

	Poster Presentations, ECHI Conference Room Research							
PR1	MMP12-REGULATED TRANSCRIPTIONAL PROGRAMS IN ALVEOLAR MACROPHAGES OF A MURINE MODEL OF CHRONIC GRANULOMATOUS-INFLAMMATION	<u>D Ogburn,</u> A Mohan, A Malur, N Leffler, E Soliman, BP Barna, LM Schnapp, SA Gharib, MJ Thomassen						
PR2	GPR65 EXERTS ANTI-TUMORAL EFFECT DURING COLITIS ASSOCIATED COLORECTAL CANCER (CAC) DEVELOPMENT	MA Marie, EJ Sanderlin, LV Yang						
PR3	MECHANISMS OF GRANULOMA PERSISTENCE IN AN ANIMAL MODEL OF SARCOIDOSIS.	<u>S Bhalla</u> , E Soliman, A Mohan, M McPeek, N Leffler, K Linder, A Malur, MJ Thomassen						
PR4	G PROTEIN COUPLED RECEPTOR 4 REGULATES PARACELLULAR GAP FORMATION IN ENDOTHELIAL CELLS UNDER ACIDIC CONDITIONS.	<u>S Nik Akhtar,</u> EA Krewson, MA Marie, LV Yang						
PR5	THE NEMATODE <i>C. ELEGANS</i> AS A MODEL SYSTEM TO STUDY DEDIFFERENTIATION-MEDIATED TUMORIGENESIS	<u>Y Park</u> , S O'Rourke, FA Taki, MA Alfhili, MH Lee						
PR6	DURATION OF TRANSITION FROM INTRAVENOUS TO ORAL DIURETICS	<u>S Jain, </u> F Kaleta, P Singh, H Alhosaini						
PR7	NON-CANDIDACY FOR KIDNEY TRANSPLANT: AN EXPERIENCE FROM RURAL EASTERN NORTH CAROLINA	<u>S Dadzie</u> , G Samuel, R Alfarra, D Basuli						
PR8	FREQUENCY OF OBESITY COUNSELING BY PHYSICIANS	<u>S Poola</u> , N Jampala, L Matarese, J Powell						
PR9	TRENDS OF HOSPITALIZATIONS WITH INVASIVE FUNGAL INFECTIONS IN PATIENTS WITH ACUTE LEUKEMIA AND HEMATOPOIETIC STEM CELL TRANSPLANTATION FROM 2005- 2014 IN UNITED STATES	<u>S Kamboj</u> , H Elias, V Kumar, C R Subramaniam, M Muzaffar						
PR10	ASSOCIATION BETWEEN IMMUNE-RELATED ADVERSE EVENTS AND CLINICAL OUTCOMES TO PD-1/PD-L1 BLOCKADE IN SMALL CELL LUNG CANCER.	B Ricciuti, AR Naqash, J Naidoo, K Sehgal, A Miller, K Kehl, D Venkatraman, J Sands, G Lamberti, G Recondo, J Zhang, S Macherla, <u>S Baig</u> , P Walker, D Rangachari, J Gainor, DB Costa, N Rizvi, L Sholl, M Nishino, B Henick, A Farago, MM Awad						
PR11	ANTI-TUMOR EFFICIENCY OF HIGH SALT ACTIVATED CD4+T LYMPHOCYTES	<u>S Amara,</u> JC Rathmell, V Tiriveedhi						

Poster Presentations, ECHI Conference Room Vignette

PV1	DISSEMINATED GONOCOCCAL INFECTION	KM Catania, T Kerkering
PV2	FULMINANT VIRAL MYOCARDITIS SECONDARY TO INFLUENZA A	<u>KM Catania.</u> A Lagasca
PV3	GROUP A STREPTOCOCCUS BACTEREMIA CAUSING UPPER EXTREMITY CELLULITIS WITH BULLAE	<u>KM Catania, </u> K Ramsey
PV4	HISTOPLASMOSIS IN PATIENT WITH SARCOIDOSIS	WM Wooten, P King, P Cook, O Obi
PV5	CRYPTOCOCCUS NEOFORMANS OSTEOMYELITIS AND PSOAS ABSCESS IN AN IMMUNOCOMPETENT HOST	<u>SR Cowles</u> , S Thomas-Nadler, R Harrison, A Lagasca
PV6	NIVOLUMAB INDUCED HYPOPHYSITIS AND SECONDARY ADRENAL INSUFFICIENCY IN A PATIENT WITH METASTATIC RENAL CELL CARCINOMA	<u>SR Cowles,</u> L Yesaulava, C Uzoka, A Drake
PV7	LIFE THREATENING HYPOCALCEMIC TETANY IN PSEUDOHYPOPARATHYROIDISM TYPE 1B MIMICKING CLOSTRIDIUM TETANI INFECTION	<u>SR Cowles,</u> S Pathak, K Aziz, V Maddipati
PV8	THE ULTIMATE DECEIVER: A CASE OF RAPIDLY FATAL RETROPERITONEAL FASCIITIS	<u>H Labuschagne.</u> J Mullins, T Adeyemi, M Sahebazamani, C Brown.
PV9	DELAYED PRESENTATION OF AORTAESOPHAGEAL FISTULA.	<u>H Labuschagne,</u> D Pemmaraju, V Maddipati.
PV10	UNUSUAL CAUSE OF HEMIDIAPHRAGMATIC PARALYSIS.	<u>H Labuschagne</u> , S Awadallah, M Sahebazamani
PV11	UNCOMMON PRESENTATION OF TUMOR LYSIS SYNDROME IN ICU.	<u>S Pathak, A Badr</u> , BA Kabchi
PV12	ASSOCIATION BETWEEN SARCOIDOSIS AND MULTIPLE MYELOMA: A CASE REPORT AND REVIEW OF LITERATURE	<u>A Faisal</u> , A Kumar
PV13	THE COLLISION OF TWO CUTTING EDGE TECHNOLOGIES IN THE WORK UP OF A SOLITARY PULMONARY NODULE	<u>P King</u> , S Durrett, S Awadallah, MR Bowling, S Alqalyoobi
PV14	DYSPHAGIA: AN ALARMING SYMPTOM OF SARCOIDOSIS	<u>P King</u> , O Obi, M Sahebazamani
PV15	ACUTE NEGATIVE PRESSURE PULMONARY EDEMA IN THE SETTING OF AN UNDIAGNOSED GOITER	<u>L Kallur</u> N Brandon V Maddipati, M Sahebazamani
PV16	MITOMYCIN INDUCED PULMONARY VENO-OCCLUSIVE DISEASE	<u>A Kunadu,</u> H Labuschagne, A Gilleland, M Ritchie, V Maddipati

PV17	NASAL PERFORATION: A RARE COMPLICATION OF SARCOIDOSIS	<u>A Kunadu,</u> Y Kataria
PV18	THE CASE OF ASCENDING PARAPARESIS FOLLOWING NINTEDANIB (OFEV)	<u>A Kunadu</u> , S Alqalyoobi, O Obi
PV19	POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME AFTER RITUXIMAB INFUSION	<u>M Hafiz,</u> M Picton, V Ramsammy
PV20	RAMPED UP LUNG TUMOR	<u>M Blaj</u> , S Nalamalapu, M Sahebazamani
PV21	NOVEL THERAPEUTIC STRATEGY IN THE TREATMENT OF A BIOLOGICALLY COMPLEX NON-SMALL CELL LUNG CANCER	<u>C. Uzoka,</u> N. Sharma
PV22	MULTIPLE PRIMARY SYNCHRONOUS TUMORS AND SECONDARY ACUTE B-LYMPHOBLASTIC LEUKEMIA IN A YOUNG PATIENT	<u>SR Polsani</u> , A Weil
PV23	TENOFOVIR ALFENAMIDE CAN INDUCE RENAL TUBULAR WASTING	<u>E Primeaux,</u> H Lai, C Parker, R Obi
PV24	OUTCOMES OF MICROSATELLITE INSTABILITY HIGH GASTROINTESTINAL TUMORS AT A SINGLE INSTITUTION	<u>A Patel,</u> M Navaid
PV25	A DIAGNOSTIC HEADACHE IN A PREGNANT WOMAN WITH DIABETES INSIPIDUS: BLAME THE PLACENTA OR THE PITUITARY?	<u>K Aziz</u> , C Houston, B Ramirez, A Pokhrel
PV26	THAT'S NOT A GASTROINTESTINAL STROMAL TUMOR (GIST): A CASE OF A GASTRIC SCHWANNOMA	<u>M Kratzer</u> , J Kinderwater, S Poola, K Regan
PV27	ADVANCED PROSTATE CANCER WITH BRAIN METASTASIS: A CASE REPORT AND REVIEW OF LITERATURE	N. Mainkar, J Alcid, V Chaudhary
PV28	DOWNHILL BLEEDING ESOPHAGEAL VARICES AS COMPLICATION OF SUPERIOR VENA CAVA SYNDROME	<u>LF Rauseo Lopez,</u> JG Alvarez Posada, W Leland
PV29	APIXABAN AND PERITONEAL DIALYSIS, IS IT SAFE?	<u>RA. Jiwani</u> , FA. Faiz. WR. Badwan.
PV30	SEVERE VITAMIN B12 DEFICIENCY MIMICKING THROMBOTIC THROMBOCYTOPENIC PURPURA	<u>S Kumar</u> , H Brody, C Knupp
PV31	DERMATOMYOSITIS WITH ANTISYNTHETASE SYNDROME: AN INPATIENT DIAGNOSTIC ADVENTURE	<u>JG Alvarez Posada,</u> T Blair, JM Bermudez
PV32	GET SMASHED IN THE HOSPITAL: A CASE OF COMPLICATED PANCREATITIS	<u>ZS Hamedi</u> , S Poola, G Sheri, B Shahid
PV33	CARDIAC ARREST SECONDARY TO INTRATHECAL BUPIVACAINE INJECTION	<u>B Vadhar</u> , J Mullin, M LeDoux, L Lindsey, M Sahebazamani



In 2008, the Annual Departmental Research Day Program was dedicated and renamed the **Yash P. Kataria Internal Medicine Research Day** to honor the many contributions of Dr. Yash P. Kataria and to support the educational and research program in the Department of Internal Medicine at the Brody School of Medicine at ECU.

Dr. Kataria is Professor Emeritus of Medicine at BSOM and continues to contribute actively to the clinical, educational and research mission of the Pulmonary and Critical Care Division at BSOM. He was the first pulmonologist in eastern NC and helped to establish the pulmonary specialty at BSOM 30 years ago and has been an integral force since the inception of

the medical school. Yash was the first Division Chief of Pulmonary Medicine at BSOM and successfully recruited and established a clinical and active laboratory research program. Yash was the section head of pulmonary at BSOM /PCMH from 1978-1995, Vice Chair of the Dept. of Medicine 1987-1992 and Interim Chair 1986-87. Yash is of course known regionally, nationally and internationally for his passion in translational research with a particular focus on Sarcoidosis. He has authored over 70 publications, has received the Trudeau Award from the American Lung Association, Lifetime Achievement Award by the NC Thoracic Society, on many occasions been listed on the "Best Doctors" list, has been a reviewer and/or on editorial boards for numerous specialty journals.

Over his 30-year career, he has cared for thousands of patients with sarcoidosis and he arguably has one of the largest sarcoid cohorts in the US. Yash is revered by his patients and families. Yash has literally trained hundreds of medical students and house staff and is cherished by them as a role model and outstanding teacher at the bedside and in clinics. Yash has been a fixture in the international sarcoid community and has contributed actively at a leadership level at ACCP, ATS and WASOG. Scientifically, Yash is perhaps best known for promulgating a paradigm shift in our understanding of sarcoid immunology. While it was accepted dogma in the 70s that sarcoidosis was a disease of "depressed immunity" and anergy, Yash proposed and championed the concept that it is a pro-inflammatory disease with involvement of activated T-cells, cytokines, etc. Yash and his group also proposed that the active "sarcoid factor" was localized to the cell walls of alveolar macrophages and monocytes or an "autologous kveim" model (this remains an intriguing hypothesis!).

One of the missions of the medical school is community service in which medical school faculty plunged deeply. Yash lived in and loved Greenville where he raised two lovely children.

He was actively involved in the J H Rose Attendance Area Foundation Advisory Committee; also served as a Member Board of Academic Boosters Club, Rose High School, Greenville, NC and President, Parent Teacher Association, Greenville Middle School, Greenville, NC. He also helped to develop support groups for patients with sarcoidosis & COPD and played leadership roles in the local American Lung Association of NC. We are honoring Dr. Kataria by dedicating our annual Internal Medicine Research Day, which he started in 1987, to the **Yash P. Kataria Internal Medicine Research Day**. We will continue to build on the tradition of encouraging research by inviting leading guest speakers and facilitating scholarship and interaction by our trainees and faculty.



Keynote Address :

"How to Succeed in Clinical Research in the 21st Century"

Marc A. Judson, MD

Professor of Medicine Chief, Division of Pulmonary and Critical Care Medicine Department of Medicine Albany Medical College

Dr. Judson is a Professor of Medicine and serves as Chief of the Division of Pulmonary and Critical Care Medicine at Albany Medical College. Dr. Judson graduated from Stanford University before entering medical school at Vanderbilt University Medical School. His training continued in the New York City area, first at Montefiore Hospital Medical Center located in the Bronx, followed by a fellowship at NYU Medical Center. Dr. Judson then served in various positions at the University of South Carolina and the Medical University of South Carolina in Charleston before accepting his current position at Albany Medical College in 2011.

Dr. Judson has had a career-long interest in sarcoidosis. He has published ~ 250 papers and 40 book chapters, with more than 150 works concerning sarcoidosis. He has also participated in more than 40 sarcoidosis trials. He is the current Editor-in-chief of Respiratory Medicine: Focus on Sarcoidosis. He has previously served as president of the American sarcoidosis medical society (Americas Association of Sarcoidosis and Other Granulomatous Disorders – AASOG) and was a member of the Executive Committee of the international sarcoidosis medical society (World Association of Sarcoidosis and Other Granulomatous Disorders- WASOG). In addition to running one of the largest sarcoidosis clinics in the Northeast, Dr. Judson's interests include both interstitial lung diseases and fungal diseases of the lung.

When not at work, Dr. Judson enjoys cycling and completing all the puzzles in the Sunday New York Times.

The Keynote Address - Celebrating 34 Years

1987	<i>Morris Reichlin, MD</i> Professor of Medicine University of Oklahoma, School of Medicine	2004	Helen Burstin, MD, MPH Director of the Center for Primary Care, Prevention and Clinical Partnerships, Agency for Healthcare Research and Quality
1988	Jesse Roth, MD Director, Intramural Research National Institute of Diabetes and Digestive and Kidney Diseases, NIH	2005	Marschall S. Runge, MD, PhD Chair, Department of Medicine University of North Carolina at Chapel Hill President, UNC Physicians
1989	Roy Patterson, MD Professor and Chair Department of Medicine Northwestern University Medical School	2006	Jose Caro, MD Vice President, Endocrine Research and Clinical Investigation Lilly Corporate Center, Indianapolis
1990	Edward W. Hook, MD Professor and Chair Department of Medicine University of Virginia, Health Sciences Center	2007	<i>William Stratford May, MD, PhD</i> Chair, Hematology and Oncology Director, Shands Cancer Center University of Florida
1991	Albert F. LoBuglio, MD Director, Comprehensive Cancer Center Director, Division of Hematology/Oncology University of Alabama at Birmingham	2008	Phillip A. Bromberg, MD Bonner Professor of Medicine Scientific Director of the Center for Environmental Medicine, Asthma and Lung Biology University of North Carolina at Chapel Hill
1992	Raj K. Goyal, MD Harvard Medical School Chief Gastroenterology Division Beth Israel Hospital	2009	Randy L. Jirtle, PhD Professor of Radiation Oncology and Pathology Duke University Medical Center
1993	Richard E. Kerber, MD Professor of Medicine Associate Director Cardiovascular Division The University of Iowa College of Medicine	2010	Robert M. Lust, PhD Interim Associate Dean, Research and Graduate Studies Chair, Department of Physiology East Carolina University, Brody School of Medicine
1994	James S. Louie, MD Chief, Division of Rheumatology Department of Medicine Harbor-UCLA Medical Center	2011	David C. Goff Jr., MD, PhD Chair, Department of Epidemiology and Prevention Division of Public Health Services Wake Forest University School of Medicine
1995	Matthew I. Gilmour, B.SC., PhD Center for Environmental Medicine and Lung Biology University of North Carolina at Chapel Hill	2012	Vinay Kumar, MBBS, MD, FRCPath Donald N Pritzker Professor and Chair Department of Pathology University of Chicago
1998	O. Michael Colvin, MD William Singleton Professor of Cancer Research Director, Duke Comprehensive Cancer Center	2013	Paul W. Nobel , MD Chair, Department of Medicine Director, Women's Guild Lung Institute Cedars-Sinai, Los Angeles, California
1999	<i>Jerry Palmer, MD</i> Professor of Medicine Director, Diabetes Research Center University of Washington	2014	Vishva Dixit, MD Vice President Early Discovery Research Genentech, Inc.
2000	Thomas Feldbush, PhD Vice Chancellor for Research and Graduate Studies Dean, Graduate School East Carolina University	2015	Jerry R. Mendell, MD Curran-Peters Chair in Pediatric Research Professor of Pediatrics and Neurology Nationwide Children's Hospital and The Ohio State University
2001	<i>William B. Applegate, MD, MPH</i> Professor and Chair Department of Internal Medicine Wake Forest University School of Medicine	2016	<i>Manoocher Soleimani, MD</i> James F Heady Professor of Medicine Department of Medicine, Nephrology and Hypertension University of Cincinnati
2002	<i>William Roper, MD, MPH</i> Dean, School of Public Health University of North Carolina at Chapel Hill.	2017	Barbara Dudley Alexander, MD Professor of Medicine and Pathology Director, Transplant Infectious Diseases Service Duke University
2003	Jeffrey P. Engel, MD Division Head, General Communicable Disease Control State Epidemiologist, Division of Public Health NC Department of Health and Human Services	2018	Lynn M. Schnapp, MD Professor of Medicine Director, Pulmonary, Critical Care, Allergy and Sleep Medicine Medical University of South Carolina, Charleston

W. James Metzger, Jr., MD Award

The W. James Metzger, Jr., M.D. award is presented to the most outstanding presentation by a junior faculty member in the Department of Internal Medicine. A peer-review process selects the winner. The recipient of the award receives a certificate and has his/her name engraved on a plaque that is displayed in the Department of Internal Medicine Library. The recipient also receives recognition on the Department of Internal Medicine web site.

Dr. Metzger, a native of Pittsburgh, Pennsylvania, was a graduate of Stanford University and Northwestern University Medical School, Chicago, Illinois. He completed his residency and research fellowship in Allergy-Clinical Immunology at Northwestern University. After serving in the United States Air Force, he came to Greenville in 1984 to join the East Carolina University School of Medicine. During his tenure at East Carolina University, Dr. Metzger rose to the rank of Professor of Medicine. He was Section Head of the Section of Allergy-Immunology and held the appointments of Vice Chairman of Research, Department of Internal Medicine; Executive Director, the Center for Asthma, Allergy, and Immunology; Assistant Vice Chancellor for Clinical Research; Assistant Dean for Clinical Research; and Director, Clinical Trials Office. He was the recipient of the East Carolina University Award for Excellence in Research and Creative Activity and the Distinguished Research Professor of Medicine. His research was published in the New England Journal of Medicine, Nature, and other journals. Dr. Metzger had mentored numerous faculty and fellows.

In August 2000 Dr. Metzger accepted a position as Professor of Allergy, Asthma and Immunology at the National Jewish Medical and Research Center and was a faculty member at the University of Colorado Medical School, Denver, Colorado. He died on November 11, 2000 at the age of 55. Dr. Metzger represented excellence in research.

2001 Recipients: Carlos A. Estrada, MD, MS Paul Mehlhop, MD

> 2003 Recipient: Lisa Staton, MD

2004 Recipient: Cassandra Salgado, MD

2005 Recipient: Barbara J. Muller-Borer, PhD Cardiology

> 2006 Recipient: Timothy P. Gavin, PhD Human Performance

2007 Recipient: Christopher Newton, MD Endocrinology 2008 Recipient:

Li Yang, PhD Hematology/Oncology

2009 Recipient: Li Yang, PhD Hematology/Oncology

2010 Recipient: Sunil Sharma, MD Pulmonary

2011 Recipient: Sunil Sharma, MD Pulmonary

2012 Recipient: Maria Ruiz-Echevarria, PhD Hematology/Oncology

2013 Recipient:

Moahad Dar, MD Endocrinology 2014 Recipient:

Mark Bowling, MD Pulmonary

2015 Recipient: Hsaio Lai, MD Nephrology

2016 Recipient: Geoffrey Stroud, PharmD

Pharmacy-LJCC

2017 Recipient : Geoffrey Stroud, PharmD

Pharmacy-LJCC

2018 Recipient :

Li Yang, PhD Hematology/Oncology

2019 Recipient :

Nitika Sharma, MD Hematology/Oncology

ABSTRACTS for ORALS

In Presentation Order

OP = Oral Presentation PR = Poster Research PV = Poster Vignette

OP1

CIRCULATING TUMOR DNA: A BIOMARKER FOR IMMUNOTHERAPY **RESPONSE IN ADVANCED LUNG CANCER**

E Appah, M Yogarajah, P Walker, M Muzaffar

Background

Circulating tumor DNA (ctDNA) can be predicative of outcomes in lung cancer. Levels can correlate with changes in tumor burden in response to therapy. We assessed the utility of ctDNA as an early indicator of response to immunotherapy.

Methods

29 patients with advanced non-small cell lung cancer treated with immune therapy either alone or in combination with chemotherapy were enrolled in the prospective trial. Patients had baseline plasma samples collected prior to therapy and serially with the initial 4 cycles of therapy. ctDNA was assessed in plasma by ctDNA NGS assay for detection and quantification of genomic alterations in 36 genes commonly mutated in NSCLC. The trends of the ctDNA allele fractions were correlated with imaging responses post 4 cycles of therapy and subsequently with interval imaging.

Results

Of the 29 patients, 7 were not evaluable at the time of analysis. Twenty-two patients had evaluable imaging assessments which was done on completion of C4 and later at intervals determined by the treating oncologist. Clinical benefit was demonstrated in 16 (55%) patients (complete response (CR, n =4), partial response (PR, n = 5) or stable disease (SD, n = 7); 6 patients had progressive disease (PD). In patients achieving CR/PR, there was no detectable ctDNA at baseline (n=4) or there was complete clearance of ctDNA after completion of 4 cycles of immune therapy (n=4), except for 1 patient who had persistent ctDNA. Follow up imaging demonstrated continued beneficial responses, with most patients who had CR continuing to be in CR and patients who had PR persisting as PR or improving to CR. Patients with SD had varying levels of ctDNA. All 6 patients with PD had detectable or increasing ctDNA at progression.

Conclusions

Decrease or clearance of ctDNA during immune therapy correlated with positive responses. Absence of detectable ctDNA was indicative of overall a good response and prognosis. Increasing or newly detectable ctDNA was indicative of progressive disease or poor overall outcome.

Notes:			



RACIAL VARIATION IN MOLECULAR PROFILE OF ADVANCED GASTROINTESTINAL CANCERS

S Macherla, S Nandimandalam, S Jayananda, E Appah, A Bulumulle, S Baig, A Patel, S Polsani, M Muzaffar

Background: Heterogeneity in the tumor molecular profile based on race is poorly understood. We sought to review the utilization of next generation sequencing (NGS) in patients with advanced gastrointestinal (GI) malignancies treated at a rural academic center and analyze inter racial variations in the molecular tumor profile.

Methods: We conducted a retrospective review of patients with advanced GI malignancies that underwent NGS between 2015 to 2018 at East Carolina University, 104 patients met eligibility criteria, but 8 patients were excluded due to insufficient tissue sampling. Patients with colorectal, gastric, pancreatic, biliary, small intestinal and esophageal cancers were included. Targeted NGS using Caris Life Sciences platform was performed to obtain molecular analysis. We conducted descriptive univariate analysis. cox regression and Kaplan-Meier survival curve analysis.

Results: Median age at diagnosis was 64yrs and 64% of patients were black. The study cohort had 41% (39) with colon cancer, 18% (17) gastric cancer, 30% (29) pancreatic cancer, 6%(6) biliary cancer, 4%(4) small intestinal cancer and 1%(1) esophageal cancer. 60% (55) had De Novo Stage IV disease. Median overall survival (OS) was 25 months (mo), 30 mo in blacks and 32 mo in whites (p value =0.46). Microsatellite stability (MSS) was seen in 94% (87) and instability in 3% (3). Overall cohort had mutations(mut) in KRAS (50%), TP53 (64%), BRAF (4%), and ERBB amplification (3%). On the cox regression model APC mutation was associated with worse outcome. Black patients have more alterations in KRAS, TP53 (not significant), and APC (p=0.02).

Conclusion: In our analysis we observed inter racial variations in molecular profile of advanced GI malignancies. Black patients had increased rates of APC, KRAS and TP 53 mutations. Further studies are required to analyze the impact of these molecular variations on outcomes.

Notes:

OP3

FACTORS INFLUENCING INPATIENT COLONOSCOPY BOWEL PREPARATION QUALITY

S Poola, N Jampala , E Ali

Background:

Colonoscopy is highly sensitive for the visualization of the entire colon. Inpatient colonoscopies pose a special risk of poor preparation. We reviewed bowel preparation methods and patient factors to identify predictors of inadequate bowel preparation for inpatient colonoscopy at our institution. The purpose of this study was to identify factors that predict inadequate bowel preparation for inpatient colonoscopies.

Methods:

All patients ages >18 years of age undergoing inpatient colonoscopy in 2017-2018 were reviewed. The primary outcome was inadequate bowel preparation and secondary outcomes were successful cecal intubation, duration of colonoscopy, and hospital LOS. Outcomes were compared using multivariable regression with stepwise covariate selection.

Results:

The analysis included 315 patients (median age = 67 years; 45% female). Visualization was deemed adequate in 56%, fair in 27%, and poor in 17% of cases. Cecal intubation was successful in 84% of cases. The median duration of colonoscopy was 25 min and LOS was 2 days. Unsuccessful cecal intubation was most likely with poor visualization compared to adequate visualization (36% vs 11%, p=0.014). There was no increased colonoscopy duration with poor visualization (p=0.075). There was no significant LOS with worse visualization quality (p=0.185). Factors predicting worse visualization quality included older age, history of CHF, cirrhosis, and motility disorders. **Conclusion**:

At our institution, patients who were older or had significant co-morbid conditions (CAD, CHF, COPD, motility disorders, or cirrhosis) were more likely to have inadequate inpatient bowel preparation. Bowel preparation type did not affect the duration, quality of visualization, or successful cecal intubation.

OP4

14

APOPTOSIS IN ALVEOLAR MACROPHAGES AND GRANULOMAS: A POSSIBLE ROLE OF OXIDIZED PHOSPHOLIPIDS IN SARCOIDOSIS <u>E Soliman</u>, AEM Elhassanny, A Malur, K Kew, ON Obi, MJ Thomassen

Introduction: Sarcoidosis is a chronic granulomatous systemic disease of unknown etiology. Previous studies have reported that apoptosis is associated with sarcoid granulomatous inflammation, however, the cause of apoptosis and its role in sarcoid pathogenesis is unclear. Furthermore, sarcoidosis patients have systemic oxidative stress and impaired surface activity of lung phospholipids. Thus, we hypothesized that oxidative stress in the lung causes the formation of cytotoxic phospholipid oxidation products (OX-PL) which results in apoptotic cell death in sarcoidosis.

Methods: To test our hypothesis, we used a multiwalled carbon nanotube (MWCNT) model for sarcoid-like granulomatous inflammation. C57BL/6 mice were instilled with MWCNT or PBS (control) and sixty days following instillation bronchoalveolar lavage (BAL) cells were collected. Oxidative stress was measured in BAL cells with CellRox reagent and in BAL fluid and lung tissue homogenate using DCFDA reagent. Apoptosis was measured in BAL cells, lung homogenate, and lung sections using caspase 3/7 activity and TUNEL assays. Lipid was extracted from whole lung homogenate and phospholipids were detected using Tandem LC/MS. We also measured oxidative stress in BAL fluid from sarcoidosis patients and healthy controls using DCFDA reagent.

Results: MWCNT instillation increased reactive oxygen species (ROS) in BAL cells, BAL fluid (P=0.02) and lung tissues (P=0.0003). ROS levels were also elevated in BAL fluid of sarcoidosis patients when compared to controls (P=0.009). Extracted lipids from the whole lung homogenates showed increased levels of phosphatidylcholine (P=0.009) and oxidized palmitoyl arachidonyl phosphocholine (OX-PAPC) (p=0.005) indicating the oxidation of phospholipids in the lung. In addition, MWCNT-instilled mice showed significant apoptosis in both BAL cells and granuloma.

Conclusion: Human pulmonary sarcoidosis and sarcoid-like granulomatous inflammation in mice are associated with oxidative stress in the lung. ROS may increase the oxidation of phospholipids in lung surfactant resulting in macrophage apoptosis in BAL and granulomas.

Notes:			

Notes:

HIGH UTILIZATION RATE OF IMPLANTABLE CARDIOVERTER DEFIBRILLATORS AMONG VICTIMS OF OUT OF HOSPITAL PREMATURE NATURAL DEATH IN A LARGE RURAL COMMUNITY <u>O Eboh.</u> V Okunrintemi, O Derbal, Y Mao, SM Hill, E Lee, A Naniwadekar, I Pursell, S Sears, J Mounsey

Background: Implantable Cardioverter-Defibrillator (ICD) therapy is indicated for primary prevention of sudden cardiac death (SCD) in patients with LVEF<35% and NYHA class II heart failure, and in ischemic cardiomyopathy with LEVF<30%. Utilization rates are thought to be low, especially in socioeconomically disadvantaged communities and racial minorities, which could lead to excess SCD in unprotected patients. Since a majority of Out of Hospital Premature Natural Deaths (OHPND) are attributed to cardiovascular causes, we studied the penetrance of ICD implantation in OHPND victims that met the criteria for ICDs from a large rural community in Eastern North Carolina.

Methods: We identified 1,316 victims of OHPND in 2016 (18-74 years old, who died out of hospital from natural causes excluding cancer), from a total of 12,575 deaths registered in 29 counties of Eastern North Carolina (Population 1.4 million). We retrospectively reviewed the electronic records of the decedents and identified cases meeting standard criteria for ICD implantation. The utilization rate and reason for non-implantation of ICD were determined by chart review

Results: A total of 70 potential ICD candidates with LVEF <35% were identified. 31 (44%) had received an ICD. 11 (16%) did not receive an ICD due to comorbid conditions that limited life expectancy, 5 (7%) did not require an ICD because their LVEF improved with medical therapy, 6 (9%) were lost to follow up, 5 (7%) refused ICD placement, 1 (1%) was yet to commence guideline directed medical therapy, and 1 (1%) received a Life Vest. Only 10 (14%) eligible decedents did not receive an ICD.

Conclusion: Utilization of ICD has been reported to be low in rural communities, but our study shows only a small percentage of eligible rural OHPND victims failed to receive the device due to guideline nonadherence. Other reasons identified for non-implantation of ICD were decreased life expectancy due to co-morbid conditions and failure to follow up.

ODE	
UPO	

Notes:

15

USE OF A TRAINED CANINE TO DETECT CLOSTRIDIOIDES DIFFICILE IN THE HOSPITAL ENVIRONMENT

<u>R Harrison</u>, K Pittman, L Pittman, P Cook.

Background: Clostridioides difficile infection (CDI) is the most common nosocomial infection in this country. The organism forms spores, which likely contribute to spread of infection in the hospital setting. Current guidelines call for special cleaning of rooms following discharge of patients who tested positive for CDI. There are currently no means to validate that cleaning has eradicated all of the spores. Canines (dogs) have been used to detect a variety of odors because of their superior olfactory abilities. A beagle was trained to detect the odor of *C. difficile* in the hospital setting. Methods: C. difficile was grown at the microbiology department at Vidant Medical Center (VMC). Culture plates containing the organism were used by a professional trainer (KP) to train a two-year old female beagle dog. The canine was taught to sit when she identified the odor. The canine was given positive reinforcement with oral treats each time she identified the odor. Once the dog was proficient in identifying the organism, the trainer used clinical stool specimens that tested either positive or negative for C. difficile. Prior to coming into the hospital setting, the canine was able to identify positive stool samples with near 100% accuracy. The dog was brought to search rooms occupied or previously occupied by patients who had CDI. The canine was also used to detect the presence (sitting) or absence (no sitting) of C. difficile on hospital cleaning carts. The study was approved by the Animal Use and Care Committee at East Carolina University and took place between November 2019 and January 2020 at VMC.

Results: The canine detected the presence of *C. difficile* in 61% of 28 rooms inhabited by patients currently being treated for CDI and in 58% of 19 rooms previously inhabited by patients that tested positive for CDI. In all positive rooms, the organism was detected on the bedrails. The canine detected the presence of *C. difficile* in 60% of 15 cleaning carts. She did not detect *C. difficile* in any positive areas after they had been cleaned with bleach wipes. **Conclusions**: Training a canine to detect *C. difficile* is an effective means of detecting the organism in the hospital environment. Use of a trained dog appears to be effective in validating the cleaning process of rooms that have been previously occupied by patients with CDI.

Notes:			

OP7

INFLUENZA VACCINATION RATES: DID WE DO BETTER? S Poola, M Freiberg, R Kilgore, J Chu, A Laughman, R Narayan, M Turner

Introduction: Influenza (flu) is a severe but a potentially preventable infection. The inactivated vaccination produced before flu season helps to decrease the incidence of the flu. Eastern North Carolina has a diverse patient population with significant co-morbid conditions such as heart disease, chronic pulmonary disease, and diabetes where hospitalizations can be devastating. Vaccination rates continue to be low despite its known benefit. Last year the clinic implemented a three-pronged approach for increased vaccination rates and this year we hope by using our previous strategies to identify faults to our methods to improve the vaccination rates. Our aim is by April 1, 2020, greater than or equal to 80% of eligible adults and children who visit the Adult Pediatric Health Clinic (APHC) will receive the influenza vaccination.

Methods: By using the EPIC electronic health record (EHR) we can track month to month percentages of all APHC patients who have received the influenza vaccination. We will use the previous three approaches implemented last year to identify, screen, and prompt providers to vaccinate. Our second strategy will be to send MyChart messages to our clinic patients to inform them of the accessibility of the flu vaccinations. Patients who have the vaccination administered in the clinic will have this documented in the EHR. Using the EHR, percentages will be tracked on a month to month basis. Patients who have no documentation of receiving the vaccination or declining the vaccination will be flagged for their next clinic visit. Results: From all clinic patients registered for APHC last year (2018-2019 season) we were able to vaccinate patients 67% by January. When extracting data to patient seen by their primary care physicians at APCH, 82% of patients were vaccinated by January. This year we have been able to document vaccination in 78% of patients from August 2019 to January 2020. Future data will be available once the above methods are implemented. Conclusion: Our implemented practices did improve access to the flu vaccination, documentation of vaccination, and rates of vaccination. This year we need to continue to improve as our rates as we remain to be under our goal of 80%. We plan to identify patients that are not vaccinated or those who have received a vaccination to reach our goal of 80%.

Notes:			

OP8

THE BURDEN OF HYPONATREMIA AND HYPERCALCEMIA ON HOSPITALIZATIONS AND MORTALITY IN LUNG CANCER PATIENTS IN THE UNITED STATES: AN ANALYSIS OF NATIONWIDE INPATIENT DATABASE

S Kamboj, V Kumar, W Acker, S Mazurkivich, C R Subramanian, M Muzaffar

Abstract: Lung cancer is the most common cause of cancer-related death in the United States consisting of 25.3% of all cancer deaths. While the incidence continues to fall, the mortality continues to be high. It is important to identify factors which are associated with worse outcomes in these patients. Hyponatremia and hypercalcemia are noted in paraneoplastic syndrome. We aim to note the trends in patients hospitalized with lung cancer who have hyponatremia and hypercalcemia. **Methods**: We used the Nationwide Inpatient Sample (2002-2013) to identify lung cancer hospitalizations with hyponatremia and hypercalcemia. We analyzed trends in incidence, inhospital mortality, length of stay (LOS) and cost. We calculated adjusted odds ratios (aOR) for outcomes including in-hospital mortality. Results: A total of 1,404,228 lung cancer patient's lung cancer were hospitalized from 2005-2014. Number of admissions has been progressively declining from 159,568 in 2005 to 123,305 in 2014 with a relative decline of 21.8%. The overall incidence of hyponatremia in these patients was 8.62%, and it has been trending up from 6.79% to 10.48% (p < 0.001) from 2005-2014 with a relative increase of 57%. Hypercalcemia was reported in 2.59% of patients admitted with lung cancer. The number of hospitalizations in lung cancer patients with hypercalcemia has increased from 2.19% to 3.17% (p<0.001) with a relative increase of 49.3%. Hospitalizations for hyponatremia and hypercalcemia were more frequent in age 50-64 years, males and smokers. Lung cancer patients with hyponatremia and hypercalcemia had an in-hospital mortality of 12.9 % and 17.1% respectively from 2005-2014. Hypercalcemia and hyponatremia were associated with increased risk of in-hospital mortality (OR 1.15, p <0.001 for hypercalcemia and OR 1.43, p <0.001 for hyponatremia). Mortality with hyponatremia among patients with lung cancer decreased from 17.15 % in 2005 to 11.84% (p < 0.001) in 2014. In-hospital mortality for hypercalcemia also decreased from 21.3 % to 16.11% (p < 0.001) in a period of 2005-2014. Conclusion: This study found that hyponatremia and hypercalcemia are associated with increased risk of in hospital mortality and increase the cost of care in lung cancer patients. Utilization of these findings in guiding management may lead to decreased hospitalizations, hospital stays, and improve outcomes for these patients.

Notes:

THE SIX-MINUTE WALK TEST AFTER CRITICAL ILLNESS: A SYSTEMATIC REVIEW AND META-ANALYSIS

<u>SR Nalamalapu,</u> S Parry, K Nunna, A Rabiee, L Friedman, E Colantuoni, DM Needham, V Dinglas, V Ramsammy.

Background and Objectives: Intensive care unit (ICU) admissions are commonly associated with post-hospital impaired physical functioning that can negatively impact health-related quality of life. The six-minute walk test (6MWT) is validated and widely used to assess functional exercise capacity in studies of ICU survivors. We synthesized existing data to: (1) evaluate mean 6MW distance (6MWD) across studies with follow-up after hospital discharge for ICU survivors, (2) compare the 6MWD between acute respiratory distress syndrome (ARDS) versus non-ARDS survivors, and (3) evaluate 6MWT association with ICU and patient-related factors. Methods: Five electronic databases (PubMed, EMBASE, Cumulative Index of Nursing and Allied Health literature, PsychINFO, and Cochrane Controlled Trials Registry) were searched using a systematic, comprehensive, and reproducible search strategy to identify studies reporting 6MWT among general (non-specialty) ICU survivors after hospital discharge. Separate linear random effects regression models were used to calculate pooled mean 6MWT findings, and associations of ARDS status, and ICU-and patientrelated variables, over the available follow-up time periods. Results: A total of 26 eligible publications reporting on 16 unique participant groups with 1755 unique patients were included. The pooled mean [95% CI] 6MWD at 3- vs. 12-months post-hospital discharge were: 361 [321-401] vs. 436 [391-481] meters, respectively (p=0.017). In ARDS (7 studies) vs. non-ARDS (9 studies) survivors, the mean [95% CI] 6MWD difference over 3, 6, and 12-month follow-up was 73 [13-133] meters lower (P=0.019). Female sex and pre-existing comorbidity also were significantly associated with shorter 6MWD, with ICU-related variables having no consistent associations. Conclusions: Significant improvement in 6MWD was reported at 12- vs. 3month follow-up. Female sex, pre-existing comorbidity, and ARDS were each

month follow-up. Female sex, pre-existing comorbidity, and ARDS were each associated with shorter 6MWD results across follow-up time periods. These factors warrant consideration when designing clinical research studies and interpreting ICU survivors' functional status using the 6MWT.

Notes:

17

TREATMENT DELAYS WITH PEMBROLIZUMAB BASED REGIMENS AND SURVIVAL OUTCOMES IN ADVANCED NON SMALL CELL CANCER

<u>A Bulumulle,</u> K Sehgal, H Brody, R Gill, S Macherla, A Qilleri, D McDonald, C Cherry, M Shea, M Huberman, P VanderLaan, G Weiss, P Walker, D Costa, D Rangachari, M Muzaffar.

Objective To evaluate an association between survival outcomes and treatment extensions or delays of pembrolizumab-based regimens in advanced NSCLC

Methods: In this retrospective study, advanced NSCLC patients treated with pembrolizumab-based regimens for at least 4 cycles at two university centers were divided into two groups: non-standard (Non-Std: ≥ 2 cycles at intervals >3 weeks \pm 3 days) and standard (Std: ≤ 1 cycle >3 weeks \pm 3 days).

Results: Among 150 patients, 92 (61.3%) had received at least 4 pembrolizumab-based cycles (Non-Std: 27, Std: 65). Patients in the Std group was more likely to receive pembrolizumab along with chemotherapy and have lower PD-L1 tumor proportion score. Median OS was significantly longer in the Non-Std than the Std group [not reached] vs 17 months, as was median PFS 23 vs 7.

Conclusions : Our data, though limited by confounding by indication and sample size, shows that a significant proportion of advanced NSCLC patients received pembrolizumab-based regimens with extended intervals or delays and with no worse outcomes than expected for those receiving it at label-specified 3-week intervals.

Notes:			

THE REAL-WORLD INCIDENCE OF IMMUNOTHERAPY-RELATED THYROID DYSFUNCTIN: A RETROSPECTIVE ANALYSIS OF A SINGLE **CENTER'S EXPERIENCE OVER FIVE YEARS**

H Brody, A Bulumulle, S Macherla, J Rahim, P Namireddy

Background and Objectives: Immunotherapy related thyroid abnormalities are well described. Any grade abnormality has been reported in 6-18% of patients. The clinical relevance of thyroid abnormalities in a real-world setting is still unclear.

Methods: We retrospectively collected data for patients who received immunotherapy of any type from 2015 to 2019. We recorded the type of immunotherapy, abnormal TSH values, and grade of abnormality using the immune checkpoint inhibitor related adverse events Common Terminology Criteria for Adverse Events (IRAE-CTCAE), number of days from start of treatment to first noted abnormal TSH, and number requiring treatment with levothyroxine. At our center, we analyze thyroid function prior to starting immunotherapy and at every treatment.

Results: Of our 374 patients, 159 patients had some grade of thyroid dysfunction after receiving immunotherapy. Of the 374, 45 received atezolizumab (A), 5 received durvalumab (D), 155 received nivolumab (N), and 116 received pembrolizumab (P). Of the 159 patients with thyroid dysfunction, 23 received A, 81 received N, and 55 received P. Within these sub-groups, the majority of the adverse events were grade one, 74% in the A group, 57% in the N group, and 76% in the P group. Of these, zero were treated with levothyroxine. Grade two toxicities were seen in 22% in the A group, 31% in the N group, and 22% in the P group. Of these, a total of eight required treatment with levothyroxine. Average time to first abnormal was 97 days in the A group, 94 days in the N group, and 130 days in the P group.

Conclusions: In our population, 42.5% of patients had some grade of thyroid dysfunction which is higher than the previously reported, however, the majority of abnormalities were grade one and self-resolved. This may indicate that transient changes in TSH are common and not necessarily clinically relevant.

DP12

Notes:

18

ETHNIC MINORITIES EXPERIENCE INFREQUENT BIOLOGIC SWITCH DESPITE ACTIVE RHEUMATOID ARTHRITIS DISEASE EL Treadwell, G Kerr

Background: The expanded therapeutic modalities in rheumatoid arthritis (RA) provide options to achieve low disease activity or remission. Yet, in routine care, the frequency and choice of switching of biologic DMARD (bDMARD) amongst ethnic subsets when there is inefficacy, is unknown. The objective of this study was to evaluate frequency and choice of biologic switch in ethnic RA subsets.

Methods: Patients enrolled in the Ethnic Minority RA Consortium (EMRAC), with at least one followup visit were analyzed. Data included clinical outcomes as assessed by RAPID3 tender/swollen joint counts; medication use (prednisone, methotrexate, other DMARD), and bDMARD (Tumor Necrosis factor inhibitors (TNFi) and non-TNFi). Minimally clinical improvement (MCI) in RAPID3 was defined as decrease of >= 3.2 points during followup. Differences between medication usage, biologic switch, and RAPID3 improvement between race and ethnicity groups while on biologics, was investigated.

Results: 1040 subjects with 3719 follow-up visits over an average of 63.2 weeks were analyzed. African Americans (AAs) and Hispanics comprised 24% and 15%, respectively. Compared to Whites, AAs and Hispanics had significantly less education (P<0.001 for both), significantly less biologic use (P<0.001 for both) and significantly less TNF use (P<0.001 for both). African Americans had significantly higher RAPID3 scores at enrollment than Whites as well (P=0.018). Switching between TNFi and non-TNFi was recorded in only 9 subjects, with only 2 patients remaining within TNFi class. There was no statistical difference between race/ethnic groups in frequency of bDMARD switching, nor within bDMARD class, bDMARD treatment led to MCI in RAPID3 in 101(38%) subjects and in more AAs (29 [48%]) and Hispanics (12 [41%]) than in Whites (49 [37%]) (but not statistically significant). Conclusion: In our cohort, disparity was seen in bDMARD use between race and ethnic groups but with similar and infrequent biologic switch. Based upon these data, efforts to eliminate biologic use disparity remains paramount and supersedes concerns regarding disparity in biologic switching.

Notes:			

Page intentionally left blank.

ABSTRACTS for POSTERS

In Presentation Order

OP = Oral Presentation PR = Poster Research PV = Poster Vignette

MMP12-REGULATED TRANSCRIPTIONAL PROGRAMS IN ALVEOLAR MACROPHAGES OF A MURINE MODEL OF CHRONIC GRANULOMATOUS-INFLAMMATION

<u>D Ogburn,</u> A Mohan, A Malur, N Leffler, E Soliman, BP Barna, LM Schnapp, SA Gharib, MJ Thomassen

Background: We previously described a murine model in which multiwall carbon nanotubes (MWCNT) elicit a pulmonary granulomatous disease markedly similar to sarcoidosis and identified *Mmp12* in alveolar macrophages (AMs) as a critical modulator of this response. Using wildtype and *Mmp12*-null mice, we investigated the transcriptional response of AMs after MWCNT exposure in both genotypes in order to identify *Mmp12*-regulated genes and pathways in chronic granulomatous lung disease.

Methods: MWCNT were instilled oropharyngeally into wild-type C57BI/6 and *Mmp12*-KO mice. At 60 days post exposure, animals were lavaged and AMs were harvested. Total RNA was extracted, and RNA-sequencing performed. To elucidate pathways differentially activated in MWCNT-induced granulomatous disease in wildtype and *Mmp12*-KO models, we applied functional enrichment analysis. Gene product interaction network analysis was performed to discover key drivers of disease pathogenesis.

Results: Compared to wildtype, *Mmp12*-null mice exposed to MWCNT demonstrated significantly reduced granuloma burden. We identified 636 genes in wildtype and 571 genes in *Mmp12*-KO mice as being differentially expressed in AMs using a false discovery rate (FDR) threshold < 0.05. However, only 134 genes were commonly differentially expressed between the two genotypes, indicating significant alterations of the AM transcriptional response to MWCNT in the absence of *Mmp12*. Indeed, the most significantly up-regulated gene in *Mmp12*-KO MWCNT model, *Fst11* (follistatin-like 1), was not changed in wildtype mice treated with MWCNT (FDR: 1.4 x 10⁻⁵² vs. 0.23). Using a pathway-focused analysis, we found both common and divergent programs enriched in wildtype and *Mmp12*-KO mice exposed to MWCNT. While many immune-associated processes were commonly up-regulated in AMs of both genotypes after exposure to MWCNT, we observed over-representation of T cell-associated pathways in wildtypes relative to *Mmp12*-null mice.

Conclusions: Animal models of chronic granulomatous inflammation are important for delineating putative mechanisms in human sarcoidosis. By comparing an *Mmp12*-KO model that displays reduced granuloma formation after MWCNT exposure with wildtype mice, we identified distinct genes and transcriptional programs activated in AMs between the genotypes and found that in the presence of *Mmp12* (i.e., wildtype) there is widespread enrichment of T cell-associated pathways. Therefore, *Mmp12* may be a critical regulator of T cell function in sarcoidosis.

Notes:			

GPR65 EXERTS ANTI-TUMORAL EFFECT DURING COLITIS ASSOCIATED COLORECTAL CANCER (CAC) DEVELOPMENT MA Marie, EJ Sanderlin, LV Yang

Background: G-protein coupled receptors are the largest group of pharmacologically targeted receptors. GPR65 (also known as T-cell death-associated gene 8, TDAG8) is a proton sensing receptor predominantly expressed on immune cells. Genome-wide association study (GWAS) identified GPR65 gene polymorphisms as a potential risk factor in inflammatory bowel disease (IBD) patients. Patients with IBD are at a higher risk of developing colorectal cancer (CRC) than the general population.

Methods: To establish the chronic colitis mouse model, wild-type (WT) (n=13) and GPR65 -/- (n=13) mice were administered 3% DSS for four (5 days) cycles in drinking water, integrated by 2 days of water-only remission cycles. Following 4th cycle water was switched back to 3% DSS for 2 final days, then mice were euthanized. Real-Time PCR using TaqMan predesigned primer probe for β -actin and GPR65 was performed for Ulcerative Colitis (UC) and Crohn's Disease (CD) patients' samples. For the colitis associated colorectal cancer (CAC) model to be established, WT (n=21) and GPR65 -/- (n=21) mice were administered one dose of AOM *i.p.* (10mg/kg) followed by three (5 day) cycles of oral administration of 4% DSS integrated by water-only recovery cycles. Mice were euthanized between 13-14 weeks post-treatment for tissue collection and tumor assessment.

Results: Macroscopic investigation indicated a significant reduction in colon shortening, mesenteric lymph node expansion, and splenic extension in WT versus GPR65 ^{-/-} mice for both the chronic colitis and CAC murine models. Leukocyte infiltration, myofibroblast activation and tissue fibrosis were reduced in WT versus GPR65 -/- mice for chronic colitis and CAC murine models. Furthermore, tumor burden (represented in tumor number and tumor volume) was significantly reduced in WT compared to GPR65 -/- mice in the CAC model. In patient samples GPR65 expression was upregulated in both UC and CD IBD lesions in comparison to healthy individuals.

Conclusions: Our results indicate that GPR65 has a role in ameliorating chronic inflammation in the colitis mouse model. Moreover, GPR65 in the CAC murine model attenuates chronic inflammation and subsequent tumor development of CAC.

Notes:

PR3

MECHANISMS OF GRANULOMA PERSISTENCE IN AN ANIMAL MODEL OF SARCOIDOSIS.

<u>S Bhalla</u>, E Soliman, A Mohan, M McPeek, N Leffler, K Linder, A Malur, MJ Thomassen

Background: Sarcoidosis is a chronic inflammatory disease characterized by granuloma formation. In most patients, the disease resolves, however 30% have progressive disease. We established a murine model of granulomatous inflammation using multi-wall carbon nanotubes (MWCNT). Instillation of C57BL/6 wild type mice with MWCNT induced chronic pulmonary granulomas which persists up to 90 days post instillation. We have also shown that the MWCNT model bears striking similarities to sarcoidosis pathophysiology, including decreased expression of peroxisome proliferator activated receptor- γ (PPAR γ) in alveolar macrophages. PPAR γ serves a crucial role in inflammatory response of alveolar macrophages. We also found that PPARy deficiency increased granuloma formation and fibrosis in the lung with MWCNT at 60 days post instillation. Whether granuloma and fibrosis persist up to 90 days with PPARy deficiency is still unknow. We hypothesized that PPARy is a critical determinant for granuloma and fibrosis progression. To address this hypothesis macrophage specific PPARyKO mice were used.

Methods: MWCNT were instilled oropharyngeally into PPAR γ KO mice. At 60- and 90-days post instillation, lungs were lavaged or harvested for histology. Paraffin embedded lungs were evaluated. RNA was extracted from bronchoalveolar lavage cells and qPCR was performed. **Results:** Surprisingly histology in PPAR γ KO mice at 90 days showed significant reduction of fibrosis and resolution of granulomas when compared to 60 days (p < 0.0001). In addition, gene expression levels of profibrotic mediators SMAD3 and PDGF α were less in 90 days instilled mice when compared to 60 days instilled mice. To determine if the biodegradation and clearance of MWCNT is higher in PPAR γ KO mice, the number of alveolar macrophage phagocytosing MWCNT was measured at 90 days post instillation. Interestingly, PPAR γ KO mice have significantly less MWCNT-engulfed alveolar macrophages at 90 days when compared to 60 days post instillation (p < 0.0012). No significant difference was observed in wild type mice.

Conclusion: These results suggest that reduction in profibrotic mediators, SMAD3 and PDGF α , is critical for resolution of granulomas.

Notes:			
	 <u> </u>	 	

PR4

G PROTEIN COUPLED RECEPTOR 4 REGULATES PARACELLULAR GAP FORMATION IN ENDOTHELIAL CELLS UNDER ACIDIC CONDITIONS.

S Nik Akhtar, EA Krewson, MA Marie, LV Yang

Background: Acidosis is a hallmark of many pathophysiological conditions such as cancer, inflammatory diseases and ischemic tissues. Research is undergoing to understand the molecular mechanism by which acidosis contributes towards these pathophysiological conditions. Acid sensing G - Protein coupled Receptor 4 (GPR4) has been shown to be activated by extracellular protons. In this study we investigated the mechanism by which endothelial cells which express GPR4 endogenously regulate paracellular gap formation. To understand the molecular mechanism, we investigated the role of different inhibitors that influence G protein signaling and cytoskeleton structure. We hypothesize that activation of GPR4 by protons increases paracellular gap formation of endothelial cells.

Methods: Paracellular gap formation assay was conducted on Human Umbilical Vein Endothelial Cells (HUVEC). The cells were grown to a confluent monolayer. The day before the experiment the cells were treated with endothelial growth media adjusted at pH of 7.6. The cells then were treated with acidic and physiological pH for five hours. Every hour pictures of the confluent area were taken to assess gap formation and the percent of gap formation was analyzed. Inhibitors such as Thiazovivin (TA), Staurosporine (STA) and Cytochalasin D (Cyto D) were used to study the molecular mechanism using the same gap formation assay.

Results: HUVEC vector cells formed gaps under acidic condition. The percentage of gaps was ~4%. In HUVEC GPR4 overexpressed cells the percentage of gaps was higher around 12%. TA, STA and Cyto D inhibited gap formation of HUVEC cells under acidic conditions. More Actin stress fibers was observed in endothelial cells under acidic conditions compared to cells that were treated with physiological pH. TA, STA and Cyto D inhibited actin stress fiber formation.

Conclusion: Acidosis regulates paracellular gap formation in HUVEC cells. In HUVEC cells overexpressing GPR4, a greater percentage of gap is observed. Inhibitors such as TA, STA and Cyto D inhibited gap formation, indicating that acidosis/GPR4 increases paracellular gap formation by remodeling actin cytoskeleton through the Rho-associated kinase (ROCK) and myosin light chain kinase pathway.

PR5

THE NEMATODE *C. ELEGANS* AS A MODEL SYSTEM TO STUDY DEDIFFERENTIATION-MEDIATED TUMORIGENESIS Y Park, S O'Rourke, FA Taki, MA Alfhili, MH Lee

Background: PUMILIO/FBF (PUF) proteins have a conserved function in stem cell regulation. *C. elegans* PUF-8 protein inhibits the translation of target mRNAs by interacting with PUF binding element (PBE) in the 3' untranslated region (3' UTR).

Method and Results: In this work, an *in silico* analysis has identified *gld-2* (a poly(A) polymerase) as a putative PUF-8 target. Biochemical and reporter analyses showed that PUF-8 specifically binds to a PBE in *gld-2* 3' UTR and represses a GFP reporter gene carrying *gld-2* 3' UTR in the *C. elegans* mitotic germ cells. GLD-2 enhances meiotic entry at least in part by activating GLD-1 (a KH motif-containing RNA-binding protein). Our genetic analyses also demonstrated that heterozygous *gld-2(+/-) gld-1(+/-)* genes in the absence of PUF-8 are competent for meiotic entry (early differentiation), but haplo-insufficient for the meiotic division (terminal differentiation) of spermatocytes. Indeed, the arrested spermatocytes return to mitotic cells via dedifferentiation, which results in germline tumors.

Conclusion: Since these regulators are broadly conserved, we thus suggest that similar molecular mechanisms may control differentiation, dedifferentiation, and tumorigenesis in other organisms, including humans.

Notes:			

PR6

DURATION OF TRANSITION FROM INTRAVENOUS TO ORAL DIURETICS

S Jain F Kaleta, P Singh, H Alhosaini

Background: Approximately 5.7 million adults in the United States have a diagnosis of heart failure which is a significant hospitalization burden. Readmission rates for acute decompensated heart failure can be as high as 50% at 6 months from discharge. Volume overload remains one of the primary reasons why patients present to the hospital and require hospitalization. Though diuretics have become a cornerstone of heart failure management, there is very little evidence-based guidelines in regard to transitioning patients from intravenous to oral diuretics when they are admitted for acute decompensated heart failure. Methods: We reviewed patients admitted with the diagnosis of heart failure exacerbation in 2016 of all adult medical services. Patients were categorized based on their current severity of heart failure via NYHA class, ejection fraction, current heart failure medication regimen, pressor requirement, and prior hospital admissions from ADHF. Only cases where intravenous diuretics were utilized were included in this study. We analyzed the timing of diuretic transition from intravenous to oral therapy with respect to discharge. **Results**: We reviewed 319 patients; the average length of stay was 6.3 days with a range of 0 to 29 days. The average duration of intravenous diuretic usage was 3.4 days with a range of 0 to 23 days. The average duration of oral diuretic usage was 2.0 days with a range 0 to 12 days. Only 230 patients used single agent for diuresis. 106 patients used either intravenous or oral bumetanide while 124 patients used either intravenous or oral furosemide only. The other 89 patients used a combination of either furosemide, bumetanide, torsemide, spironolactone, and metolazone. Only 169 patients out of 319 patients had over 24 hours of oral diuretic usage prior to discharge. 155 if the 319 patients had 30-day admission rates and of those 155 patients, only 29 patients had PO diuretics for greater than 24 hours prior to discharge. **Conclusion**: This retrospective study highlights the variability of practice in regard to transition from intravenous to oral diuretics for heart failure exacerbation as we had suspected. Nearly half of these patients had readmission within 30 days with only 29 of these patient's being transition based on the AHA expect recommendations. This finding has prompted a guality improvement project at our institution to investigate who we can adhere more closely to these expect recommendations and hopefully reduce these readmission rates.

Notes:

NON-CANDIDACY FOR KIDNEY TRANSPLANT: AN EXPERIENCE FROM RURAL EASTERN NORTH CAROLINA

S Dadzie, G Samuel, R Alfarra, D Basuli

Background: Kidney transplant is the optimal therapy for the end-stage renal disease patients in order to improve the expectancy and quality of life. Recently there are many studies investigating how to improve the referral process to improve the access to kidney transplantation. However, there is not much data looking into the rate and causes disapproval of these referred patients by the transplant program to be activated in the waiting list. Thus it is important to study the disapproved population so that we can identify the barriers and intervene to improve kidney transplant rates.

Methods: The electronic health records of 309 ESRD patients undergoing dialysis by one major dialysis practice, East Carolina University were accessed manually to obtain information about the referral by the nephrologists for a transplant and the decision of the transplant selection committee. Disapproval rate for transplant was calculated by percent, and any disparities in disapproval was measured based on gender and race of the patients. Statistical analysis was conducted with t-test and a p<0.05 was considered significant.

Results: Our preliminary data shows although all ESRD patients were referred for transplant within 1 year of initiation of dialysis, about 63 percent of the referred ESRD patients were initially disapproved for further evaluation for a transplant. 40 percent of these patients were disapproved because of modifiable factors like smoking, alcohol abuse, overweight, not completing age appropriate screening tests. Only 40% of these patients were able to successfully modify the risk factors and were accepted as transplant candidates in following transplant evaluation visits. Interestingly, 83% of the disapproved patients were African Americans, and 41% were females.

Conclusion: Our reports shows that there are major barriers to transplant in ESRD patients in eastern North Carolina even after patients have been referred early. Majority of the disapproved patients were African Americans and only less than half of the patients with modifiable risk factors were able to be enlisted for transplant after proper intervention. More quality improvement endeavors are required to reduce the disparity in race and to support ESRD patients to overcome modifiable barriers to improve transplant rates in this population.

Notes:			

PR8

FREQUENCY OF OBESITY COUNSELING BY PHYSICIANS <u>S Poola</u>, N Jampala, L Matarese, J Powell

Background: Obesity is a growing epidemic that has significant morbidity and mortality. Healthcare in the United States has moved toward best practice quality metrics during office visits; however, obesity has yet to be a quality metric studied for improvement. Centers for Medicare & Medicaid Services (CMS) has specific guidelines on follow up and intense counseling for obese patients. The purpose of this study is to identify areas of improvement for screening and interventions for obesity in the primary and specialty care setting.

Methods: A survey of physicians at VMC/ECU teaching services was conducted to evaluate their practice of identifying obese patients during office visits, providing counseling, and arranging adequate follow up. **Results:** Eighty-six physicians responded to this survey, including primary care providers (n=70) and specialty care (n=16). Forty-nine (57%)respondents felt that the majority of their patient population were obese. Although 79% of responders felt they gave face-to-face counseling during clinic visits, only 6% counseled appropriately per CMS recommendations. Counseling included lifestyle modification, medications, surgery, nutrition and physical therapy referrals; the majority of respondents offered lifestyle modification, surgery, nutrition, and exercise program referral (99%, 51%, 77%, and 54%, respectively). Most physicians felt the barriers to obesity therapy included patient motivation and lack of access (78% and 51%). Only 22% felt that physician indifference was a barrier to obesity therapy, and 49% felt the lack of physician time was a barrier to therapy. The majority of the physicians surveyed were non-obese (BMI < 30, 87%). Fewer non-obese physicians cited indifference as a barrier to counseling compared to obese physicians (19% vs 45%).

Conclusion: This survey found that most primary care and specialty care physicians have counseled patients during office visits but do not abide by CMS recommendations. Barriers to counseling include patient motivation, compliance, lack of access, physician motivation, and lack of physician time. According to our survey, less than 50% of physicians felt the lack of time was a barrier to counseling and even less felt indifference was a barrier. CMS will pay for counseling in primary care setting and specialty care setting; therefore, this can be done in most clinics with appropriate staffing.

Notes:

PR9

TRENDS OF HOSPITALIZATIONS WITH INVASIVE FUNGAL INFECTIONS IN PATIENTS WITH ACUTE LEUKEMIA AND HEMATOPOIETIC STEM CELL TRANSPLANTATION FROM 2005-2014 IN UNITED STATES

S Kamboj, H Elias, V Kumar, C R Subramaniam, M Muzaffar

Background: Invasive fungal infections (IFI) are a cause of morbidity, mortality and increased health costs in patients with Acute Leukemia (AL) and hematopoietic stem cell transplant (HSCT). With this study, we aim to examine trends of IFI related hospitalizations in patients with AL and HSCT in theUnited States.

Methods: We utilized Nationwide Inpatient Sample (NIS) data from 2005-2014 and identified patients with AL (acute lymphoblastic leukemia and acute myelogenous leukemia) and HSCT hospitalization using ICD 9 CM codes. Patients with missing information on age, gender and mortality were excluded. Patients with age less than 18 years were excluded as well. IFI (candidemia, aspergillosis, zygomycosis) were identified by using appropriate ICD 9 codes in secondary diagnosis field. P-values for trends were generated using Cochran Armitage test.

Results: A total of 666,567 hospitalizations with HM were identified. Out of which 15,316 (2.31%) had IFIs. A majority were males (57.8%), Caucasian (58%) and belong to age group 50-64 (36.8%). Overall Incidence of fungemia was 2.3% and remained stable over 11 years (2.16% in 2005 to 2.2 % in 20114, relative increase = 7.25%, p trend-0.0064). Overall In-hospital mortality was 21.84% (unchanged over 11 years with a relative decrease of 8.1 % with p trend - 0.131). After stratifying for specific IFIs, in-hospital mortality for candidemia (35.0%), zygomycosis (26.51%) and aspergillosis (18.48%). None of whichhave changed over 11 years. In multivariate analysis, old age (age > = 65 years), female gender was associated with higher mortality and elective admissions were associated with lower mortality.

Conclusions: Despite much advances in fungemia treatment and prophylaxis, incidence and outcomes of IFI have not changed over last decade. Future studies to identify limiting factors are needed to provide crucial information to prevent fungemia and improve outcomes

Notes:			



ASSOCIATION BETWEEN IMMUNE-RELATED ADVERSE EVENTS AND CLINICAL OUTCOMES TO PD-1/PD-L1 BLOCKADE IN SMALL CELL LUNG CANCER.

B Ricciuti, AR Naqash, J Naidoo, K Sehgal, A Miller, K Kehl, D Venkatraman, J Sands, G Lamberti, G Recondo, J Zhang, S Macherla, <u>S Baig</u>, P Walker, D Rangachari, J Gainor, DB Costa, N Rizvi, L Sholl, M Nishino, B Henick, A Farago, MM Awad

Importance: The development of immune-related adverse events (irAEs) has been associated with improved efficacy of immune checkpoint inhibitors (ICIs) in patients with urothelial cancer, melanoma and non-small cell lung cancer. Whether this association exists in patients with small cell lung cancer (SCLC) is currently unknown. Objective: To evaluate the impact of irAEs on immunotherapy efficacy in SCLC. Design: Retrospective cohort study. Setting: This study was performed at six academic institutions in United States. Participants: A total of 183 patients with advanced SCLC who were treated with ICIs between July 2014 and December 2018 were included in this study. Exposures: The development of irAEs during treatment with PD-(L)1 inhibition alone or in combination with CTLA-4 inhibition. Main Outcomes and Measures: Kaplan-Meier methodology was used to estimate event-time distributions and log-rank tests were used to test for differences in event-time distributions. Taking into account the lead-time bias due to the time-dependent nature of irAEs, the development of irAEs was considered as a time-varving covariate in univariate and multivariate Cox proportional hazard models. Results: Among the 183 patients included, the median age was 64 (range: 34-84) and 103/183 (56.3%) of patients were female. In the entire cohort 73 (39.9%) patients experienced at least one irAE. The median time to irAEs onset was 24 days (IQR: 14-55). At a median follow-up of 24 months (95%CI:17.0-31.6), the median progression-free survival (mPFS) was significantly longer in the irAE group compared to the non-irAE group (3.8 versus 1.3 months, P<0.0001). The median overall survival (mOS) was also significantly longer among patients with irAEs compared patients without irAEs (13.8 versus 2.9 months, P < 0.0001). When analyzed as a time-varving covariate, the development of irAEs was associated with a significant improvement in PFS (HR:0.45 [95%CI:0.30-0.67], P <0.001) and OS (HR:0.46 [95%CI:0.31-0.68], P <0.001). Conclusions and Relevance: The development of irAEs is associated with improved clinical outcomes to ICIs in patients with advanced SCLC.

Notes:

ANTI-TUMOR EFFICIENCY OF HIGH SALT ACTIVATED CD4+T LYMPHOCYTES

S Amara, JC Rathmell, V Tiriveedhi

Background: Cell based immunotherapy is rapidly emerging as a promising alternative to conventional chemotherapy-based treatment for cancer. Previous studies have shown that high salt treatment induces naïve CD4+T lymphocytes to differentiate into a highly pro-inflammatory Th17 phenotype. In our current study, we analyzed the ability of salt treatment to induce cancer-specific Th17 lymphocytes.

Methods: Naïve CD4+T cells isolated by immunomagnetic bead isolation from splenocytes of 10-week-old mice were treated *in vitro* with high salt (Δ 0.05 M NaCl) along with CD3 monoclonal antibodies (mAbs), CD28 mAbs and IL-2 for 4 days along with heat killed 4T1 breast cancer cells. The isolated cells were tested for IL-17 expression by flow cytometry and determined to be >95% pure. Orthotopic murine tumor breast models established by injection of 4T1 cells into the mammary fat pad of Nu/J mice were administered two doses of (1 x 10⁶) salt induced Th17 cells on day 7 and day 12, post-tumor implantation.

Results: By day 28, the high salt induced Th17 cells cohort demonstrated significantly reduced tumor growth (97 \pm 34 mm³ vs 512 \pm 91 mm³, untreated control, p<0.05) and lung metastasis. However, no effect on tumor growth was noted when these 4T1 sensitized high salt treated Th17 cells were injected into Nu/J mice with prostate (RM1) and lung tumors (KLN205), thus suggesting that the specificity of salt induced Th17 cells to breast tumors. Similarly, in vitro high salt mediated differentiation of Th17 cells when co-treated with heat killed RM1 and KLN205 cancer cells were able to induce respective murine tumor regression. Mechanistic studies demonstrated that the high salt induction to the Th17 phenotype was mediated by the tonicity dependent transcription factor, NFAT5. The knockdown of NFTAT5 abrogated the induction of the Th17 phenotype and expression of pro-inflammatory cytokines IL-17, IL-1 β and IL-6.

Conclusion: Taken together, our data suggests that high salt mediated *in vitro* differentiation of Th17 cells could induce tumor specific anti-cancer CD4+T lymphocytes, which may give rise to a cell based anti-cancer immunotherapy application.

Notes:			

Page intentionally left blank.

DISSEMINATED GONOCOCCAL INFECTION KM Catania. T Kerkering

Objectives: The pathophysiology and predisposing factors that lead to disseminated gonococcal infections that can result in arthritis or arthralgias, tenosynovitis, and multiple skin lesions. Those on Eculizumab are at high risk and symptoms can worsen during menses.

Case Information: The patient is a 33 year old African American female with past medical history of hemolytic uremic syndrome requiring intermittent dialysis followed by a splenectomy and renal transplant in 2013 on Tacrolimus, Prednisone, Mycophenolate and Eculizumab who presented to the ED with complaints of acute onset of right foot pain followed by significant neck pain and stiffness. White blood cell count at the time of admission was 45,000 and imaging of her foot was negative. CT Brain was negative. Lumbar Puncture was performed and was significant for meningitis. Work up including blood and urine cultures were negative. No virus or fungi was detected in the CSF. Gonorrhea PCR from her CSF was sent out to confirm Disseminated gonococcal infection. The patient had a prior diagnosis of gonorrhea from a cervical swab two months prior. Her and her partner were treated.

Summary: Disseminated gonococcal infection (DGI) results from bacteremic spread of the sexually transmitted pathogen, Neisseria gonorrhea, which can lead to a variety of clinical symptoms and signs, such as arthritis or arthralgias, tenosynovitis, and multiple skin lesions. Eculizumab is a monoclonal antibody to C5 that is used in certain conditions, such as complement-mediated hemolytic uremic syndrome, and has been associated with severe meningococcal infections. Eculizumab could also increase the risk of DGI given the risk with other acquired complement deficiencies. Nevertheless, there have only been rare reports of DGI among patients treated with Eculizumab.Menses is associated with phenotypic changes of N. gonorrhea from opaque strains to transparent strains (those with altered membrane protein expression). Genital secretions during menses are more alkaline, which may facilitate gonococcal growth Increased concentrations of transferrin and heme at mucosal surfaces during menstruation may be used as a source of iron by N. gonorrhea.

 Notes:			

PV2

FULMINANT VIRAL MYOCARDITIS SECONDARY TO INFLUENZA A KM Catania, A Lagasca

Learning Objectives: Fulminant Viral Myocarditis. Risk factors for more severe disease in the setting of Influenza A versus Influenza B. The role of IV Peramivir versus Oral Peramivir in fulminant/critically ill. The role of IVIG and/or steroids in this setting.

Case Information: 43 year old Female with PMH of atypical hemolytic uremic syndrome and CKD on tapering Eculizumab after one episode of HUS. She presented to Carteret General with generalized body aches, nausea and vomiting and shortness of breath. She was swabbed positive for influenza A and received one dose of Oseltamivir prior to transfer for worsening kidney function and hyperkalemia. She was admitted to Vidant MIU but developed a large pericardial effusion and tamponade with transfer to the CICU. 200 cc removed with pericardiocentesis with 378 WBC (63% monocytes). Echo post drainage showed EF 20-25% with mild concentric LVH and was felt to be viral myocarditis. During her ICU course, she was found to be in a low cardiac output state and she was started on inotropic support. CRRT was started for renal failure. She eventually developed cardiac arrest and underwent ACLS with emergent cannulation for ECMO.EF has been <15% since code but just trace pericardial effusion. Her cardiac output remains very low. CRRT has been initiated. Her platelets continue to drop and she remains in hepatic and renal failure with bleeding from lines requiring FFP and cryoprecipitate. She is currently on Peramivir 600 mg IV daily x 5 days

Summary: Presumed fulminant viral myocarditis secondary to influenza A with cardiogenic shock and multisystem organ failure. Typical management (despite lack of randomized data) consists of IV antiviral therapy, steroids and IVIg. There are also concerns about oral absorption of PO Oseltamivir in critically ill. Peramivir once daily for 5 days is recommended as off label use in this situation. Large Cochran review demonstrating no benefit of IVIg in adults, but multiple case reports and case series as well as other data sets suggesting that it may be beneficial, particularly with known viral insult. More data in pediatrics. Steroids have not been demonstrated in a large Cochran review to provide a mortality benefit, but remains employed by most centers as it may improve cardiac function.

GROUP A STREPTOCOCCUS BACTEREMIA CAUSING UPPER EXTREMITY CELLULITIS WITH BULLAE KM Catania, K Ramsey

Learning Objectives: 1) The presentation, causes, and treatment of cellulitis. 2) The complications and surgical emergency that can be associated with severe cellulitis. 30 The need for testing and treatment of close family members if the cellulitis is secondary to Group A Streptococcus.

Case Information: The patient is a 46 year old female who was transferred from a referring hospital after presenting for left upper extremity swelling. erythema, left arm pain and fever. Her symptoms started in early December, and after they worsened over 2-days she presented to an emergency department. The erythema initially started along her left hand that progressively traveled up and is now involving most of his left upper extremity and left part of her back. She also has developed blisters, or bullae, that were tense and have progressively worsened in size and about 4-5 in number. She was initially hypotensive and required ICU care but then moved on to regular floor. At the outside hospital, her blood cultures were positive for Strep pyogenes and her antibiotics were changed to clindamycin and penicillin G. She reports that she had similar erythema in September along her left upper extremity and was treated for shingles, but later on she was told that she did not have shingles. Her pain, swelling and ervthema resolved on its own, but the severity of that episode was nothing in comparison to her pain, erythema and edema now. The patient was transferred for concern of sepsis due to Group A strep/cellulitis and concern for necrotizing fasciitis.

Summary: Considering the severity of her cellulitis with bullae, Plastic Surgery and Burn Surgery were consulted for care. There was concern for necrotizing fasciitis as well as compartment syndrome considering her clinical picture. No surgical intervention was performed. The patient was treated with Penicillin; however, due to the severity of her disease Clindamycin was added. Her daughter had a recent Strep throat diagnosis; thus, the whole family is likely passing this organism thru chronic carriage, and now a family member has presented with a very serious illness. We recommended that each of the immediate family unit undergo a throat culture, and treat if positive, to prevent further severe illness due to throat carriage.

HISTOPLASMOSIS IN PATIENT WITH SARCOIDOSIS WM Wooten, P King, P Cook, O Obi

A patient with sarcoidosis presented with persistent shortness of breath after being diagnosed with a virus and suspected sarcoidosis flare. He was treated with supportive measures and steroids, but did not improve. In a patient receiving immunosuppression to control an autoimmune disease, it is important to have a high suspicion for opportunistic infections.

51-year-old male with history of sarcoidosis was admitted three times in three weeks with fevers, chills, sweats, non-productive cough, and headaches. A computerized tomography (CT) of the chest showed extensive mediastinal/hilar adenopathy and worsening of pre-existing parenchymal lung disease. During the first two hospital admissions, the patient tested positive for coronavirus and was treated supportively. He was also treated with steroids for a possible flare of his sarcoidosis. Because of lack of improvement, fungal infection was considered. Cultures from bronchoscopy with bronchoalveolar lavage and transbronchial biopsy of the right upper lobe revealed Histoplasma capsulatum. Because of persistent headaches, the patient underwent a lumbar puncture which also demonstrated Histoplasma capsulatum in the cerebrospinal fluid. He was diagnosed with disseminated histoplasmosis and started on amphotericin B. Symptoms resolved and respiratory status returned to baseline. He completed about 1 1/2 weeks of amphotericin before being transitioned to itraconazole. He completed three months of itraconazole before being switched to posaconazole due to drug intolerances. Urine histoplasma antigen was undetectable at 6-month followup. Immunosuppressive regimen was judiciously decreased to balance controlling his sarcoidosis while decreasing his risk for reigniting the histoplasmosis future and developing opportunistic infections.

Histoplasma is found in the soil from bird droppings and typically in the Midwest. However, it can be found on the east coast, and patients receiving immunosuppression to control their respective autoimmune disease are at risk for fungal infections such as Histoplasma. These opportunistic infections must be ruled out before administering high-dose steroids, which can further exacerbate the acute illness and vastly increase mortality.

Notes:			

Notes:

CRYPTOCOCCUS NEOFORMANS OSTEOMYELITIS AND PSOAS ABSCESS IN AN IMMUNOCOMPETENT HOST

SR Cowles, S Thomas-Nadler, R Harrison, A Lagasca

Learning Objectives: Osteomyelitis is a rare manifestation of cryptococcosis. Notoriously encountered in those with advanced HIV, it may rarely present in immunocompetent hosts. Radiographic features may be nonspecific and may mimic tuberculosis or malignancy. We describe a case of extrapulmonary cryptococcal infection with osteomyelitis and psoas abscess in an immunocompetent host. Case Information: A 64-yearold African American male presented with left hip pain that progressed over 3 weeks. Medical history notable for non-Hodgkin lymphoma treated with rituximab 18 years prior. Vital signs were normal. Physical exam notable for inability to bear weight on left leg. Labs revealed an elevated erythrocyte sedimentation rate and C reactive protein at 107mm/hr and 31.0mg/L respectively. A CT left hip revealed ill-defined sclerotic changes in the left femoral neck possibly metastatic disease. MRI revealed L4 osteomyelitis and a left psoas muscle abscess. CT chest was notable for a spiculated left upper lobe nodule. Blood cultures were negative. Abscess aspirate cytology was negative for malignancy. The aspirate culture grew cryptococcus neoformans at day 5. QuantiFERON gold test. HIV test and hepatitis C antibody testing was negative. Serum cryptococcal antigen titer was high at 100. Cerebrospinal fluid revealed negative cryptococcal antigen, elevated white blood cell count at 83UL with elevated monocytes 97% and decreased lymphocytes 3%. Protein was elevated at 51mg/dL. He was treated with amphotericin B 5mg/kg intravenously daily and flucytosine 25mg/kg intravenously every 6 hours for 1 week followed by oral fluconazole 800mg daily for 6 months with resolution of hip and back pain. Summary: In this case, there was evidence of initial pulmonary inoculation which then disseminated to the skeleton through hematogenous seeding. There were no known provoking factors as our patient did not have symptoms of systemic infection, sarcoidosis and no known immunodeficiency.

Cryptococcosis should be considered in the differential diagnosis for sclerotic lesion in bone in addition to other pyogenic infections, tuberculosis and malignancy, especially those who present without signs of systemic infection. There are opportunities for researching the pathogenesis of cryptococcal infection in healthy individuals and identifying subpopulations at risk for disseminated disease.

Notes:			

NIVOLUMAB INDUCED HYPOPHYSITIS AND SECONDARY ADRENAL INSUFFICIENCY IN A PATIENT WITH METASTATIC RENAL CELL CARCINOMA

SR Cowles, L Yesaulava, C Uzoka, A Drake

Learning Objectives: Nivolumab is an IgG4 monoclonal antibody that blocks the PD-1 receptor and rarely induces complement mediated destruction of the pituitary. Vague symptoms of headache, fatigue and anorexia make hypophysitis a diagnostic challenge. We describe a case of nivolumab induced hypophysitis with acute adrenal insufficiency. Case Information: A 55 year old male with metastatic renal cell carcinoma presented with abdominal pain, nausea and vomiting for 3 weeks. Previously treated with a left nephrectomy. 4 cycles of ipilimumab/nivolumab 7 months prior and 2 cycles of maintenance nivolumab 8 weeks prior to presentation. On exam blood pressure was 81/50mmHg, somnolent with diffuse abdominal tenderness. Though initially fluid responsive, hypotension recurred with fever of 39.3 degrees Celsius and seizure. Head CT showed no acute findings or metastatic disease. Electroencephalogram showed no epileptiform activity. Cerebrospinal fluid cytology, chemistry and cultures were normal. There was concern for immune mediated cerebritis and high-dose Dexamethasone was initiated. A random serum cortisol level from specimen prior to administration of steroids was undetectable, confirming adrenal insufficiency. Adrenocorticotrophic hormone level and renin activity was low. MRI of the pituitary revealed thickening of the infundibulum consistent with hypophysitis. Hypothalamic Pituitary Thyroid axis was preserved. Hypothalamic Pituitary Gonadotrophin axis was consistent with primary hypogonadism. Dexamethasone was discontinued and physiologic replacement dose of hydrocortisone was initiated. His encephalopathy, abdominal pain and hypotension resolved with steroid administration. Summary: Our patient presented with classic symptoms of acute adrenal insufficiency due to hypophysitis from Nivolumab given 8 weeks prior. Pituitary MRI, testing thyroid and gonadal axes, along with cosyntropin testing is helpful in diagnosis. Corticosteroids should not be withheld for hormone testing in life threatening situation of acute adrenal insufficiency. The adrenal insufficiency with check point inhibitor hypophysitis may be irreversible, requiring lifelong corticosteroid replacement. With increasing use of immunotherapy in cancer treatment and vague initial symptoms, it is imperative to maintain clinical suspicion for development of hypophysitis and adrenal insufficiency and be aware of the diagnosis and management.

Notes:

LIFE THREATENING HYPOCALCEMIC TETANY IN PSEUDOHYPOPARATHYROIDISM TYPE 1B MIMICKING *CLOSTRIDIUM TETANI* INFECTION

SR Cowles, S Pathak, K Aziz, V Maddipati

Learning Objectives: Pseudohypoparathyroidism type 1B is characterized by hypocalcemia and hyperphosphatemia resulting from diminished renal cAMP response to the action of parathyroid hormone due to alterations in GNAS1 gene regulation. Management of acute hypocalcemia and tetany is infrequently encountered in this disorder and challenging to manage in setting of rhabdomyolysis. We present a rare case of hypocalcemic tetany from pseudohypoparathyroidism type 1b presenting with opisthotonos, risus sardonicus, rhabdomyolysis, shock and renal failure. Case Information: A 47-year-old male with pseudohypoparathyroidism type 1B was found on the floor, immobile and confused. Blood pressure was 68/49mmHg, pulse 130 and hypothermic. Exam revealed frontal bossing on head, opisthotonos, risus sardonicus, positive Chvostek and Trousseau signs and a distended bladder. EKG showed atrial fibrillation, peaked T waves and prolonged QTc at 592ms. Ionized calcium was 2.5mg/dL, potassium 6.4mEq/L, blood urea nitrogen 254mg/dL, creatinine 13.19mg/dL, creatinine phosphokinase 36,405 U/L, intact parathyroid hormone 139.5 mg/dL, total vitamin D 8.3ng/ml. CT head notable for bilateral basal ganglia calcifications. Continuous renal replacement therapy was initiated. Anti-tetanus immunoglobulin was administered. A calcium gluconate intravenous infusion was started at 2mg elemental calcium/kg/hr. Intravenous calcitriol 0.5mcg was administered daily. Tetany and encephalopathy resolved after 72 hours and his calcium infusion was titrated down by 0.2mg/kg/hr until serum calcium level was 8.0. He was discharged on 0.25mg oral calcitriol twice daily and calcium carbonate 1gram twice daily, ergocalciferol 50,000 units weekly and cholecalciferol 500 units daily was prescribed. This was decreased after 2 weeks to calcium carbonate 500mg twice daily to reduce risk of hypercalciuria. **Summary:** Those with pseudohypoparathyroidism may rarely develop hypocalcemic tetany and rhabdomyolysis mimicking clostridium tetani infection with opisthotonos. During rhabdomyolysis, calcium binds to damaged tissues exacerbating hypocalcemia. Treatment involves aggressive repletion of calcium intravenously and administration of calcitriol for goal serum calcium level of 8mg/dL. Oral calcium carbonate may be adjusted judiciously to avoid hypercalciuria and nephrolithiasis.

Notes:			



THE ULTIMATE DECEIVER: A CASE OF RAPIDLY FATAL RETROPERITONEAL FASCIITIS

<u>H Labuschagne</u>, J Mullins, T Adeyemi, M Sahebazamani, C Brown.

Learning Objectives: Retroperitoneal necrotizing fasciitis is a rare and rapidly fatal condition. Diabetic patients may be more susceptible to necrotizing fasciitis due to immunodeficiency associated with poor alvcemic control and tissue hypoxia. Emergency Computed Tomography (CT) may assist with early diagnosis. We report a case of rapidly fatal retroperitoneal necrotizing fasciitis in a young diabetic patient with non-specific CT findings. Case information: A 42-year-old female with uncontrolled Diabetes presented to the Emergency Department complaining of right sided low back and extremity pain, fever and chills for 2 days. Physical exam exhibited sinus tachycardia, right medial thigh tenderness and multiple excoriations on extremities. Labs revealed a leukocytosis of 19.8, negative rapid strep group A screen and creatine kinase (CK) of 86. Patient was discharged home after intravenous hydration. Two days later, patient returned to the ED with increased right thigh and back pain with difficulty in walking, diarrhea and global weakness. She was tachycardic and hypotensive. Physical exam revealed mild erythema and edema of the anterior thigh below the anterior inquinal ligament. Labs revealed lactic acid of 4.8, creatinine of 1.9 and CK of 20000. Throat culture grew group A strep. Abdominal CT revealed nonspecific retroperitoneal edema/fat stranding which extended to pelvis and presacral spaces. Psoas musculature was mildly prominent. Patient was admitted to ICU due to shock and concern for myositis. Patient continued to have increased vasopressor requirements with bulla formation on the skin and surgery was consulted. She underwent emergency surgery with extensive intraoperative findings of necrosis involving the anterior thigh and retroperitoneum. It was determined that this was not a survivable event and surgery was aborted. She subsequently died. Summary: The incidence of retroperitoneal fasciitis remains unknown with only a few case reports/series published. Group A Streptococcal retroperitoneal fasciitis is even more limited. Diabetes is a known risk factor for necrotizing infection. This condition is often under recognized since

cutaneous signs are absent initially with a resultant high mortality rate. Emergency CT can assist in the early recognition and extent of disease but surgical exploration is crucial for diagnosis.

Notes:

DELAYED PRESENTATION OF AORTAESOPHAGEAL FISTULA. <u>H Labuschagne</u>, D Pemmaraju, V Maddipati.

Learning objectives: Aortoesophageal fistula (AEF) is a rare but catastrophic cause of upper gastrointestinal bleeding. Secondary AEF is a serious complication following aortic repair with a vascular prosthesis, esophageal malignancy, radiation, or foreign bodies. Primary AEF occurs without former aortic manipulation. Clinically presents as a triad of midthoracic pain or dysphagia followed by a sentinel hemorrhage episode and delayed massive hematemesis. The prognosis for untreated AEF is universally grim. We report a case of secondary AEF with a fatal outcome. Case Information: 33-year-old Caucasian male with medical history of descending aortic transection post thoracic endovascular aortic repair (TEVAR) due to an accident in 2006, ANCA-associated vasculitis, and systolic heart failure was initially admitted for generalized weakness and worsening renal function that progressed to end-stage-renal-disease requiring hemodialvsis. He had a deep vein thrombosis of right lower extremity and was initiated on anticoagulation. However, two weeks later he developed hematemesis. Esophagogastroduodenoscopy showed a cratered esophageal ulcer in the upper third of the esophagus. Anticoagulation was held and proton-pump inhibitor therapy was initiated. Days after resuming anticoagulation, patient had massive hematemesis. Chest roentgenogram revealed a widened aortic arch and Chest Computed Tomography (CT) angiogram showed an aortic pseudoaneurysm with contrast extravasation outside the stent concerning for fistula. Barium swallow study confirmed AEF. He underwent emergent TEVAR for thoracic pseudoaneurysm. Patient was maintained nothing by mouth and total parenteral nutrition was administered whilst he awaited esophageal reconstruction. His protracted stay was further complicated by cardiac arrest with return of spontaneous circulation achieved after resuscitation and intubated for airway protection. Post-extubation, patient developed intractable vomiting with CT-angiogram revealing an aneurysm of the superior mesenteric artery not amenable to endovascular approach. The patient subsequently expired. Summary: Since the evolution of stenting for treatment of aortic pathologies, newer complications, such as AEF, ensued. AEF usually presents within a few months after TEVAR and should be ruled out in a patient presenting with upper gastrointestinal bleeding and prior history of aortic manipulation.

Notes:			

PV10

UNUSUAL CAUSE OF HEMIDIAPHRAGMATIC PARALYSIS. <u>H Labuschagne</u>, S Awadallah, M Sahebazamani.

Learning objectives: Hemidiaphragmatic paralysis is usually associated with surgical/traumatic injuries, malignancy or neurodegenerative disorders and rarely with viral infections. Diaphragmatic paralysis (DP) due to herpes zoster (shingles) is uncommon. DP is frequently asymptomatic and unrecognized. We report a case of an 82-year-old female who presented with exertional dyspnea after an episode of herpes zoster. Case information: 82-year-old female presented to our clinic for follow-up of obstructive sleep apnea and reported new onset exertional dyspnea since last visit. Medical history included atrial fibrillation, coronary artery disease. hypertension, and hypothyroidism. She reported a recent episode of cervical herpes zoster and developed dyspnea shortly thereafter. She denied recent surgery, trauma and weight change. Chest roentgenogram revealed an elevated left hemidiaphragm which was new compared to prior imaging. Chest Computed Tomography (CT) showed an elevated left hemidiaphragm without any other abnormalities. Hemoglobin and thyroid stimulating hormone level were normal. Mild restriction with normal diffusion capacity for carbon monoxide was noted on pulmonary function testing. Echocardiogram showed preserved ejection fraction with annuloplasty ring in the mitral position. Thus, other causes for her dyspnea were excluded. Diaphragmatic fluoroscopy with sniff testing confirmed hemidiaphragm paralysis. She continues to follow-up in clinic for conservative management of her dyspnea. Summary: Herpes zoster can affect any part of the central nervous system, but it has a predilection for the sensory system. It rarely affects the peripheral motor system either by direct invasion of anterior horn cells by the virus or diffusion of virus from dorsal route ganglia. At the C3-C5 level, this can lead to phrenic nerve palsy with resultant hemidiaphragmatic paralysis. Postherpetic DP is a rare entity but may be an underdiagnosed condition. Immunosuppression and older age are the most important risk factors for DP. Hemidiaphragmatic paralysis is usually an incidental finding on chest radiographs. Patients may be asymptomatic and some develop exertional dyspnea and/or decreased exercise tolerance. Other causes of DP such as malignancy should always be excluded. Unfortunately, in the vast majority of reported cases of postherpetic DP, there was no resolution. Treatment of DP is mainly supportive. Close follow-up is recommended.

Notes:

UNCOMMON PRESENTATION OF TUMOR LYSIS SYNDROME IN ICU. <u>S Pathak, A Badr</u>, BA Kabchi

Background: The lysis of malignant cells results in a profound release of cellular contents, most common in hematologic malignancies after chemotherapy and usually mild in severity. Tumor lysis syndrome (TLS) is a constellation of metabolic derangements including hyperuricemia. hyperkalemia, hyperphosphatemia, and hypocalcemia, usually initiated by cytotoxic chemotherapy. We describe a patient who developed severe TLS after carboplatin/paclitaxel for high-grade endometrial adenocarcinoma. **Case:** A 61-year-old female presented to hospital with abdominal pain one after her third cycle of chemotherapy with paclitaxel/carboplatin for recently diagnosed stage IV endometrial adenocarcinoma. Initial work up showed leukocytosis with neutrophilia, hyperphosphatemia, hyperkalemia and hyperuricemia. Patient rapidly declined requiring vasopressors, mechanical ventilation and admission to ICU. On arrival to unit labs showed pancytopenia, creatinine 3.0 mg/dL, potassium 6 mEg/L, phosphate 10.7 mmol/L, calcium of 6 mg/dL, and uric acid of 14.7 mg/dL. Continuous renal replacement therapy was initiated. CT of abdomen/pelvis showed endometrial gas bubbles concerning for tumor necrosis vs infection. All cultures remained negative. Surgical and medical oncology services were consulted, and suspicion was low for tumor lysis syndrome due low incidence in solid malignancies and usual benign course. Bowel ischemia or sepsis were considered more likely. Surgery was not offered due to high mortality. Patient was made do not resuscitate and despite maximum treatment passed away on day four of hospitalization. Discussion: In a ten-year retrospective study TLS was found to have a 5% incident rate in gynecologic cancer (GOC). 94% of the cases were associated with high-grade GOC. Two-thirds of patients with TLS died. Laboratory criteria for TLS include uric acid > 8mg/dL potassium > 6 mEg/L, phosphorus > 4.5 mg/dL, and calcium < 7 mg/dL. Clinical TLS is graded on a scale of 0-5, with 0 being asymptomatic and 5 being death. Shock is a criterion of grade 4 and creatine > 3 times the upper levels of normal is a criterion of grade 3. In severe cases, electrolyte abnormalities should be managed with dialysis. Rasburicase can aid in hyperuricemia. In closing, TLS is rare with GOC however can be associated with significant mortality. Hence, TLS is an oncological emergency. Early recognition and prompt management is paramount to improve outcomes.

Notes:			



ASSOCIATION BETWEEN SARCOIDOSIS AND MULTIPLE MYELOMA: A CASE REPORT AND REVIEW OF LITERATURE A Faisal. A Kumar

Learning Objectives: This case highlights the association between sarcoidosis and plasma cell disorders. It also illustrates the diagnostic challenges associated with atypical presentation of sarcoidosis and concurrent presence of multiple myeloma.

Case Information: A 59-year-old male presented with complaints of nausea, vomiting, diarrhea and shortness of breath for 7 days, CBC showed abnormal WBC (1.3x10^3/uL), Hemoglobin and platelets were normal. CMP showed acute renal injury with Cr of 7.28mg/dL and hypercalcemia with Ca levels of 12.1mg/dL. Peripheral smear showed neutropenia with leukopenia and relative monocytosis. CT scan of the chest showed peri lymphatic nodules with mediastinal and hilar adenopathy. There were no skeletal lytic lesions. Extensive work up ruled out infection, rheumatologic, endocrinologic causes for these lab abnormalities. Renal work up for vasculiditis was negative as well. SPEP was notable for a monoclonal band which was shown to be IgG-kappa by immunofixation. Serum immunoglobulin levels showed a high IgG level of 2417 mg/dL, IgA 147 mg/dL, IgM 33 mg/dL. UPEP with immunofixation showed modest proteinuria. Serum kappa free light chain was 771 mg and serum lambda free light chains were 13.44 mg/dL. Bone marrow biopsy showed 27% plasma cells. Bronchoscopy demonstrated presence of non-caseating granulomas suggestive of sarcoidosis. A renal biopsy was also performed and showed diffuse interstitial granulomatous nephritis confirmatory for sarcoidosis. Patient was started on steroid therapy with 30 mg of daily prednisone for his diagnosis of sarcoidosis involving the lung and kidney. Since he was visiting from another state, he preferred to undergo treatment at a local hospital for further management.

Summary: We found 16 reported case of concurrent multiple myeloma and sarcoidosis in the literature. Retrospective summative analysis of existing literature suggests a possible association between sarcoidosis and plasma cell disorders. Whether sarcoidosis is a primary insult, or a secondary phenomenon remains unclear.

Notes:

THE COLLISION OF TWO CUTTING EDGE TECHNOLOGIES IN THE WORK UP OF A SOLITARY PULMONARY NODULE

P King, S Durrett, S Awadallah, MR Bowling, S Alqalyoobi

Learning Objectives: A left ventricular assist device (LVAD) is a complex, highly advanced therapy offered to very select patients. Pursuing bronchoscopy in these individuals requires meticulous consideration of parameters such as sedation and hemodynamic monitoring in an otherwise routine procedure. Electromagnetic Navigational Bronchoscopy (ENB) allows for sampling of peripheral lesions. The LVAD's complex technology could potentially interfere with the mechanics of this tool, thereby leading to misdiagnosis and delay in patient care. To our knowledge, ENB has never been used in a LVAD patient, and here we present the first reported case.

Case Information: A 71-year old female with a LVAD (HeartMate II[™]) placed as destination therapy for severe heart failure presented with cough and dyspnea for four weeks. A Computed Tomography (CT) of the chest showed an 8mm semi-solid right upper lobe (RUL) pulmonary nodule located 2.5cm from the pleura in a patient at high risk for malignancy. A Positron Emission Tomography (PET) scan revealed hypermetabolic activity in the RUL and mediastinal and hilar lymph nodes (LN) concerning for malignancy. She arrived at the endoscopy suite accompanied by two large battery packs to maintain power to the LVAD. Hemodynamic monitoring was accomplished using non-invasive blood pressure cuff and transcutaneous pulse oximetry, and standard medications for moderate sedation were administered. ENB was used to localize the lesion, successfully obtain biopsies, and place fiducial markers. The patient tolerated the procedure without complications.

Summary: ENB and LVAD technologies have been used in clinical practice for several years. However, the combination of these entities has been unheard of until this case and offers unique considerations and challenges. Procedural sedation in LVAD patients can lead to hemodynamic compromise. Also, while interference from external sources of electricity in LVAD patients has notoriously been a topic of debate, it remains unclear if the LVAD itself is a source of interference in other technologies such as ENB whose mechanics rely heavily on electromagnetic fields. Any such interference could have a meaningful impact on patient care.

Notes:			



DYSPHAGIA: AN ALARMING SYMPTOM OF SARCOIDOSIS <u>P King</u>, O Obi, M Sahebazamani

Learning Objectives: Sarcoidosis is a granulomatous inflammatory disorder with multisystem involvement and can present with a myriad of symptoms. Esophageal involvement and dysphagia are extremely rare, and therefore are often overlooked as manifestations of this complex disease. The following series of cases highlights presentations of this rare manifestation.

Case Information: Three patients with biopsy-proven sarcoidosis presented with dysphagia and chest pain.

Case #1: A 31-year-old male presented with acute onset of dysphagia and chest pain. Chest Computed Tomography (CT) revealed significantly enlarged mediastinal lymphadenopathy (LAD) resulting in near occlusion of the esophageal lumen with concern for perforation. His initial chest CT, four weeks earlier, did not show evidence of luminal narrowing. He underwent surgery for esophageal perforation due to enlarged lymph node (LN) compression.

Case #2: A 45-year-old male was admitted for dysphagia and dyspnea. Videofluoroscopic swallowing study and esophagogastroduodenoscopy (EGD) were unremarkable. Etiology of dysphagia was felt to be secondary to LAD. The patient was started on oral steroids and eventually discharged home. He reported complete resolution of dysphagia in follow-up visit. Case #3: A 50-year old male on immunosuppressive agents for pulmonary sarcoidosis developed new-onset dysphagia. Barium esophagram and EGD were unrevealing. Dysphagia was felt to be secondary to mechanical compression from bulky mediastinal LAD. He was started on anti-tumor necrosis factor alpha with marked improvement in dysphagia. Summary: Gastrointestinal involvement is an uncommon manifestation of sarcoidosis with a prevalence of 0.1 to 0.9% of patients with the disease, and esophageal involvement is relatively unheard of with only a handful of case reports to date. Dysphagia is the most common symptom of esophageal involvement and can be seen at any stage of the disease and while on therapy. While this symptom can be attributed to various mechanisms such as extrinsic compression, direct esophageal wall infiltration, and cranial neuropathy, it remains an important point of consideration as these underlying issues can manifest as near-fatal complications of sarcoidosis.

Notes:

ACUTE NEGATIVE PRESSURE PULMONARY EDEMA IN THE SETTING OF AN UNDIAGNOSED GOITER

L Kallur N Brandon V Maddipati M Sahebazamani

Learning Objectives: Negative pressure pulmonary edema (NPPE) is a non- cardiogenic pulmonary edema caused by breathing against an obstructed airway. While most reported cases are seen secondary to laryngospasm post anesthesia during extubation, NPPE developing secondary to an underlying undetected mediastinal goiter is rare. Case Information: A 68 year-old-male with hypertension, anxiety and atrial fibrillation was admitted for a sacroplasty. He became agitated and developed respiratory distress. with his respiratory rate being 38/ minute, blood pressure 223/144, pulse 124. Patient was diaphoretic and restless, using his accessory muscles to breathe and a palpable fullness was present in his anterior neck. He was promptly intubated with resistance being reported by the operator upon passing vocal cords. Laboratory derangements include troponin 1.03 and BNP 367. Electrocardiogram (EKG) revealed evidence of ST depression. Chest radiograph showed diffuse reticulonodular opacities in both lungs with tracheal deviation to the right side. Cardiology team recommended cardiac catheterization which revealed normal coronaries. Computed tomography of neck showed heterogenous enlargement of thyroid gland with thyroid tissue extending in to the upper mediastinum with rightward deviation of the airway. ENT was consulted and patient underwent a total thyroidectomy with planned tracheostomy. Surgical pathology report revealed nodular hyperplasia (colloid) without malignancy. Patient was successfully weaned to room air with tracheostomy. Summary: Negative pressure pulmonary edema (NPPE) is a rapidly progressive condition most commonly seen in acute or chronic upper airway obstruction. The likely mechanism precluding NPPE was a strong inspiratory effort against a blocked airway causing a decrease in intrathoracic pressure, increase venous return and pulmonary blood volume that finally lead to increased hydrostatic pressure. Accurate diagnosis is key, as our patient could have easily been misconstrued as an acute cardiac event given the premeditating EKG changes and rising troponin. Treatment for NPPE includes addressing the underlying etiology along with supportive care and positive pressure ventilation.

Notes:			



MITOMYCIN INDUCED PULMONARY VENO-OCCLUSIVE DISEASE A Kunadu, H Labuschagne, A Gilleland, M Ritchie, V Madddipati

Learning Objectives: Pulmonary veno-occlusive disease (PVOD) is a rare form of pulmonary hypertension (PH). It is characterized by widespread fibrous intimal proliferation of septal veins and pre septal venules. It is often associated with pulmonary capillary dilatation and proliferation. Although the incidence of PVOD is very rare in the general population, its incidence in patients with squamous cell anal cancer is higher and underrecognized especially following treatment with Mitomycin (MMC). Herein, we present a case of Mitomycin Induced PVOD in a patient with Metastatic anal cancer. Case Information: 50-year-old male presented with shortness of breath and orthopnea over 4 months duration. Past medical history of locally metastatic squamous cell cancer for which he had received local radiation, Mitomycin and 5- fluoro-uracil a year prior to admission. Exam revealed a cachectic man who was hypoxic in respiratory distress, had elevated Jugular venous pressure, tachycardic and hypotensive with narrow pulse pressure and cold extremities. He had crackles on lung auscultation. He was found to be in hypoxic respiratory failure and cardiogenic shock. Echo was consistent with right ventricle pressure and volume overload. Chest Computed Tomography showed interlobular septal thickening, diffuse multifocal regions of groundglass opacities, lymphadenopathy, pleural effusions and enlarged central pulmonary arteries. Right heart catheterization: mean Pulmonary artery pressure of 63 mm Hg, wedge pressure of 17 mm Hg, Cardiac output of 2.65 L/min and Pulmonary vascular resistance of 17 Wood units. He was managed on intravenous Epoprostenol and inotropes which were ultimately slowly weaned off. He was discharged home on the IV Epoprostenol. Summary: Although PVOD is rare, it should be entertained in the differential diagnosis in patients presenting with precapillary PH and characteristic but nonspecific radiographic findings as stated above with relatively normal left heart function. Patients with PVOD have out-of-proportionally low DLCO on pulmonary function testing and severe hypoxia. They may develop acute pulmonary edema in response to pharmacologic agents either during a vasodilator challenge during right heart catheterization or during treatment with pulmonary vasodilators. PVOD is very rare and needs a high index of suspicion for diagnosis.

NASAL PERFORATION: A RARE COMPLICATION OF SARCOIDOSIS <u>A Kunadu</u>, Y Kataria

Learning Objectives: Sarcoidosis is a chronic granulomatous multisystemic disorder of unknown etiology affecting young and middle-aged adults. Sinonasal involvement can occur as part of systemic disease but may represent limited disease of the nose and sinuses. It presents with nonspecific symptoms like nasal polyps, epistaxis, recurrent sinusitis, Hyposmia/anosmia. Septal perforation, nasal bone destruction and saddle nose deformity can occur in severe disease. We present a patient with sarcoidosis who developed nasal septal perforation (NSP), a rare complication of sarcoidosis.

<u>Case Information:</u>61-year-old Black woman with Sarcoidosis diagnosed at age 36. Presenting symptoms were dry cough and voice hoarseness. She had hypertrophic nodular nasal mucosa with congestion, greyish nodules on the lips and granular rash on her upper eyelids. Biopsy of lip nodules showed noncaseating granulomas. She later developed nasal ulceration which progressed to Anterior nasal septal perforation (NSP). She was managed on varying doses of Plaquenil, methotrexate and prednisone over the years with marked improvement in her symptoms but she has had persistent NSP with occasional mild epistaxis

Summary: Diagnosis of sarcoidosis can be challenging as it is one of exclusion. Involvement of the of the upper respiratory tract epithelium is rare but nasal symptoms may be the first manifestation of the disease. NSP, though uncommon, is well described in sarcoidosis. It is characterized by loss of cartilage and/or bony structures along with the mucoperichondrium and mucoperiosteum lining them. It can also be caused by many systemic diseases or local trauma. Diagnosis of sinoatrial sarcoidosis is based on clinical findings of crusting friable nasal mucosa with polypoid changes or characteristic vellowish submucosal nodularity endoscopic features, CT findings and histologic appearance of non-caseating granulomas. Two-thirds of patients affected are asymptomatic. Sarcoidosis is self-limiting in 80% of cases. Mainstay of treatment in more progressive symptomatic cases includes systemic and/or local corticosteroids. Pharmacologic treatment for head and neck sarcoidosis is not different from treatment of symptomatic disease in general. Rarely head and neck involvement may compromise the airway requiring intubation or surgical intervention (Septoplasty).

Notes:			

PV18

THE CASE OF ASCENDING PARAPARESIS FOLLOWING NINTEDANIB (OFEV)

<u>A Kunadu</u>, S Alqalyoobi, O Obi

Learning Objectives: Idiopathic pulmonary fibrosis (IPF) is an incurable, progressive fibrosing interstitial lung disease reflected by a decline in lung function, worsening dyspnea, exercise capacity, and overall poor prognosis. Nintedanib is one of two anti-fibrotic therapies approved for the treatment of IPF. We present the case of a patient who presented with ascending paraparesis following Nintedanib and here by hope to shed light on treatment of IPF and potential but unproven side effects on Nintedanib.

Case Information: 39-year-old male with history of familial IPF secondary to short telomere syndrome who presented with bilateral progressive upper and lower extremity paresthesia and weakness which started shortly after he was commenced on Nintedanib for pulmonary fibrosis. This progressed to numbness and weakness till he could barely walk or lift his arms against gravity by day 5. He denied any preceding upper respiratory tract or gastrointestinal symptoms. Physical exam was significant for bibasilar fine velcro crackles in the lungs, hyporeflexia and flaccid tone with power of 3/5 in all extremities. He had negative autoimmune work up. Cerebro-spinal fluid analysis, Pan spinal MRI and MRI of the brain were unrevealing. Electromyogram was significant for motor neuropathy. Management was mainly supportive with physical therapy and patient gradually regained his strength back to baseline.

Summary: Nintedanib inhibits multiple tyrosine kinases and targets growth factors like vascular endothelial growth factor receptor, fibroblast growth factor receptor and platelet-derived growth factor receptor which have been implicated in the pathogenesis of idiopathic pulmonary fibrosis. It is important to monitor potential adverse effects aside from what was noted in the relevant trials of which diarrhea was the commonest. Other side effects were bronchitis, upper respiratory tract symptoms, nausea, vomiting, cough weight loss and back ache. Our patient presented with paresthesias and ascending paresis after taking Nintadenib. He had negative extensive work up for other causes of ascending paralysis. His weakness gradually improved after stopping the medication and with Physical therapy. To the best of our knowledge, this is the first reported case of ascending paresis following the use of Nintedanib.

No	otes
----	------

POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME AFTER RITUXIMAB INFUSION

M Hafiz, M Picton

LEARNING OBJECTIVES

Posterior reversible encephalopathy syndrome (PRES) is a syndrome of acute onset neurological changes including headache and altered mental status, and radiologic findings of reversible vasogenic edema in the posterior cerebral white matter. Common precipitants include acute elevations of blood pressure (BP), fluid retention, and immunosuppressive drugs like rituximab.

CASE INFORMATION

56-year-old woman with extranodal marginal zone lymphoma of mucosaassociated lymphoid tissue (MALT) presented to the emergency department (ED) with a headache. Two days before presentation, the patient had received the first dose of rituximab for stage III MALT lymphoma. Headache started on the evening of the infusion. Patient was found to have BP of 150's systolic. She denied history of hypertension. CT scan of the head was normal. Headache improved with conservative management. She was discharged home. She received the second dose of rituximab. 4 days after the second dose, patient returned to the ED complaining of headache with dizziness, blurred vision and vomiting. Her BP was elevated at 200's systolic. MRI of the brain showed features consistent with PRES. Patient reported feeling better as her BP improved. Repeat MRI showed significant improvement of the edema. She was eventually discharged home with no residual symptoms.

SUMMARY

Recently PRES has been found to be associated with rituximab infusions. Although uncommon, PRES as a potential side effect of rituximab should be discussed with patients before initiation of the therapy. High suspicion for PRES should be maintained when patients on rituximab therapy present with acute onset of mild to severe neurological manifestations as timely identification can be lifesaving and prevent the patient from future reexposure to the agent.

Notes:

37

RAMPED UP LUNG TUMOR

M Blaj, S Nalamalapu, M Sahebazamani

Background: Osteosarcoma is a primary malignancy of the bone. The lung is the most common site of metastasis. Chondroblastic is one of the histologic types of osteosarcoma comprising about 25% of cases. We would like to emphasize the surveillance interval of chondroblastic osteosarcoma through our case. We are presenting a 39 year old male with osteosarcoma diagnosis now with recurrent metastasis even with recommended follow up periods.

Case: 39 y/o caucasian male with history of high grade chondroblastic osteosarcoma of left tibia. He underwent surgery and chemotherapy. Two years later, patient had first occurrence of metastatic lung disease . He had right lower lobe (RLL) thoracoscopic wedge resection and repeated chemotherapy (ifosfamide and etoposdie). PET scan performed 4 months after surgery was negative and, CT chest performed 8 months after surgery was also negative. 10 weeks after the last CT, patient presented with fatigue, cough, exertional dyspnea, and 10lbs weight loss for two weeks. CT chest showed large RLL lung mass with size of 6.7 x 4.6 cm and pleural effusion. Endobronchial biopsy showed metastatic osteosarcoma.

Conclusion: Recurrence of osteosarcoma is seen in 80% of patients with metastasis within the first 3 years and has a 5-year survival rate of 20%. Doubling time for osteosarcoma depends on the cell line which has been reported varying from 1 to >7days. Current recommendations advise 3-month follow up. Unfortunately, even with 3 month close follow up interval, our patient developed large lung mass within 10 weeks. Optimal time interval for follow up is not clear. With the aggressive nature of this tumor, treated metastatic population might warrant closer follow up within a month rather than 3 months to prevent late diagnosis like in our case.

Notes:			
	 	 · · · · · · · · · · · · · · · · · · ·	

NOVEL THERAPEUTIC STRATEGY IN THE TREATMENT OF A BIOLOGICALLY COMPLEX NON-SMALL CELL LUNG CANCER C. Uzoka, N. Sharma

LEARNING OBJECTIVES

To emphasize the standard treatment for metastatic non squamous Non-Small Cell Lung Cancer (NSCLC) is the combination of immunotherapy with Pembrolizumab to a platinum chemotherapy doublet of Carbo (Cis)platin and Pemetrexed.

To identify genomic alterations that preclude response to the above hitherto described regimen.

To recognize the novel treatment approach utilized to overcome a therapeutic quagmire posed by the heterogenic molecular complexity of these genomic mutations and reestablish antitumor immunity.

CASE INFORMATION

A 58-year-old patient with an aggressive metastatic non squamous NSCLC presented with acute respiratory failure. The tumor bore multiple molecular alterations that conferred an aggressive biology, with limited benefit from the current standard of care treatment with chemo-immunotherapy. The molecular profile of the tumor KRAS^{G12C} driver mutation that has limited response to platinum chemotherapy and STK11 mutation associated with poor clinical outcome from the addition of pembrolizumab to carboplatin and pemetrexed. She was treated with a novel regimen that included Nab-paclitaxel, Pemetrexed, Bevacizumab and Pembrolizumab. This translated to a rapid and marked clinical response.

SUMMARY

Our patient presented with bulky and symptomatic disease which appeared resistant to the current standard of care treatment. A novel therapeutic approach which leveraged antiangiogenic therapy, Bevacizumab, that converted the "cold" tumor microenvironment, (paucity of tumor T cell infiltration) to a T cell inflamed phenotype in the bid to reestablish an effective antitumor immunity, by adding pembrolizumab to a chemotherapy backbone that did not include a platinum which has no benefit in KRAS^{G12C} mutated lung cancers. This synergistic response requires further studies to refine this therapeutic approach for heterogeneously complex NSCLC.

Notes:			



MULTIPLE PRIMARY SYNCHRONOUS TUMORS AND SECONDARY ACUTE B-LYMPHOBLASTIC LEUKEMIA IN A YOUNG PATIENT SR Polsani, A Weil

LEARNING OBJECTIVES: Importance of being aware of secondary primary malignancies as cancer survival increases.

CASE INFORMATION: A 39-year-old with no significant family or personal history was diagnosed with IgG kappa Plasma Cell Myeloma (PCM) and PDGFRA mutation+ Gastric GIST along with a L Renal Lesion concerning for Renal Cell carcinoma in February 2016. He received Carfilzomib. Lenalidomide and Dexamethasone for 6 cycles for PCM achieving very good partial response followed by Autologous Stem Cell Transplant on 11/15/16 followed by Lenalidomide maintenance and has achieved complete response. For GIST post R0 resection he received approximately 3 years of Imatinib while the left renal lesion concerning for Renal Cell Carcinoma is being monitored with serial imaging. Genetic testing for KIT. NF1. PDGF RA. SDH B. SDHC, SDH D. SDH A was negative. Approximately 3 years into Lenalidomide maintenance peripheral blasts were noted on a routine CBC with flow cytometry revealing 31% blasts, immunophenotypically (CD10+, CD19 dim, CD22 dim, CD34+, TdT+) most compatible with B-Lymphoblastic Leukemia. Bone marrow biopsy confirmed B-Lymphoblastic Leukemia with 88% blasts. We plan to start a pediatric inspired regimen CALGB 10403.

SUMMARY: Multiple solid and hematologic neoplasms in a young patient not fitting any known hereditary syndromes raises questions about causality and association based on an as yet undetermined genetic or molecular mechanism. With increased survival of patients with PCM a new phenomenon of secondary primary malignancies (SPM) is being observed. Secondary Acute Lymphoblastic Leukemia is very rarely reported though.

Notes:

TENOFOVIR ALFENAMIDE CAN INDUCE RENAL TUBULAR WASTING <u>E Primeaux</u>, H Lai, C Parker, R Obi

Case information:

29 years old male with congenital HIV on Biktarvy for the past 6 months, Cryptococcus meningitis, complicated by Dural venous thrombosis presented to the ED because hypokalemia. Patient was seen for routine visit 5 days prior and referred to ED for severe hypokalemia 2.4. In the ED he reported "feeling fine". Physical exam was unremarkable, labs showed normal kidney function, leukocytosis 15.000, hypokalemia 1.8, high anion gap 18, and high lactic acid: 4.1. EKG was normal. After two days of IV potassium repletion hypokalemia persist. Work up showed Urine K: 12.5meq (Random), Urine Na 46, and Glucose: +3.

Diarrhea and diuretics use were excluded in the Differential diagnosis since patient did not respond to potassium replacement. A renal K wasting was suspected and Tenofovir Alafenamide was stopped. Only until day 9 after admission, the serum K improved to a normal level. Lactic acidosis was also monitored and it mildly improved during hospital stay.

PCP office	Admission Day	ED	Day 2	Day 9
2.4*	POTASSIUM	1.8>3.0	3.0*	4.2

Learning objectives:

Proximal tubulopathy is a classic presentation of Tenofovir nephrotoxicity. Chronic tubule interstitial damage from direct nephrotoxicity with decline in GFR with or without low level proteinuria is another common presentation. This patient was recently taking Tenofovir Alafenamide that is a new nucleoside reverse transcriptase inhibitor developed specifically with the intent to lower renal toxicity compared with Tenofovir disoproxil fumarate by achieving lower plasma levels and reduce kidney exposure. There are a few cases reported that show renal toxicity can still develop. Although it is less frequent with the newer Tenofovir formulation.

Summary: This case showed that hypokalemia presented after starting use of Tenofovir alafenamide and furthers that newer Tenofovir Alfenamide can cause renal toxicity such as proximal tubular dysfunction.

Notes:			



Notes:

39

OUTCOMES OF MICROSATELLITE INSTABILITY HIGH GASTROINTESTINAL TUMORS AT A SINGLE INSTITUTION <u>A.Patel</u>, M Navaid

LEARNING OBJECTIVES: Gastrointestinal cancers are prevalent with colon cancer being the third leading cause of cancer in the United States. Despite advances with chemotherapeutic treatments, advanced stage colorectal cancers have an average overall survival of approximately 15 to 22 months. Standard upfront treatment consists of an Oxaliplatin based regimen. Upon progression, treatment is often individualized based on the presence of any actionable mutations. MSI-H (microsatellite instability high) is one such mutation and occurs when a cell is unable to repair replication errors. MSI-H tumors are rare, comprising approximately 5% of metastatic colorectal cancers. When MSI-H tumors are present, however, the addition of immunotherapy has increased the overall response rate to approximately 60% with a complete response rate of 7%.

<u>CASE INFORMATION:</u> At our institution, we have identified seven cases of MSI-H gastrointestinal tumors. Of the seven cases, six cases were identified as stage III or IV colorectal cancer and one case was a stage IV pancreatic cancer. Each of these patients initially received an Oxaliplatin based chemotherapy. Upon progression, each patient received immunotherapy with Pembrolizumab 200mg every three weeks. Patients had a radiologic response at a median of 3.3 months. To date, four of the seven cases have resulted in a complete radiologic response and one case resulted in a partial response after initiation of immunotherapy. Two of the seven patients who achieved a complete remission are on surveillance with tumor markers and imaging. The stage IV pancreatic cancer patient resulted in a complete response with immunotherapy.

<u>SUMMARY</u>: The data from our institution exceeded the average, demonstrating almost a 71% overall response to immunotherapy and a 28% complete response. These results support the importance of identifying the MSI status in gastrointestinal malignancies, as it has shown improved outcomes in MSI-H tumors. At our institution, it is increasingly becoming routine to assess for MSI status on all tissue biopsies. This case series reviewed the use of immunotherapy at the time of progression. We aim to study outcomes with the use of immunotherapy in the frontline setting.

A DIAGNOSTIC HEADACHE IN A PREGNANT WOMAN WITH DIABETES INSIPIDUS: BLAME THE PLACENTA OR THE PITUITARY? K Aziz, C Houston, B Ramirez, A Pokhrel

Background

Diabetes insipidus (DI) occurs in 1/30,000 pregnancies .The most common etiology is excess production of placental vasopressinase, which degrades maternal anti-diuretic hormone. We present the case of a pregnant woman presenting with diabetes insipidus and pituitary apoplexy.

Clinical case

We were called to see a 33 year old female with polyuria and polydipsia on post-partum day #1. She had presented to the ED at 29.4 weeks of her 5th pregnancy (G5P4) with an unrelenting headache, nausea, and vomiting for 12 hours. Admission labs included serum sodium of 147m Eq/L (n 136-145), serum potassium 2.8 m Eg/L (n 3.4-4.4), and urine specific gravity of 1.003 (n 1.005-1.030). She remained tachycardic despite vigorous IV fluid administration. It was noted that she had produced 8L of urine over the preceding 24 hours. Serum sodium was 159 mEg/L with urine osmolality of 78 mOsmol/kg (n 300-900). A presumptive diagnosis of gestational DI was made and 2 mcg of subcutaneous DDAVP was given. Shortly thereafter she delivered a healthy infant. Maternal blood loss was minimal. Over the next 12 hours her urine became concentrated and her serum sodium decreased, but by the next morning she re-developed dilute polyuria. At the time of our evaluation, she had no apparent signs of glucocorticoid or thyroxine deficiency but had not begun to lactate. Biochemical evaluation included early morning cortisol of 4.6 ug/dL (n 3.5-18.3), TSH 0.46 uIU/mL (n 0.35-4.94), free T4 0.76 ng/dL (n 0.70-1.48), and prolactin 26.6 ng/mL (n 5.2-26.5). Pituitary MRI showed a mildly enlarged pituitary gland with central T1 hyperintensity, consistent with apoplexy.

Conclusion

The rapid physiologic growth of the pituitary during pregnancy may increase the risk of apoplexy. A severe headache is the most common symptom and may be accompanied by signs of pituitary dysfunction. Although diabetes insipidus more often results from placental physiology, pituitary apoplexy must also be considered in a pregnant woman with concurrent neurologic symptoms.

Notes:			



THAT'S NOT A GASTROINTESTINAL STROMAL TUMOR (GIST): A CASE OF A GASTRIC SCHWANNOMA

M Kratzer, J Kinderwater, S Poola, K Regan

Learning Objectives: There are multiple subtypes of gastric mesenchymal tumors which vary in malignant potential. Endoscopic ultrasound can help to characterize these neoplasms. The majority (60-70%) are Gastrointestinal Stromal tumors (GIST), which have malignant potential and are derived from the interstitial cells of Cajal. Less common are leiomyomas, derived from smooth muscle, which are typically benign. Even more rare, accounting for only 0.2% of gastric neoplasms, are gastric schwannomas (GS) which arise from Auerbach's plexus. We present a case of gastric schwannoma which was discovered incidentally during routine preoperative evaluation.

Case Information: A 35-year-old morbidly obese Caucasian female with a history of hypertension, hyperlipidemia, diabetes mellitus, and hypothyroidism presented for bariatric surgery evaluation prior to sleeve gastrectomy. She reported symptoms of reflux, globus sensation, decreased appetite, and bloating. She underwent an upper endoscopy which found a subepithelial, non-bleeding mass within the gastric fundus. Endoscopic ultrasound with fine needle aspiration demonstrated a 29 mm x 32 mm vascular, irregular, lobulated, subepithelial mass that appeared to originate in the muscularis propria. Fine needle aspiration revealed a spindle cell neoplasm with CD117 negative staining. Laparoscopic sleeve gastrectomy was performed, and the entire mass was removed with clear margins. Pathology report confirmed the diagnosis of gastric schwannoma and immunohistochemical stains were negative for CD117, Actin, and Desmin, and positive for S100 (diagnostic for schwannoma).

Summary: While GS shares similar clinical features with GIST, they possess extremely low malignant potential. These neoplasms are typically incidentally found in middle-age females with vague or no gastrointestinal symptoms, as with our patient. Malignant gastric schwannomas are exceedingly rare (case reports only) and typically present as a central mass with ulceration that may metastasize. Treatment involves resection with clear margins. Recurrence is rare and is usually due to incomplete surgical margin, therefore postsurgical surveillance is not recommended.

tes
tes

ADVANCED PROSTATE CANCER WITH BRAIN METASTASIS: A CASE REPORT AND REVIEW OF LITERATURE

N. Mainkar, J. Alcid, V. Chaudhary

Learning Objectives:

Prostate cancer is known to metastasize to several locations, most commonly, bone, lung and liver. Brain metastases are exceedingly rare, ranging from 0.16-2%, and occurring with disseminated disease. We report a case of prostate cancer with initial presentation of metastasis to the brain.

Case:

A 52-year-old man presented with right facial paresis, right lower extremity weakness and confusion for 1 month prior to seeking medical attention. MRI brain revealed multiple lesions, in the basal ganglia, corona radiata, superior frontal gyrus and cerebellum. CT chest, abdomen and pelvis revealed multiple skeletal and pulmonary metastases, intra-abdominal lymphadenopathy, an enlarged prostate and bladder thickening. PSA was 156. Biopsy of a rib lesion revealed findings consistent with metastatic non-small cell carcinoma, but IHC could not be performed. Based on this prostate primary was suspected. He underwent a prostate biopsy, which confirmed metastatic prostate adenocarcinoma. Due to the extremely aggressive nature of his prostate cancer with bulky disease and symptomatic brain metastases, he was started on treatment with androgen deprivation therapy along with docetaxel 75mg/m2 q3 weeks with prednisone, denosumab and was offered gamma knife radiosurgery for the brain lesions.

Summary:

Prostate cancer is the fourth most common malignancy in the world, and the second most common in men. Brain metastasis from prostate cancer remains rare. Our patient was diagnosed initially with several brain lesions. There is no gold standard for the management of brain metastasis from prostate cancer, however the established approach includes radiotherapy, surgery and radiosurgery, along with combination androgen deprivation therapy and/or systemic chemotherapy, which is the standard for advanced prostate cancer. JC, our patient, was diagnosed initially with multiple foci of metastasis, including several intraparenchymal brain lesions. One study reports that the median survival for prostate carcinoma with brain metastasis is 2.8 months. With early diagnosis, high clinical suspicion and rapid treatment, our patient is currently still alive, 4 months out from initial presentation.

Notes:			

DOWNHILL BLEEDING ESOPHAGEAL VARICES AS COMPLICATION OF SUPERIOR VENA CAVA SYNDROME

LF Rauseo Lopez, JG Alvarez Posada, W Leland

Learning Objectives:

Bleeding esophageal varices is a rare complication of superior vena cava (SVC) syndrome that is not related to the presence of hepatic disease. **Case Information:**

A 34-year-old male presented with two weeks of nausea followed by sudden hematemesis, melena, and epigastric pain radiated to chest. In 2016, he developed symptomatic SVC syndrome after a tunneled right internal jugular dialysis catheter complicated with a deep venous thrombosis. Since then he has been on oral anticoagulation and had three hospital admission for hematemesis, with esophagogastroduodenoscopy (EGD) in each opportunity showing grade III esophageal varices that were banded and erosive esophagitis with ulceration in the distal esophagus. On admission, physical exam was significant for tachycardia and superficial venous collaterals over the entire chest wall arising from aneurysmal left upper extremity arteriovenous fistula. Complete blood cell counts showed hemoglobin 7.5 g/dL, and complete chemistry with liver panel was normal. Abdominal ultrasound with duplex doppler showed no signs of advanced liver disease, nor abnormalities of portal flow or pressures. EGD showed grade III varices in the upper third (downhill) and medium size varices in the mid-distal third of esophagus. Due to concern for varices arising from SVC we consulted cardiothoracic surgery. Patient underwent SVC-to-right-atrium bypass with aortic homograft and was discharged home after recovery. Since then patient remains asymptomatic. Summary:

Esophageal varices are a known complication of cirrhosis with portal hypertension. Rarely (0.4%-10%) they originate instead from SVC obstruction and they may be an overlooked etiology of upper gastrointestinal bleed. SVC syndrome is usually caused by external compression from tumors or thrombosis caused by central venous catheters or implanted ports. Complications are mostly related to blood stasis and esophageal wall edema rather than bleeding. Diagnosis is by direct visualization through endoscopy and/or imaging modalities (i.e. doppler ultrasound of neck/thorax, CT scan of abdomen/chest with contrast). Treatment is with variceal banding or sclerosis, but prognosis may be poor without resolution of SVC obstruction.

Notes:

APIXABAN AND PERITONEAL DIALYSIS, IS IT SAFE? RA Jiwani, FA Faiz, WR Badwan.

Learning Objectives: Hemorrhagic cardiac tamponade (HCT) is a rare disorder caused by the rapid accumulation of blood in the pericardium resulting in hemodynamic collapse. In literature, there are less than 30 case reports of HCT with the use of direct oral anticoagulants (DOACs), and none reported in patients with end stage renal disease (ESRD). Case Report: We describe a case of a 31-year-old female with a past medical history of ESRD as a result of stage 4 lupus nephritis, systemic lupus erythematosus, rheumatoid arthritis and hypertension who presented to our hospital with severe nausea, vomiting and chest pain for the past 24 hours. This patient had recently been started on peritoneal dialysis. Physical exam was notable for an audible friction rub over the precordium and lower extremity edema. Chemistries were remarkable for hyperkalemia at 5.7 mEg/L, and significantly elevated blood urea nitrogen (BUN) and creatinine at 86 mg/dL and 21.66 ma/dL, respectively. Subsequent transthoracic echocardiogram (TTE) showed a 1.1 cm pericardial effusion but no evidence of increased pericardial pressure. She was treated with hemodialysis with resolution of her symptoms. During the admission she was found to have a right brachial deep vein thrombosis (DVT) and was started on Apixaban before discharge, at the regular recommended dose for the general population. The patient returned to the hospital 48 hours later, with complaint of chest pain radiating to her back and left arm. She was hypotensive and hemoglobin was found to be 6.1 grams per deciliter (g/dL). Repeat TTE showed a large pericardial effusion with resulting tamponade physiology. She was treated with red blood cell transfusion and emergent pericardiocentesis, evacuating 1.2 liters of bloody fluid, leading to resolution of her hemodynamic compromise. Anticoagulation was discontinued and the patient was discharged with close follow up. Summary: We present a unique case of HCT following initiation of Apixaban therapy for DVT treatment in an ESRD patient. HCT is potentially life threatening and requires urgent evaluation and treatment. Although the use of DOACs in ESRD patients is becoming increasingly common, provider awareness of the serious complications of DOAC use, such as HCT, needs to be considered when initiating anticoagulation. Furthermore, more data is needed to best understand the differences between low dose DOAC and regular dose in the ESRD population.

Notes:			

PV30

SEVERE VITAMIN B12 DEFICIENCY MIMICKING THROMBOTIC THROMBOCYTOPENIC PURPURA S Kumar, H Brody, C Knupp

Learning Objectives: Vitamin B12 is a necessary vitamin for hematopoiesis, required for production of purines, functioning as a cofactor for thymidylate synthase, an enzyme required for cell growth and DNA repair. If there is deficiency, not only is erythropoiesis decreased, but there is cell fragility with intramedullary cell destruction (ineffective erythropoiesis). As all blood cells require vitamin B12, other cell lines are affected, including platelets. Anemia with evidence of red cell fragility on peripheral smear and thrombocytopenia can mimic microangiopathy with intravascular red cell and platelet destruction, as seen with Thrombotic Thrombocytopenic Purpura (TTP), a life-threatening condition requiring immediate aggressive treatment. **Case Information:** Our patient is a 49 year old female who presented to the ED for symptomatic anemia. She had a history of pernicious anemia but had stopped parenteral vitamin B12 therapy several years before. Hemoglobin was 5.4 a/dl. platelet count 114 K/uL. d-dimer 24.224 ng/ml. lactate dehydrogenase 8,296 U/L, bilirubin 3.3 mg/dl and haptoglobin <8 mg/dl. Reticulocyte count was 2.69%. Schistocytes were diffusely present on peripheral smear. Hyper-segmented neutrophils were seen. Folate was 15.2 ng/ml and vitamin B12 was <146 pg/ml. She refused hospital admission, was given a vitamin B12 injection and discharged home with outpatient follow up and continued subcutaneous vitamin B12 supplementation. ADAMTS 13 activity assay was sent and ultimately resulted at a normal value of 92%. Three days later the hemoglobin was 6.0 g/dl, reticulocyte count 13.89% and platelet count 164.000.

Summary: This case illustrates how vitamin B12 deficiency with severe anemia and thrombocytopenia can mimic life-threatening microangiopathic disorders, such as TTP, which requires hospital admission, invasive treatments, including placing a vascular catheter, plasma exchange therapy and high doses of corticosteroids. There are other published case reports of patients who were treated for TTP before a diagnosis of Vitamin B12 deficiency was established, usually after the ADAMTS 13 activity level was found to be normal and there had been no response to the TTP therapy. As our patient had a history of pernicious anemia, we were able to quickly make this distinction and avoid unnecessary and potentially harmful treatments.

Notes:

DERMATOMYOSITIS WITH ANTISYNTHETASE SYNDROME: AN INPATIENT DIAGNOSTIC ADVENTURE JG Alvarez Posada. T Blair. JM Bermudez

Learning Objectives: We present an interesting case of weakness presenting to the ED. The patient was originally sent by his PCP after abnormal chest imaging that was concerning for infection or malignancy. Ultimately, he was found to have an underlying rheumatologic disease rather than a pulmonary process.

Case Information: A 62 v/o M with PMH of HTN. HLD. and tobacco abuse reported one-month h/o B/L painful, swollen hands accompanied by an inability to raise his arms above his shoulders. He had been on a steroid taper, which partially relieved his symptoms. He had no viral prodrome. FH was significant for RA, SLE, and Addison's disease. SH was concerning for smoking 40 PPY. Exam findings included B/L proximal LE weakness and proximal/distal UE weakness. Labs were notable for elevated CPK which peaked at 12469, elevated transaminases, ANA <40, ESR 20 and CRP of 35. Hepatitis panel and HIV tests were negative. His Anti-SM antibody was positive at 25, Aldolase was elevated at 265. A CT Chest revealed B/L ground glass opacities: a LLL consolidated mass-opacity and calcified mediastinal lymphadenopathy. Rheumatology recommended a LE MRI that revealed varying degrees of mild to moderate B/L thigh muscle edema seen with inflammatory myopathy. Muscle biopsy results showed lymphocytic infiltrates in both the perimysial and endomysial regions, seen in dermatomyositis and antisynthetase syndromes. Pulmonology evaluated the patient and expressed concerns for ILD related to dermatomyositis with antisynthetase syndrome. He continued high dose steroid therapy with outpatient follow-up for further evaluation after his weakness largely resolved and his labs returned to normal.

Summary: Antisynthetase syndrome can present in up to 30% of patients with inflammatory myopathies. It can lead to proximal muscle weakness, "mechanic hands", non-erosive arthritis, constitutional symptoms, and interstitial lung disease. The lung is the most common organ involved and it is the leading cause of mortality in this disorder. Diagnosis requires high clinical suspicion. Muscle biopsy in addition to rheumatologic lab-work, dedicated imaging and appropriate Rheumatology and Pulmonology consultation allows for differentiation and definitive diagnosis.

Notes:

GET SMASHED IN THE HOSPITAL: A CASE OF COMPLICATED PANCREATITIS

ZS Hamedi, S Poola, G Sheri, B Shahid

Learning Objectives: Acute pancreatitis is one of the most common diseases of the GI tract with many etiologies. The most common etiologies of pancreatitis are due to bile stones or alcohol abuse. This is a rare case of hypertriglyceridemia and alcohol-induced pancreatitis that was complicated with a portal vein thrombus and acute cholangitis from an obstructing gallstone.

Case Information: A 61-year-old Caucasian male with a history of binge alcohol drinking and pancreatitis 3 years ago, presented with sudden onset of abdominal pain, nausea, and vomiting. Initial work up demonstrated an elevated lipase greater than 4800 U/L and triglyceride greater than 4560 mg/dl. The patient was managed with an insulin drip and after one session of plasmapheresis his triglycerides dropped to 538 IU/ml. He had clinical improvement however was noted to have a slow rise of his total bilirubin from 1.5 mg/dl to 5.5 mg/dl. A RUQ US showed a dilated CBD to 9 mm. MRCP demonstrated a CBD dilation with a 4-5 mm stone. The patient subsequently developed fever and was started on antibiotics for concern of cholangitis and had a CT scan that demonstrated severe peri-pancreatic fat stranding compatible with progressive pancreatitis and a new portal vein thrombosis. The patient underwent ERCP with successful CBD stone removal, CBD stent, and PD stent placement. The patient had improved bilirubinemia and was discharged home on oral anticoagulation for his portal vein thrombus.

Summary: Gallstones are the most common cause of acute pancreatitis followed by alcohol. Hypertriglyceridemia is a rare cause of pancreatitis and serum triglyceride concentrations above 1000 mg/dL can precipitate attacks of pancreatitis. There have been no cases of concurrent gallstone and hypertriglyceridemia pancreatitis. This case highlights the need to evaluate all etiologies of hyperbilirubinemia despite having a suspected source. Treatment involves a multidisciplinary approach with plasmapheresis and endoscopic therapy to reduce triglyceride levels and remove the obstructing stone. This patient was also found to have a portal vein thrombus. Despite theoretical hemorrhagic complications, anticoagulation was initiated for concern of clot extension that may result in hepatic decompensation or bowel compromise.

Notes:

CARDIAC ARREST SECONDARY TO INTRATHECAL BUPIVACAINE INJECTION

B Vadhar, J Mullin, M LeDoux, L Lindsey, M Sahebazamani

LEARNING OBJECTIVES: Intrathecal injection and continuous epidural infusions are both accepted modalities of analgesia in obstetric patients. Through this case report we highlight the possibility of accidental intradural/ intrathecal injection of large doses of bupivacaine and the disastrous cardiovascular effects that it may cause. We would also like to highlight upon the precautions one can take for safe administration of epidural agents. **CASE INFORMATION:** A 19 year old thin primigravida with spontaneous rupture of membranes underwent L3/L4 epidural catheter placement. Placement was confirmed. She was started on ropivacaine infusion, however the effects wore out. Hence a bolus of 10cc of 0.5% bupivacaine was administered. Vitals were initially stable but twenty minutes later patient had a cardiopulmonary arrest with asystole. ROSC was achieved after 5 minutes of CPR and 1mg epinephrine. Patient was intubated and taken for emergent C-section. She remained tachycardic throughout the procedure. Post procedure she was extubated. It was noted then that patient had bit her tongue and was maintaining bilateral wrist flexion. . Intralipid was administered to treat possible seizure-like activity but no change was noted. Patient was intubated. CXR revealed diffuse pulmonary edema. Echocardiogram showed LVEF at 15%. Head CT done interestingly showed pneumocephalus at left frontal horn. She was started on APRV mode and inhaled nitric oxide. She was in cardiogenic shock and was started on Lasix drip and pressors. The possibility of ECMO was discussed but patient eventually improved on above measures. **SUMMARY:** High neuraxial block due to accidental intrathecal injection and CNS/cardiac toxicities due to high dose anesthetic are the most dreaded complications of local anesthetic agents and can be fatal. The former is termed as TSA-total spinal anesthesia and the latter is termed as LAST-Local anaesthetic systemic toxicity. While CT brain made us question about the site of bupivacaine injection being intrathecal instead of epidural, the dose used for this patient was also larger with respect to her LBW. The

overall incidence for these complications was found to be 1.8 in 1000 patients. Although this is rare, its fatal potential warrants awareness about this condition.

Notes:			

Page intentionally left blank.

Notes: