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Henry Ford Health System Publication List – April 2017

This bibliography aims to recognize the scholarly activity and provide ease of access to journal articles, meeting abstracts, book chapters, books and other works published by Henry Ford Health System personnel. Searches were conducted in PubMed, Embase, Web of Science, and Google Scholar during the beginning of May, and then imported into EndNote for formatting. There are 162 unique citations listed this month. Because of various limitations, this does not represent an exhaustive list of all published works by Henry Ford Health System authors.

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Administration

Omar J, **Heidemann DL**, **Blum-Alexandar B**, **Uju-Eke C**, **Alam Z**, **Willens DE**, and **Wisdom K**. Fresh prescription: Improving nutrition education and access to fresh produce in detroit *J Gen Intern Med* 2017; 32(2):S752. PMID: Not assigned. Abstract

J. Omar, Henry Ford Hospital, Macomb, United States

STATEMENT OF PROBLEM OR QUESTION (ONE SENTENCE): Lack of basic knowledge of nutrition and limited access to fresh produce contribute to difficulty in controlling chronic diseases like obesity, diabetes, and cardiovascular disease among underserved adults in Detroit. OBJECTIVES OF PROGRAM/INTERVENTION (NO MORE THAN THREE OBJECTIVES): To improve patient's knowledge of nutrition and confidence in their ability to eat healthy. To improve access to fresh produce by 1) providing financial support, 2) introducing patients to new local Detroit farmer's markets. DESCRIPTION OF PROGRAM/INTERVENTION, INCLUDING ORGANIZATIONAL CONTEXT (E.G. INPATIENT VS. OUTPATIENT, PRACTICE OR COMMUNITY CHARACTERISTICS): Fresh Prescription is a program that serves patients at several different sites in the Detroit area. We implemented Fresh Prescription at our tertiary-care academic institution in the outpatient Internal Medicine clinic. Eligible participants with body mass index >25 and motivation to learn healthy eating habits were enrolled by their primary care physician from July- September 2016. Participants were given a $10 reward on a rechargeable debit card for completing a nutrition educational counseling session, which could include tele-counseling, cooking demonstrations, and other events. They were able to redeem their reward at local farmer's markets or with boxed food deliveries to receive a maximum total of $40 in fresh produce. Patients underwent a total of 4 counseling sessions over 6 weeks and received an additional $20 boxed food delivery for returning for a 12 week follow up. MEASURES OF SUCCESS (DISCUSS QUALITATIVE AND/OR QUANTITATIVE METRICS WHICH WILL BE USED TO EVALUATE PROGRAM/INTERVENTION): Success was measured through comparison of pre- and post-survey responses. FINDINGS TODATE (IT IS NOT SUFFICIENT TOSTATE FINDINGS WILL BEDISCUSSED):Atotal of 149 patients were referred to the program by their primary care physician. 39 of these patients were enrolled, and 28 patients completed the program (72% completion rate). Post-survey responses are available for 27 of the 39 patients enrolled in the program. 96% of participants reported they were better able to manage their health and their chronic conditions. 78% of participants reported an increase in their daily intake for fresh fruits and vegetables, with an average increase of 2 cups/day. 48% of participants reported a decrease in their intake of unhealthy food items, with an average decrease of 1 item/day. There was an increase in measures of knowledge base, which included ability to select, prepare, and store fresh produce. 85% of participants reported better knowledge of where to buy fresh produce. Price, access, and transportation were still noted to be barriers for many participants. Of the 39 patients who completed the program, 16 returned for follow up on biometrics, including weight and blood pressure. 5 of 16 participants had weight loss, and 5 of 16 had improvement in blood pressure. KEYLESSONS FORDISSEMINATION(WHATCAN OTHERS TAKE AWAY FOR IMPLEMENTATION TO THEIR PRACTICE OR COMMUNITY?): Increasing general nutrition knowledge base among participants led to an increase in the amount of fresh produce consumed, a decrease in unhealthy food items consumed, and increase in ability to manage chronic health conditions. Providing financial resources and improving access to fresh produce are important in supporting patients in an underserved population while encouraging healthy eating habits.

Allergy and Immunology
Liu AH, **Zoratti EM**, Pongracic JA, Babineau DC, Visness CM, Gergen PJ, Togias A, and Busse WW. The multimorbid polysensitized phenotype is associated with the severity of allergic diseases Reply *J Allergy Clin Immunol* 2017; 139(4):1408-1409. PMID: Not assigned. Full Text

[Liu, Andrew H.] Childrens Hosp Colorado, Aurora, CO 80045 USA. [Liu, Andrew H.] Univ Colorado, Sch Med, Aurora, CO 80045 USA. [Zoratti, Edward M.] Henry Ford Hlth Syst, Detroit, MI USA. [Pongracic, Jacqueline A.] Ann & Robert H Lurie Childrens Hosp Chicago, Chicago, IL 60611 USA. [Babineau, Denise C.; Visness, Cynthia M.] Rho Fed Syst Div, Chapel Hill, NC USA. [Gergen, Peter J.; Togias, Alkis] Natl Inst Allergy & Infect Dis, Bethesda, MD USA. [Busse, William W.] Univ Wisconsin, Sch Med & Publ Hlth, Madison, WI USA.
Liu, AH (reprint author), Childrens Hosp Colorado, Aurora, CO 80045 USA.; Liu, AH (reprint author), Univ Colorado, Sch Med, Aurora, CO 80045 USA. Andrew.liu@childrenscolorado.org

Allergy and Immunology
Mann ET, **Havstad SL**, **Sitarik A**, **Bellemore SM**, **Levin AM**, Lynch SV, Ownby DR, **Johnson CC**, Lukacs NW, **Zoratti EM**, **Woodcroft KJ**, and **Bobbitt KR**. Characterization of basophils in infants in the microbes, allergy, asthma and Pets (MAAP) birth cohort *J Allergy Clin Immunol* 2017; 139(2):AB168. PMID: Not assigned. Abstract

E.T. Mann, Henry Ford Health System, Detroit, United States

RATIONALE: Basophils are mature circulating granulocytic cells that play an important role in IgE-dependent immune responses. The objective of this study was to prospectively examine, in very early life, basophils for FcεRIa and activation markers, which are involved in a Th2 response. METHODS: Cord blood and venous blood at 6 months of age were obtained from 65 infants enrolled in the MAAP (Microbes, Allergy, Asthma and Pets) birth cohort. Basophil percentages were determined by manual differential count of 200 cells in whole blood smears. The enriched granulocyte fraction collected after Ficoll separation of peripheral blood mononuclear cells was examined by flow cytometry. Basophils were defined as low side scatter/Class II 2/CD123+ cells. Cells expressing FcεRIa or the activation markers CD203c or CD63 were examined and were reported as % of basophils expressing these markers. Paired t-tests were used to assess change over time. RESULTS: Basophils represented a mean 0.78% (range 0 to 2.5%) and 0.88% (range 0 to 4.0%) of the differential among cord and 6 month blood samples, respectively. There was a statistically significant increase from birth to 6 months of age in the proportion of basophils expressing FcεRIa (mean increase 12.7%, p=0.007), CD203c (mean increase 16.7%, p<0.001) or CD63 (mean increase 20.3%, p<0.001). CONCLUSIONS: The longitudinal investigation of basophils in samples from the first months of life makes this study distinctive. The increase in the proportion of basophils that were either CD203c+, CD63+, or FcεRIa+ suggests the rapid development of this aspect of innate immunity during the earliest prenatal period.

Allergy and Immunology
Orandi D, **Havstad S**, **Sitarik A**, **Bobbitt K**, **Jones K**, **Levin A**, Lukacs N, Lynch SV, **Wegienka G**, **Woodcroft K**, Ownby D, Johnson C, and **Zoratti E**. An analysis of potential associations between delivery mode and dog-keeping to basophil FCER1 and activation marker expression during infancy *J Allergy Clin Immunol* 2017; 139(2):AB167. PMID: Not assigned. Abstract

D. Orandi, Henry Ford Health System, Detroit, United States

RATIONALE: Early-life exposures, including dog-keeping and vaginal delivery, are associated with lower rates of childhood allergy. The underlying immune mechanism(s) are unknown. Basophils are innate immune cells capable of promoting Th2 polarization and allergy development. We explored associations of these exposures with basophil FcεR1 and activation marker expression during the first 6 months of life. METHODS: Basophil-lineage cells (low side scatter/Class II-/CD123+ from the enriched granulocyte fraction) FcεR1, CD63 and CD203c were identified by flow cytometry in cord blood and at age 6 months in the Microbes, Allergy, Asthma and Pets birth cohort. Concomitant total IgE levels were determined. Dog-keeping during pregnancy and delivery mode data was collected prospectively. Analysis included non-parametric testing using Kruskal-Wallis and Wilcoxon rank sum comparisons. RESULTS: No associations between dog-keeping (any vs. none) and basophil marker expression were apparent. However, children from homes with >1 dog had lower proportions of basophils expressing CD63 at 6 months (median=11.9%, n=18) than those with 0 or 1 dog (median=21.3%, n=33; median=30.7%, n=26, respectively; p=0.045). A trend for lower percentage FcεR1 expression with >1 dog was noted (p=0.096). Vaginal delivery was associated with proportionally fewer basophils expressing FcεR1 versus c-section in cord blood only (median=13.7%, n=80; median=50%, n=16, respectively; p=0.031). Cord and 6 month IgE levels did not correlate with basophil marker expression. CONCLUSIONS: Early-life exposure to multiple dogs is associated with lower proportions of basophils expressing

CD63 at 6 months. Natural parturition is associated with lower proportions of basophils expressing FcεR1 in cord blood. These associations may relate to lowered allergy risk.

Cardiology
Abdelrahim E, **Eng M**, **Gorgis S**, **Mawri S**, **Wang DD**, **Greenbaum A**, **Mahan M**, **Wyman J**, **Paone G**, and **O'Neill W**. Predictors of late bleeding in the tavr population *J Am Coll Cardiol* 2017; 69(11):1298-1298. PMID: Not assigned. Abstract

[Abdelrahim, Elsheikh; Eng, Marvin; Gorgis, Sarah; Mawri, Sagger; Wang, Dee Dee; Greenbaum, Adam; Mahan, Meredith; Wyman, Janet; Paone, Gaetano; O'Neill, William] Henry Ford Hosp, Detroit, MI 48202 USA.

Cardiology
Al-Darzi W, **Nowak R**, **Hudson M**, **Moyer ML**, **Jacobsen G**, and **McCord J**. Ischemicst-segment changes on electrocardiogram in acute myocardial infarction-still common? *J Gen Intern Med* 2017; 32(2):S235-S236. PMID: Not assigned. Abstract

W. Al-Darzi, Henry Ford Hospital, Detroit, United States

BACKGROUND: Prior studies report ischemic ST-segment changes on electrocardiogram (ECG) in 40-60% of patients with acute myocardial infarction (AMI) with important diagnostic and prognostic implications. Additionally, 1 to 6% of AMI patients had normal ECG on prior studies. These findings may have changed on the era of more sensitive cardiac troponin (cTn) assays. METHODS: In a single-center we prospectively studied 569 patients who were evaluated for possible AMI in the emergency department from May 2013 to April 2015. Diagnosis of AMI was adjudicated by 2 independent physicians in accordance with the universal definition of AMI using all clinical information and required cTnI > 0.04 ng/ml (Siemens Ultra-cTnI). In situations where there was disagreement between the adjudicators, a third Cardiology adjudicator reviewed the case for final determination. Patients with ECG findings that led to immediate reperfusion therapy were excluded. RESULTS: There were 45 (8%) patients with a diagnosis of AMI. Among AMI patients, the most common ECG findings were T-wave inversion 13 (29%) and normal 13 (29%) while 6 (13%) ECGs demonstrated ST Depression ≥ 1 mm. Comparing patients with and without ST-segment elevation or depression, there was non-significantly higher cTnI levels (13.2 ± 28.3 vs. 5.9 ± 15.6 ng/ml; p = 0.355). CONCLUSIONS: ST-segment changes on ECG are becoming less common in AMI. This may relate to smaller AMIs identified by more sensitive cTn assays which should be verified in larger trials. (Table Presented).

Cardiology
Al-Mallah MH, **Ahmed A**, **Qureshi W**, **Elshawi R**, **Brawner C**, **Blaha M**, **Ahmed H**, **Ehrman J**, **Keteyian S**, and **Sakr S**. Using machine learning to define the association between cardiorespiratory fitness and all-cause mortality: The fit (henry ford exercise testing) project *J Am Coll Cardiol* 2017; 69(11):1612-1612. PMID: Not assigned. Abstract

Henry Ford Hosp, Detroit, MI 48202 USA. King Saud bin Abdulaziz Univ Hlth Sci, King Abdulaziz Med City, Riyadh, Saudi Arabia.

Cardiology
Babaliaros VC, **Greenbaum AB**, Khan JM, Rogers T, **Wang DD**, **Eng MH**, **O'Neill WW**, **Paone G**, Thourani VH, Lerakis S, Kim DW, Chen MY, and Lederman RJ. Intentional percutaneous laceration of the anterior mitral leaflet to prevent outflow obstruction during transcatheter mitral valve replacement: First-in-human experience *JACC Cardiovasc Interv* 2017; 10(8):798-809. PMID: 28427597. Full Text

Structural Heart and Valve Center, Emory University Hospital, Atlanta, Georgia.
Center for Structural Heart Disease, Henry Ford Health System, Detroit, Michigan.
Cardiovascular and Pulmonary Branch, Division of Intramural Research, National Heart Lung and Blood Institute, National Institutes of Health, Bethesda, Maryland.
Structural Heart and Valve Center, Emory University Hospital, Atlanta, Georgia; Children's Healthcare of Atlanta, Emory University, Atlanta, Georgia.
Cardiovascular and Pulmonary Branch, Division of Intramural Research, National Heart Lung and Blood Institute, National Institutes of Health, Bethesda, Maryland. Electronic address: lederman@nih.gov.

OBJECTIVES: This study sought to use a new catheter technique to split the anterior mitral valve leaflet (AML) and prevent iatrogenic left ventricular outflow tract (LVOT) obstruction immediately before transcatheter mitral valve

replacement (TMVR). BACKGROUND: LVOT obstruction is a life-threatening complication of TMVR, caused by septal displacement of the AML. METHODS: The procedure was used in patients with severe mitral valve disease and prohibitive surgical risk. Patients either had prior surgical mitral valve ring (n = 3) or band annuloplasty (n = 1) or mitral annular calcification with stenosis (n = 1). Iatrogenic LVOT obstruction or transcatheter heart valve dysfunction was predicted in all based on echocardiography and computed tomography. Transfemoral coronary guiding catheters directed an electrified guidewire across the center and base of the AML toward a snare in the left atrium. The externalized guidewire loop was then electrified to lacerate the AML along the centerline from base to tip, sparing chordae, immediately before transseptal TMVR. RESULTS: Five patients with prohibitive risk of LVOT obstruction or transcatheter heart valve dysfunction from TMVR successfully underwent LAMPOON, with longitudinal splitting of the A2 scallop of the AML, before valve implantation. Multiplane computed tomography modeling predicted hemodynamic collapse from TMVR assuming an intact AML. However, critical LVOT gradients were not seen following LAMPOON and TMVR. Doppler blood flow was seen across transcatheter heart valve struts that encroached the LVOT, because the AML was split. Transcatheter heart valve function was unimpeded. CONCLUSIONS: This novel catheter technique, which resembles surgical chord-sparing AML resection, may enable TMVR in patients with prohibitive risk of LVOT obstruction or transcatheter heart valve dysfunction.

Cardiology

Butler J, Hamo CE, Udelson JE, O'Connor C, **Sabbah HN**, Metra M, Shah SJ, Kitzman DW, Teerlink JR, Bernstein HS, Brooks G, Depre C, DeSouza MM, Dinh W, Donovan M, Frische-Danielson R, Frost RJ, Garza D, Gohring UM, Hellawell J, Hsia J, Ishihara S, Kay-Mugford P, Koglin J, Kozinn M, Larson CJ, Mayo M, Gan LM, Mugnier P, Mushonga S, Roessig L, Russo C, Salsali A, Satler C, Shi V, Ticho B, van der Laan M, Yancy C, Stockbridge N, and Gheorghiade M. Reassessing phase II heart failure clinical trials consensus recommendations *Circ Heart Fail* 2017; 10(4):1-8. PMID: 28356300. Full Text

[Butler, Javed] SUNY Stony Brook, Dept Med, Stony Brook, NY USA. [Udelson, James E.] Tufts Med Ctr, Div Cardiol, CardioVasc Ctr, Boston, MA USA. [O'Connor, Christopher] Inova Heart & Vasc Inst, Div Cardiol, Falls Church, VA USA. [Sabbah, Hani N.] Henry Ford Hosp, Dept Med, Div Cardiovasc Med, Detroit, MI USA. [Metra, Marco] Univ Brescia, Div Cardiol, Civil Hosp, Brescia, Italy. [Shah, Sanjiv J.] NW Univ Feinberg Sch Med, Div Cardiol, Chicago, IL USA. [Kitzman, Dalane W.] Univ Calif San Francisco, Cardiovasc Med, Wake Forest Sch Med, Winston Salem, NC USA. [Teerlink, John R.] Univ Calif San Francisco, Div Cardiol, San Francisco, CA USA. [Bernstein, Harold S.] Merck & Co Inc, Kenilworth, NJ USA. [Brooks, Gabriel; Hellawell, Jennifer; Satler, Carol] Gilead Sci, Foster City, CA USA. [Depre, Christophe; Kozinn, Marc] Amgen Inc, Thousand Oaks, CA USA. [DeSouza, Mary M.; Donovan, Mark; Frost, Robert J.; Mugnier, Pierrre; Mushonga, Sekayi; Russo, Cesare] Bristol Myers Squibb, Princeton, NJ USA. [Dinh, Wilfried] Bayer, Wuppertal, Germany. [Dinh, Wilfried] Univ Hosp Witten Herdecke Germany, Dept Cardiol, HELIOS Clin Wuppertal, Wuppertal, Germany. [Donovan, Mark] AstraZeneca, Gaithersburg, MD USA. [Frische-Danielson, Regina; Hellawell, Jennifer] AstraZeneca, Gothenburg, Sweden. [Garza, Dahlia; Ishihara, Shiro] Relypsa Inc, Redwood City, CA USA. [Kay-Mugford, Patricia] Vifor Pharma, Opfikon, Switzerland. [Russo, Cesare] Nippon Med Sch Musashi Kosugi Hosp, Dept Cardiol, Kawasaki, Kanagawa, Japan. [Roessig, Lothar] Novartis Pharmaceut Inc, Hanover, NH USA. [Salsali, Afshin] Bayer Pharma AG, Wuppertal, Germany. [Larson, Christopher J.] Columbia Univ, Med Ctr, New York, NY USA. [Salsali, Afshin; Ticho, Barry] Pharmaceut Inc, Boehringer Ingelheim Pharmaceut Inc, Ridgefield, CT USA. [Stockbridge, Norman] Moderna Therapeut, Feinberg Sch Med, Cambridge, MA USA. [Gheorghiade, Mihai] United States Food & Drug Adm, Div Cardiovasc & Renal Prod, Silver Spring, MD USA. [Stockbridge, Norman; Gheorghiade, Mihai] SUNY Stony Brook, Div Cardiol, Room 080, Stony Brook, NY 11794 USA.
Butler, J (reprint author), SUNY Stony Brook, Dept Med, Stony Brook, NY USA.
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The increasing burden and the continued suboptimal outcomes for patients with heart failure underlines the importance of continued research to develop novel therapeutics for this disorder. This can only be accomplished with successful translation of basic science discoveries into direct human application through effective clinical trial design and execution that results in a substantially improved clinical course and outcomes. In this respect, phase II clinical trials play a pivotal role in determining which of the multitude of potential basic science discoveries should move to the large and expansive registration trials in humans. A critical examination of the phase II trials in heart failure reveals multiple shortcomings in their concept, design, execution, and interpretation. To further a dialogue on the challenges and potential for improvement and the role of phase II trials in patients with heart failure, the Food and Drug Administration facilitated a meeting on October 17, 2016, represented by clinicians, researchers, industry members, and regulators. This document summarizes the discussion from this meeting and provides key recommendations for future directions.

Cardiology
Evans KL, Wirtz H, Li J, **She RC**, Maya J, Depre C, Hamer A, and **Lanfear D**. Genetics of heart rate observational study (genhrate) *J Am Coll Cardiol* 2017; 69(11):685-685. PMID: Not assigned. Abstract

Henry Ford Hosp, Detroit, MI 48202 USA. Amgen Inc, Thousand Oaks, CA USA.

Cardiology
Frisoli TM, **Afana M**, **Mawri S**, **Hadid M**, **Sayed L**, **O'Neill WW**, **Parikh S**, **Wang DD**, **Khandelwal A**, and **Alaswad K**. Respect the septal perforator: Septal artery perforation during cto pci resulting in massive interventricular septal hematoma and biventricular cardiac obstructive shock *JACC Cardiovasc Interv* 2017;PMID: 28456700. Full Text

Henry Ford Hospital, Detroit, Michigan. Electronic address: Tfrisoli@gmail.com.

Cardiology
Gindi R, and **Parikh S**. For the love of loeffler *J Am Coll Cardiol* 2017; 69(11):2348-2348. PMID: Not assigned. Abstract

[Gindi, Ryan; Parikh, Sachin] Henry Ford Hosp, Detroit, MI 48202 USA.

Cardiology
Gupta RC, **Singh-Gupta V**, and **Sabbah HN**. Long-term therapy with elamipretide normalizes activation of the mitochondrial signal transducer and activator of transcription 3 (mstat3) in of left ventricular myocardium of dogs with chronic heart failure *J Am Coll Cardiol* 2017; 69(11):923-923. PMID: Not assigned. Abstract

[Gupta, Ramesh C.; Singh-Gupta, Vinita; Sabbah, Hani N.] Henry Ford Hosp, Detroit, MI 48202 USA.

Cardiology
Hansen JW, Foy A, Yadav P, Gilchrist I, Kozak M, **Wang A**, **Wang DD**, **Eng M**, **Greenbaum A**, and **O'Neill W**. Death and dialysis risk after transcatheter aortic valve replacement *J Am Coll Cardiol* 2017; 69(11):1212-1212. PMID: Not assigned. Abstract.

Penn State Milton S Hershey Med Ctr, Hershey, PA USA. Henry Ford Hlth Syst, Detroit, MI USA.

Cardiology
Jain T, **Nowak R**, **Hudson M**, **Moyer M**, **Jacobsen G**, and **McCord J**. How often does troponin elevation identify acute myocardial infarction in the emergency department? *J Am Coll Cardiol* 2017; 69(11):1191-1191. PMID: Not assigned. Abstract

[Jain, Tarun; Nowak, Richard; Hudson, Michael; Moyer, Michele; Jacobsen, Gordon; McCord, James] Henry Ford Hosp, Detroit, MI 48202 USA.

Cardiology
Jain T, **Wang DD**, **Eng M**, **Isley M**, **Paone G**, **Greenbaum A**, and **O'Neill W**. Transcatheter mitral valve-in-ring implantation after failure of surgical mitral ring annuloplasty *J Am Coll Cardiol* 2017; 69(11):1262-1262. PMID: Not assigned. Abstract

[Jain, Tarun; Wang, Dee Dee; Eng, Marvin; Isley, Michael; Paone, Gaetano; Greenbaum, Adam; O'Neill, William] Henry Ford Hosp, Detroit, MI 48202 USA.

Cardiology
Kassier A, **Tawney A**, **Nona P**, and **Ananthasubramaniam K**. Impact of echo contrast agents on ventricular assist devices (vad) hemodynamics: Are they safe to use? *J Am Coll Cardiol* 2017; 69(11):1632-1632. PMID: Not assigned. Abstract

[Kassier, Adnan; Tawney, Adam; Nona, Paul; Ananthasubramaniam, Karthikeyan] Henry Ford Hlth Syst, Detroit, MI USA.

Cardiology
Lavie CJ, **Keteyian SJ**, and Ventura HO. Therapeutic cardiorespiratory fitness to prevent and treat heart failure *JACC Heart Fail* 2017; 5(5):375-376. PMID: 28396039. Full Text

Department of Cardiovascular Diseases, John Ochsner Heart and Vascular Institute, Ochsner Clinical School, The University of Queensland School of Medicine, New Orleans, Louisiana. Electronic address: clavie@ochsner.org.
Division of Cardiovascular Medicine, Henry Ford Hospital, Detroit, Michigan.
Department of Cardiovascular Diseases, John Ochsner Heart and Vascular Institute, Ochsner Clinical School, The University of Queensland School of Medicine, New Orleans, Louisiana.

Cardiology
Meraj PM, Doshi R, Schreiber T, Maini B, and **O'Neill WW**. Impella 2.5 initiated prior to unprotected left main PCI in acute myocardial infarction complicated by cardiogenic shock improves early survival *J Interv Cardiol* 2017;PMID: 28419573. Full Text

Department of Cardiology, Northwell Health, Manhasset, New York.
Department of Cardiology, Detroit Medical Center, Detroit, Michigan.
Department of Interventional Cardiology and Transcatheter Therapy, Charles E. Schmidt College of Medicine, Delray Beach, Florida.
Department of Interventional Cardiology and Structural Heart, Henry Ford Medical Center, Detroit, Michigan.

OBJECTIVES: To assess post-procedural outcomes when Impella 2.5 percutaneous left ventricular assist device (pLVAD) support is initiated either prior to or after percutaneous coronary intervention (PCI) on unprotected left main coronary artery (ULMCA) culprit lesion in the context of acute myocardial infarction cardiogenic shock (AMICS). BACKGROUND: Initiation of Impella 2.5 pLVAD prior to PCI is associated with significant survival benefit in the setting of AMICS. Outcomes of those presenting with a ULMCA culprit lesion in this setting have not been well characterized. METHODS: Thirty-six consecutive patients in the cVAD Registry supported with Impella 2.5 pLVAD for AMICS who underwent PCI on ULMCA culprit lesion were included in our multicenter study. RESULTS: The average age was 69.8 +/- 14.2 years, 77.8% were male, 72.7% were in CS at admission, 44.4% sustained one or multiple cardiac arrests, and 30.6% had anoxic brain injury. Baseline characteristics were comparable between the Pre-PCI group (n = 20) and Post-PCI group (n = 16). Non-ST segment elevation myocardial infarction and greater coronary disease burden were significantly more frequent in the Pre-PCI group but they had significantly better survival to discharge (55.0% vs 18.8%, P = 0.041). Kaplan-Meier 30-day survival analysis showed very poor survival in Post-PCI group (48.1% vs 12.5%, Log-Rank P = 0.004). CONCLUSIONS: Initiation of Impella 2.5 pLVAD prior to as compared with after PCI of ULMCA for AMICS culprit lesion is associated with significant early survival. As previously described, patients supported after PCI appear to have very poor survival at 30 days.

Cardiology
Nketiah E, **McCord J**, and **Koenig G**. Cardiac electrical biomarker response during percutaneous coronary intervention *J Am Coll Cardiol* 2017; 69(11):1193-1193. PMID: Not assigned. Abstract

[Nketiah, Emmanuel; McCord, James; Koenig, Gerald] Henry Ford Hlth Syst, Detroit, MI USA.

Cardiology
Nona P, **Mittal A**, **Pattiala K**, **Brooks K**, **Moore MT**, and **Ananthasubramaniam K**. Do cardiovascular health screening programs and focused counseling have impact on patient habits and lifestyle change? Early results of the heart smart screening program *J Am Coll Cardiol* 2017; 69(11):1815-1815. PMID: Not assigned. Abstract

[Nona, Paul; Mittal, Aayush; Pattiala, Karthik; Brooks, Kristen; Moore, Maria Tyler; Ananthasubramaniam, Karthikeyan] Henry Ford Hlth Syst, Detroit, MI USA.

Cardiology
O'Neill W, **Basir M**, Dixon S, Patel K, Schreiber T, and Almany S. Feasibility of early mechanical support during mechanical reperfusion of acute myocardial infarct cardiogenic shock *JACC Cardiovasc Interv* 2017; 10(6):624-625. PMID: 28335901. Full Text

Cardiology
Patel R, **Abdelrahim E**, **Ali M**, **Desai N**, **Singh A**, **Sudasena D**, **Wang DD**, **Eng MH**, **O'Neill W**, and **Greenbaum A**. Outcomes and their predictors in acute transcatheter aortic heart valve-in-transcatheter aortic heart valve therapy *J Am Coll Cardiol* 2017; 69(11):1990-1990. PMID: Not assigned. Abstract

[Patel, Ruchir; Abdelrahim, Elsheikh; Ali, Mahmoud; Desai, Nirmit; Singh, Aditya; Sudasena, Daryl; Wang, Dee Dee; Eng, Marvin H.; O'Neill, William; Greenbaum, Adam] Wayne State Univ, Henry Ford Hosp, Detroit, MI USA.

Cardiology
Patel R, **Ali M**, **Nair S**, **Alqarqaz M**, **Koenig G**, **Zaidan M**, **Kim H**, **O'Neill W**, and **Alaswad K**. Innovative technique to achieve hemostasis with large bore access for percutaneous hemodynamic support devices *J Am Coll Cardiol* 2017; 69(11):1114-1114. PMID: Not assigned. Abstract

[Patel, Ruchir; Ali, Mahmoud; Nair, Steven; Alqarqaz, Mohammad; Koenig, Gerald; Zaidan, Mohammad; Kim, Henry; O'Neill, William; Alaswad, Khaldoon] Wayne State Univ, Henry Ford Hosp, Detroit, MI USA.

Cardiology
Qureshi W, **Ahmed A**, **Blaha M**, **Brawner C**, **Ehrman J**, **Kupsky D**, **Keteyian S**, **Ahmed H**, and **Al-Mallah M**. Chronotropic incompetence and long-term risk of heart failure: The henry ford exercise testing project *J Am Coll Cardiol* 2017; 69(11):691-691. PMID: Not assigned. Abstract

Henry Ford Hosp, Detroit, MI 48202 USA. King Saud bin Abdulaziz Univ Hlth Sci, King Abdulaziz Med City, Riyadh, Saudi Arabia.

Cardiology
Schuger CD, and **Singh G**. Tying Ourselves in Knots to Avoid Ventricular Pacing in Sick Sinus Syndrome. Does it Matter?* *JACC: Clinical Electrophysiology* 2017;PMID: Not assigned. Full Text

C.D. Schuger, Cardiac Electrophysiology Section, Edith and Benson Ford Heart and Vascular Institute, Henry Ford Health System, 2799 West Grand Boulevard, M322, Detroit, Michigan 48202

Cardiology
Shah R, **Nasr Y**, **Raymond T**, **Khandelwal A**, and **Tita C**. Proof is in the paclitaxel: Catheter directed intracoronary paclitaxel as salvage therapy for refractory cardiac allograft vasculopathy *J Am Coll Cardiol* 2017; 69(11):2462-2462. PMID: Not assigned. Abstract

[Shah, Rajan; Nasr, Youssef; Raymond, Timothy; Khandelwal, Akshay; Tita, Cristina] Henry Ford Heart & Vasc Inst, Detroit, MI USA.

Cardiology
Singh G, **Lahiri MK**, **Khan A**, and **Schuger CD**. Bundle branch reentrant ventricular tachycardia after transcatheter aortic valve replacement *HeartRhythm Case Reports* 2017; 3(3):177-185. PMID: Not assigned. Article Request Form

G. Singh, Section of Cardiac Electrophysiology, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, United States

Cardiology

Singh V, Yadav PK, **Eng MH**, Macedo FY, Silva GV, Mendirichaga R, Badiye AP, Sakhuja R, Elmariah S, Inglessis I, Alfonso CE, Schreiber TL, Cohen M, Palacios I, and **O'Neill WW**. Outcomes of hemodynamic support with Impella in very high-risk patients undergoing balloon aortic valvuloplasty: Results from the Global cVAD Registry *Int J Cardiol* 2017;PMID: 28377189. Full Text

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BACKGROUND: Reports on the role of hemodynamic support devices in patients with severe aortic stenosis (AS) and left ventricular (LV) dysfunction undergoing balloon aortic valvuloplasty (BAV) are limited. METHODS: Patients were identified from the cVAD registry, an ongoing multicenter voluntary registry at selected sites in North America that have used Impella in >10 patients. RESULTS: A total of 116 patients with AS who underwent BAV with Impella support were identified. Mean age was 80.41+/-9.03years and most patients were male. Mean STS score was 18.77%+/-18.32, LVEF was 27.14%+/-16.07, and 42% underwent concomitant PCI. In most cases Impella was placed electively prior to BAV, whereas 26.7% were placed as an emergency. The two groups had similar baseline characteristics except for higher prevalence of CAD and lower LVEF in the elective group, and higher STS score in the emergency group. Elective strategy was associated higher 1-year survival compared to emergency placement (56% vs. 29.2%, p=0.003). One-year survival was higher when BAV was used as a bridge to definitive therapy as opposed to palliative treatment (90% vs. 28%, p<0.001). On multivariate analysis, STS score and aim of BAV (bridge to definitive therapy vs. palliative indication) were independent predictors of mortality. CONCLUSION: In this large cohort of patients with AS and severe LV dysfunction undergoing BAV, our results demonstrates feasibility and promising long-term outcomes using elective Impella support with the intention to bridge to a definitive therapy.

Cardiology

Solomon R, **Nowak R**, **Hudson M**, **Moyer M**, and **McCord J**. Is duration of symptoms predictive of acute myocardial infarction? *J Am Coll Cardiol* 2017; 69(11):247-247. PMID: Not assigned. Abstract

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Cardiology

Ting C, **Singh A**, **Solomon R**, **Murad A**, **Woolley R**, and **Michaels A**. No maggic in predicting heart failure readmissions *J Am Coll Cardiol* 2017; 69(11):788-788. PMID: Not assigned. Abstract

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Background: Readmission for acute decompensated heart failure represents a significant burden to healthcare in the United States with nearly a quarter of patients being readmitted by 30 days. Here, we evaluate the ability of two robust risk tools derived from ambulatory cohorts, the MAGGIC score and Seattle Heart Failure Model (SHFM), to predict 30-day readmission in an urban heart failure population. Methods: This single center retrospective cohort study analyzed a total of 1172 patients admitted for acute systolic or combined systolic-diastolic heart failure. All patients were assigned a discharge NYHA class 2 status. The primary endpoint was readmission with primary diagnosis of decompensated heart failure. Patients with end-stage renal disease, isolated diastolic heart failure, history of or awaiting heart transplant, and ventricular assist devices were excluded. Data from all variables identified in the MAGICC and SHFM risk scores were abstracted from this cohort, as well as BNP and renal function. The association of SHFM or MAGICC variables and 30-day readmission risk was evaluated with univariate binary logistic regression models. Results: Of 1172 patients included in the study, there were 245 readmissions. 43 patients who expired or placed in hospice at the index encounter were removed prior to analysis, leaving 1129 in the final analysis. The average age was 69.3 years, with 43% female and 49% white. Neither risk tool, SHFM (OR 0.96, 95% CI 0.79-1.17, p=0.7) or MAGGIC (OR 1.0, 95% CI 0.98-1.02, p = 0.892), demonstrated utility in stratifying hospitalized patients at discharge for risk of readmission. Conclusions: The MAGGIC and Seattle Heart Failure Model are two

robust risk models of all-cause mortality in ambulatory heart failure patients but fail to predict 30-day readmission in acute decompensated heart failure. Assessing readmission risk in a heart failure patient is complex and likely dependent on many patient-level factors that are not readily quantifiable in current risk-prediction tools. Traditional risk factors identified for mortality may not be sufficient in predicting readmission risk and future endeavors may benefit from evaluating socioeconomic influences.

Center for Health Policy and Health Services Research
Friedly JL, Comstock BA, Turner JA, Heagerty PJ, Deyo RA, Bauer Z, Avins AL, Nedeljkovic SS, **Nerenz DR**, Shi XR, Annaswamy T, Standaert CJ, Smuck M, Kennedy DJ, Akuthota V, Sibell D, Wasan AD, Diehn F, Suri P, Rundell SD, Kessler L, Chen AS, and Jarvik JG. Long term effects of repeated injections of local anesthetic with or without corticosteroid for lumbar spinal stenosis: a randomized trial *Arch Phys Med Rehabil* 2017;PMID: 28396242. Full Text

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OBJECTIVE: To determine the overall long term effectiveness of treatment with epidural corticosteroid injections for lumbar central spinal stenosis and the impact of repeat injections, including crossover injections, on outcomes through 12 months. DESIGN: Multicenter, double-blind, randomized trial comparing epidural injections of corticosteroid plus lidocaine versus lidocaine alone SETTING: 16 U.S. clinical sites PARTICIPANTS: 400 participants with imaging-confirmed lumbar central spinal stenosis INTERVENTIONS: Participants were randomized to receive either epidural injections with corticosteroid plus lidocaine or lidocaine alone with the option of blinded crossover after 6 weeks to receive the alternate treatment. Participants could receive 1-2 injections from 0-6 weeks and up to 2 injections from 6-12 weeks. After 12 weeks, participants received usual care. MAIN OUTCOME MEASURES: Primary outcomes were the Roland-Morris Disability Questionnaire (RDQ; range 0 to 24; higher scores indicate greater disability) and leg pain intensity (range 0='no pain' to 10='pain as bad as you can imagine'). Secondary outcomes included opioid use, spine surgery and crossover rates. RESULTS: At 12 months, both treatment groups maintained initial observed improvements, with no significant differences between groups on the RDQ (adjusted mean difference:

-0.4; 95% confidence interval [CI]: -1.6, 0.9; p=0.55); leg pain (adjusted mean difference: 0.1; 95% CI: -0.5, 0.7; p=0.75); opioid use (corticosteroid plus lidocaine (41.4%) versus lidocaine alone (36.3%), p=0.41); or spine surgery (corticosteroid plus lidocaine (16.8%) versus lidocaine alone (11.8%), p=0.22). Fewer participants randomized to corticosteroid plus lidocaine (30%, n=60) versus lidocaine alone (45%, n=90) crossed over after 6 weeks (p=0.003). Among participants who crossed over at 6 weeks, the 6-12 week RDQ change did not differ between the two randomized treatment groups (adjusted mean difference -1.0; 95% CI: -2.6 to 0.7, p=0.24). In both groups, participants crossing over at 6 weeks had worse 12-month trajectories compared with participants who did not choose to cross over. CONCLUSIONS: For lumbar spinal stenosis symptoms, epidural injections of corticosteroid plus lidocaine offered no benefits from 6 weeks to 12 months beyond that of injections of lidocaine alone in terms of self-reported pain and function or reduction in use of opioids and spine surgery. In patients with improved pain and function 6 weeks after initial injection, these outcomes were maintained at 12 months. However, the trajectories of pain and function outcomes after 3 weeks did not differ by injectate type. Repeated injections of either type offered no additional long-term benefit if injections in the first 6 weeks did not improve pain.

Center for Health Policy and Health Services Research

Gold LS, Bryan M, Comstock BA, Bresnahan BW, Deyo RA, Nedeljkovic SS, **Nerenz DR**, Heagerty P, and Jarvik JG. Associations between relative value units and patient-reported back pain and disability *Gerontol Geriatr Med* 2017; 3:2333721416686019. PMID: 28405596. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5384601/

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Objective: To describe associations between health care utilization measures and patient-reported outcomes (PROs). Method: Primary data were collected from patients >/=65 years with low back pain visits from 2011 to 2013. Six PROs of pain and functionality were collected 12 and 24 months after the index visits and total and spine-specific relative value units (RVUs) from electronic health records were tabulated over 1 year. We calculated correlation coefficients between RVUs and 12- and 24-month PROs and conducted linear regressions with each 12- and 24-month PRO as the outcome variables and RVUs as predictors of interest. Results: We observed very weak correlations between worse PROs at 12 and 24 months and greater 12-month utilization. In regression analyses, we observed slight associations between greater utilization and worse 12- and 24-month PROs. Discussion: We found that 12-month health care utilization is not strongly associated with PROs at 12 or 24 months.

Center for Health Policy and Health Services Research

Gui H, Kwok M, Baum L, Sham PC, Kwan P, and Cherny SS. SNP-based HLA allele tagging, imputation and association with antiepileptic drug-induced cutaneous reactions in Hong Kong Han Chinese *Pharmacogenomics J* 2017;PMID: 28398356. Article Request Form

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Human leukocyte antigen (HLA) genes control the regulation of the human immune system and are involved in immune-related diseases. Population surveys on relationships between single nucleotide polymorphisms (SNP) and HLA alleles are essential to conduct genetic association between HLA variants and diseases. Samples were obtained from our in-house database for epilepsy genetics and pharmacogenetics research. Using 184 epilepsy patients with both genome-wide SNP array and HLA-A/B candidate gene sequencing data, we sought tagging SNPs that completely represent sixHLA risk alleles; in addition, a Hong Kong population-specific reference panel was constructed for SNP-based HLA imputation. The performance of our new panel was compared to a recent Han Chinese panel. Finally, genetic associations of HLA variants with mild skin rash were performed on the combined sample of 408 patients. Common SNPs rs2571375 and rs144295468 were found to successfully tag HLA risk alleles A*31:01 and B*13:01, respectively. HLA-B*15:02 can be predicted by rs144012689 with >95% sensitivity and specificity. The imputation reference panel for the Hong Kong population had comparable performance to the Han

Chinese panel due to the large sample size for common HLA alleles, though it retained discordance for imputing rare alleles. No significant genetic associations were found between HLA genetic variants and mild skin rash induced by aromatic antiepileptic drugs. This study provides new information on the genetic structure of HLA regions in the Hong Kong population by identifying tagging SNPs and serving as a reference panel. Moreover, our comprehensive genetic analyses revealed no significant association between HLA alleles and mild skin rash in Hong Kong Han Chinese.The Pharmacogenomics Journal advance online publication, 11 April 2017; doi:10.1038/tpj.2017.11.

Center for Health Policy and Health Services Research

Lim HW, Collins SAB, Resneck JS, Jr., Bolognia JL, Hodge JA, Rohrer TA, Van Beek MJ, Margolis DJ, Sober AJ, Weinstock MA, **Nerenz DR**, Smith Begolka W, and Moyano JV. Contribution of health care factors to the burden of skin disease in the United States *J Am Acad Dermatol* 2017;PMID: 28427793. Full Text

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The American Academy of Dermatology has developed an up-to-date national Burden of Skin Disease Report on the impact of skin disease on patients and on the US population. In this second of 3 manuscripts, data are presented on specific health care dimensions that contribute to the overall burden of skin disease. Through the use of data derived from medical claims in 2013 for 24 skin disease categories, these results indicate that skin disease health care is delivered most frequently to the aging US population, who are afflicted with more skin diseases than other age groups. Furthermore, the overall cost of skin disease is highest within the commercially insured population, and skin disease treatment primarily occurs in the outpatient setting. Dermatologists provided approximately 30% of office visit care and performed nearly 50% of cutaneous surgeries. These findings serve as a critical foundation for future discussions on the clinical importance of skin disease and the value of dermatologic care across the population.

Center for Health Policy and Health Services Research

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Genome-wide association studies (GWAS) have identified >300 loci associated with measures of adiposity including body mass index (BMI) and waist-to-hip ratio (adjusted for BMI, WHRadjBMI), but few have been identified through screening of the African ancestry genomes. We performed large scale meta-analyses and replications in up to 52,895 individuals for BMI and up to 23,095 individuals for WHRadjBMI from the African Ancestry Anthropometry Genetics Consortium (AAAGC) using 1000 Genomes phase 1 imputed GWAS to improve coverage of both common and low frequency variants in the low linkage disequilibrium African ancestry genomes. In the sex-combined analyses, we identified one novel locus (TCF7L2/HABP2) for WHRadjBMI and eight previously established loci at P < 5x10-8: seven for BMI, and one for WHRadjBMI in African ancestry individuals. An additional novel locus (SPRYD7/DLEU2) was identified for WHRadjBMI when combined with European GWAS. In the sex-stratified analyses, we identified three novel loci for BMI (INTS10/LPL and MLC1 in men, IRX4/IRX2 in women) and four for WHRadjBMI (SSX2IP, CASC8, PDE3B and ZDHHC1/HSD11B2 in women) in individuals of African ancestry or both African and European ancestry. For four of the novel variants, the minor allele frequency was low (<5%). In the trans-ethnic fine mapping of 47 BMI loci and 27 WHRadjBMI loci that were locus-wide significant (P < 0.05 adjusted for effective number of variants per locus) from the African ancestry sex-combined and sex-stratified analyses, 26 BMI loci and 17 WHRadjBMI loci contained </= 20 variants in the credible sets that jointly account for 99% posterior probability of driving the associations. The lead variants in 13 of these loci had a high probability of being causal. As compared to our previous HapMap imputed GWAS for BMI and WHRadjBMI including up to 71,412 and 27,350 African ancestry individuals, respectively, our results suggest that 1000 Genomes imputation showed modest improvement in identifying GWAS loci including low frequency variants. Trans-ethnic meta-analyses further improved fine mapping of putative causal variants in loci shared between the African and European ancestry populations.

Center for Health Policy and Health Services Research

Salas J, Scherrer JF, Schneider FD, Sullivan MD, Bucholz KK, Burroughs T, Copeland LA, **Ahmedani BK**, and Lustman PJ. New-onset depression following stable, slow, and rapid rate of prescription opioid dose escalation *Pain* 2017; 158(2):306-312. PMID: 28092649. Full Text

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Recent studies suggest that longer durations of opioid use, independent of maximum morphine equivalent dose (MED) achieved, is associated with increased risk of new-onset depression (NOD). Conversely, other studies, not accounting for duration, found that higher MED increased probability of depressive symptoms. To determine whether rate of MED increase is associated with NOD, a retrospective cohort analysis of Veterans Health Administration data (2000-2012) was conducted. Eligible patients were new, chronic (>90 days) opioid users, aged 18 to 80, and without depression diagnoses for 2 years before start of follow-up (n = 7051). Mixed regression models of MED across follow-up defined 4 rate of dose change categories: stable, decrease, slow increase, and rapid increase. Cox proportional hazard models assessed the relationship of rate of dose change and NOD, controlling for pain, duration of use, maximum MED, and other confounders using inverse probability of treatment-weighted propensity scores. Incidence rate for NOD was 14.1/1000PY (person-years) in stable rate, 13.0/1000PY in decreasing, 19.3/1000PY in slow increasing, and 27.5/1000PY in rapid increasing dose. Compared with stable rate, risk of NOD increased incrementally for slow (hazard ratio = 1.22; 95% confidence interval: 1.05-1.42) and rapid (hazard ratio = 1.58; 95% confidence interval: 1.30-1.93) rate of dose increase. Faster rates of MED escalation contribute to NOD, independent of maximum dose, pain, and total opioid duration. Dose escalation may be a proxy for loss of control or undetected abuse known to be associated with depression. Clinicians should avoid rapid dose increase when possible and discuss risk of depression with patients if dose increase is warranted for pain.

Center for Health Policy and Health Services Research

Truitt AR, Monsell SE, Avins AL, **Nerenz DR**, Lawrence SO, Bauer Z, Comstock BA, Edwards TC, Patrick DL, Jarvik JG, and Lavallee DC. Prioritizing research topics: a comparison of crowdsourcing and patient registry *Qual Life Res* 2017;PMID: 28382522. Full Text

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PURPOSE: A cornerstone of patient-centered outcome research is direct patient involvement throughout the research process. Identifying and prioritizing research topics is a critical but often overlooked point for involvement, as it guides what research questions are asked. We assess the feasibility of involving individuals with low back pain in identifying and prioritizing research topics using two approaches: an existing patient registry and an online crowdsourcing platform. We compare and contrast the diversity of participants recruited, their responses, and resources involved. METHODS: Eligible participants completed a survey ranking their five highest priority topics from an existing list and supplying additional topics not previously identified. We analyzed their responses using descriptive statistics and content analysis. RESULTS: The patient registry yielded older (mean age 72.4), mostly White (70%), and well-educated (95% high school diploma or higher) participants; crowdsourcing yielded younger (mean age 36.6 years), mostly White (82%), and well-educated (98% high school diploma or higher) participants. The two approaches resulted in similar research priorities by frequency. Both provided open-ended responses that were useful, in that they illuminate additional and nuanced research topics. Overall, both approaches suggest a preference towards topics related to diagnosis and treatment over other topics. CONCLUSION: Using a patient registry and crowdsourcing are both feasible recruitment approaches for engagement. Researchers should consider their approach, community, and resources when choosing their recruitment approach, as each approach has its own strengths and weaknesses. These approaches are likely most appropriate to supplement or to complement in-person and ongoing engagement strategies.

Community Health Equity and Wellness

Omar J, **Heidemann DL**, **Blum-Alexandar B**, **Uju-Eke C**, **Alam Z**, **Willens DE**, and **Wisdom K**. Fresh prescription: Improving nutrition education and access to fresh produce in detroit *J Gen Intern Med* 2017; 32(2):S752. PMID: Not assigned. Abstract

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STATEMENT OF PROBLEM OR QUESTION (ONE SENTENCE): Lack of basic knowledge of nutrition and limited access to fresh produce contribute to difficulty in controlling chronic diseases like obesity, diabetes, and cardiovascular disease among underserved adults in Detroit. OBJECTIVES OF PROGRAM/INTERVENTION (NO MORE THAN THREE OBJECTIVES): To improve patient's knowledge of nutrition and confidence in their ability to eat healthy. To improve access to fresh produce by 1) providing financial support, 2) introducing patients to new local Detroit farmer's markets. DESCRIPTION OF PROGRAM/INTERVENTION, INCLUDING ORGANIZATIONAL CONTEXT (E.G. INPATIENT VS. OUTPATIENT, PRACTICE OR COMMUNITY CHARACTERISTICS): Fresh Prescription is a program that serves patients at several different sites in the Detroit area. We implemented Fresh Prescription at our tertiary-care academic institution in the outpatient Internal Medicine clinic. Eligible participants with body mass index >25 and motivation to learn healthy eating habits were enrolled by their primary care physician from July- September 2016. Participants were given a $10 reward on a rechargeable debit card for completing a nutrition educational counseling session, which could include tele-counseling, cooking demonstrations, and other events. They were able to redeem their reward at local farmer's markets or with boxed food deliveries to receive a maximum total of $40 in fresh produce. Patients underwent a total of 4 counseling sessions over 6 weeks and received an additional $20 boxed food delivery for returning for a 12 week follow up. MEASURES OF SUCCESS (DISCUSS QUALITATIVE AND/OR QUANTITATIVE METRICS WHICH WILL BE USED TO EVALUATE PROGRAM/INTERVENTION): Success was measured through comparison of pre- and post-survey responses. FINDINGS TODATE (IT IS NOT SUFFICIENT TOSTATE FINDINGS WILL BEDISCUSSED):Atotal of 149 patients were referred to the program by their primary care physician. 39 of these patients were enrolled, and 28 patients completed the program (72% completion rate). Post-survey responses are available for 27 of the 39 patients enrolled in the program. 96% of participants reported they were better able to manage their health and their chronic conditions. 78% of participants

reported an increase in their daily intake for fresh fruits and vegetables, with an average increase of 2 cups/day. 48% of participants reported a decrease in their intake of unhealthy food items, with an average decrease of 1 item/day. There was an increase in measures of knowledge base, which included ability to select, prepare, and store fresh produce. 85% of participants reported better knowledge of where to buy fresh produce. Price, access, and transportation were still noted to be barriers for many participants. Of the 39 patients who completed the program, 16 returned for follow up on biometrics, including weight and blood pressure. 5 of 16 participants had weight loss, and 5 of 16 had improvement in blood pressure. KEYLESSONS FORDISSEMINATION(WHATCAN OTHERS TAKE AWAY FOR IMPLEMENTATION TO THEIR PRACTICE OR COMMUNITY?): Increasing general nutrition knowledge base among participants led to an increase in the amount of fresh produce consumed, a decrease in unhealthy food items consumed, and increase in ability to manage chronic health conditions. Providing financial resources and improving access to fresh produce are important in supporting patients in an underserved population while encouraging healthy eating habits.

Dermatology

Bousquet E, **Zarbo A**, Tournier E, Chevreau C, Mazieres J, Lacouture ME, and Sibaud V. Development of papulopustular rosacea during nivolumab therapy for metastatic cancer *Acta Derm Venereol* 2017; 97(4):539-540. PMID: 27826614. https://www.medicaljournals.se/acta/content/abstract/10.2340/00015555-2566

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Dermatology

Eichenfield LF, and **Gold LFS**. Addressing the immunopathogenesis of atopic dermatitis: Advances in topical and systemic treatment *Semin Cutan Med Surg* 2017; 36:S45-S48. PMID: Not assigned. Abstract

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Several immunologic mediators-phosphodiesterase (PDE), interleukin (IL), small molecules, and Janus kinase-have been implicated in the pathogenesis of atopic dermatitis, and evidence has shown that blocking these mediators can help modify the disease process. Several new topical medications have been developed that target the enzyme PDE; crisaborole was recently approved by the US Food and Drug Administration (FDA) for the treatment of atopic dermatitis, and phase II studies have been completed on OPA-15406. The phase III clinical trial results of the systemic medication dupilumab, an inhibitor of the IL-4 receptor a subunit (which inhibits both IL-4 and IL-13 signaling), are currently being reviewed by the FDA. (C) 2017 published by Frontline Medical Communications

Dermatology

Eichenfield LF, and **Gold LFS**. Practical strategies for the diagnosis and assessment of atopic dermatitis *Semin Cutan Med Surg* 2017; 36:S36-S38. PMID: Not assigned. Abstract

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Atopic dermatitis (AD) has a significant, lifelong clinical impact on affected individuals and has profound effects on quality of life both for patients and their families. The diagnosis usually can be reliably established on the basis of the history and physical examination. In patients with skin of color, blanching of the skin may be helpful to detect erythema, lichenification, follicular accentuation, and hypopigmentation (all of which are more common than in lighter-skinned patients). Once the diagnosis of AD is established, an assessment of severity, persistence, and impact on the patient's and family's life is important as a guide to treatment decisions. (C) 2017 published by Frontline Medical Communications

Dermatology
Gold LFS, and Eichenfield LF. Nonpharmacologic strategies and topical agents for treating atopic dermatitis: An update *Semin Cutan Med Surg* 2017; 36:S42-S44. PMID: Not assigned. Abstract

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The signs and symptoms of atopic dermatitis can be safely and effectively controlled in most patients; in many cases, the disease can be improved to the point that signs and symptoms are absent or minimal. In addition, flares can be effectively controlled and, in some cases, prevented. New topical medications, improved strategies for the use of topical corticosteroids and topical calcineurin inhibitors, and judicious use of nonpharmacologic regimens including bathing, bleach baths, and early use of emollients have led to better disease management and improved quality of life for patients and their families. (C) 2017 published by Frontline Medical Communications

Dermatology
Gold LFS, and Eichenfield LF. Atopic dermatitis progression: Evaluating intervention strategies *Semin Cutan Med Surg* 2017; 36:S39-S41. PMID: Not assigned. Abstract

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Several risk factors have been identified that appear to be consistently and strongly associated with the development of atopic dermatitis (AD): a family history of atopy, an inherited genetic predisposition, and active and passive exposure to tobacco smoke. Recent studies also have demonstrated that a simple intervention from birth-the daily application of an emollient moisturizer-seems to protect susceptible infants from the development of AD. (C) 2017 published by Frontline Medical Communications

Dermatology
Kircik L, Sung JC, **Stein-Gold L**, and Goldenberg G. United States food and drug administration product label changes *J Clin Aesthet Dermatol* 2017; 10(2):20-29. PMID: 28367259.
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5367870/

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Once a drug has been approved by the United States Food and Drug Administration and is on the market, the Food and Drug Administration communicates new safety information through product label changes. Most of these label changes occur after a spontaneous report to either the drug manufacturing companies or the Food and Drug Administration MedWatch program. As a result, 400 to 500 label changes occur every year. Actinic keratosis treatments exemplify the commonality of label changes throughout the postmarket course of a drug. Diclofenac gel, 5-fluorouracil cream, imiquimod, and ingenol mebutate are examples of actinic keratosis treatments that have all undergone at least one label revision. With the current system of spontaneous reports leading to numerous label changes, each occurrence does not necessarily signify a radical change in the safety of a drug.

Dermatology
Lim HW, Collins SAB, Resneck JS, Jr., Bolognia JL, Hodge JA, Rohrer TA, Van Beek MJ, Margolis DJ, Sober AJ, Weinstock MA, **Nerenz DR**, Smith Begolka W, and Moyano JV. Contribution of health care factors to the burden of skin disease in the United States *J Am Acad Dermatol* 2017;PMID: 28427793. Full Text

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The American Academy of Dermatology has developed an up-to-date national Burden of Skin Disease Report on the impact of skin disease on patients and on the US population. In this second of 3 manuscripts, data are presented on specific health care dimensions that contribute to the overall burden of skin disease. Through the use of data derived from medical claims in 2013 for 24 skin disease categories, these results indicate that skin disease health care is delivered most frequently to the aging US population, who are afflicted with more skin diseases than other age groups. Furthermore, the overall cost of skin disease is highest within the commercially insured population, and skin disease treatment primarily occurs in the outpatient setting. Dermatologists provided approximately 30% of office visit care and performed nearly 50% of cutaneous surgeries. These findings serve as a critical foundation for future discussions on the clinical importance of skin disease and the value of dermatologic care across the population.

Dermatology
Mehta D, and **Ozog D**. Use of ablative fractional co2 laser for scars in skin type iv-vi *Lasers Surg Med* 2017; 49:31-31. PMID: Not assigned. Abstract

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Dermatology
Nicholson C, **Hamzavi I**, and **Ozog D**. The role of the carbon dioxide laser in the treatment of advanced hidradenitis suppurativa and in post-surgical complications *Lasers Surg Med* 2017; 49:32-32. PMID: Not assigned. Abstract

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Dermatology
Pariser D, Bukhalo M, Guenthner S, Kempers S, Shideler S, **Gold LS**, Tschen E, Berg J, Ferdon MB, and Dromgoole S. Two multicenter, randomized, double-blind, parallel group comparison studies of a novel enhanced lotion formulation of halobetasol propionate, 0.05% versus its vehicle in adult subjects with plaque psoriasis *J Drugs Dermatol* 2017; 16(3):234-240. PMID: 28301619. Full Text

BACKGROUND: A novel lotion formulation of halobetasol propionate, 0.05% (HBP Lotion) with enhanced vehicle characteristics of a cream while preserving the ease of use and cosmetic elegance of a lotion has been developed to treat plaque psoriasis. OBJECTIVE: Determine the safety and effectiveness of HBP Lotion in patients with plaque psoriasis. METHODS: Two prospective, randomized, vehicle-controlled clinical studies were conducted in 443 adult subjects with moderate-severe plaque psoriasis. Subjects applied the test article to psoriatic plaques within the treatment area twice daily for 14 days. Efficacy data are based upon treatment "success" defined as those subjects that achieved scores of 0=clear or 1=almost clear with at least a two-grade improvement relative to baseline for an Investigator's Global Assessment (IGA) and clinical signs (plaque elevation, erythema, scaling). Safety data are presented as adverse events and local skin reactions. RESULTS: After two weeks of treatment with HBP Lotion, 44.5% of the HBP Lotion treated subjects in each study achieved (a) treatment "success" (ie, an IGA score of 0=clear or 1=almost clear and >2 grade improvement compared to baseline) and (b) a notable reduction in plaque elevation, erythema, scaling, and pruritus. In contrast, only 6.3% and 7.1% of VEH subjects in Studies 1 and 2, respectively, achieved treatment success and the reduction of disease related signs was materially lower. Statistically, at day 15 in both Phase 3 studies, treatment success with HBP Lotion was superior to VEH (P less than 0.001). From a safety perspective the outcomes were in general unremarkable with similar findings in the HBP Lotion and VEH treatment

groups. CONCLUSIONS: The results demonstrate the safety and effectiveness of HBP Lotion in the treatment of plaque psoriasis. Furthermore, this novel HBP lotion formulation is also distinguished by its moisturization qualities and ease of use.

Dermatology
Porto D, and **Ozog D**. Creating an effective laser procedural video *Lasers Surg Med* 2017; 49:34-34. PMID: Not assigned. Abstract

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Dermatology
Smith MK, **Mohammad TF**, and **Hamzavi IH**. Assessment of dietary supplementation in the treatment of vitiligo *Open Dermatol J* 2017; 11:12-21. PMID: Not assigned. Article Request Form

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Background: Vitiligo is the most common acquired pigmentary disorder in the world. Due to alterations in physical appearance, vitiligo is a psychologically devastating disease. Although treatment options exist, a cure for this disease has yet to be discovered. Of recent interest in vitiligo is the relationship between diet and disease. Objective: To review various dietary modifications and supplementation used in the management of vitiligo. Materials and Methods: A thorough evaluation of recent literature using the keywords “vitiligo, diet, supplement, antioxidant, vitamin, mineral, zinc, copper, gluten-free, celiac disease, alternative medicine” in the NCBI PubMed search function was performed. Results: A total of 39 relevant articles were reviewed and critically evaluated. Conclusion: Initial studies regarding the treatment of vitiligo through dietary modification are promising, although further studies are needed in multiple populations to explore the therapeutic value of these interventions.

Dermatology
Sugarman JL, **Gold LS**, Lebwohl MG, Pariser DM, Alexander BJ, and Pillai R. A phase 2, multicenter, double-blind, randomized, vehicle controlled clinical study to assess the safety and efficacy of a halobetasol/tazarotene fixed combination in the treatment of plaque psoriasis *J Drugs Dermatol* 2017; 16(3):197-204. PMID: 28301614. Full Text

BACKGROUND: Psoriasis is a chronic, immune-mediated disease that varies widely in its clinical expression. Treatment options focus on relieving symptoms, reducing inflammation, induration, and scaling, and controlling the extent of the disease. Topical corticosteroids are the mainstay of treatment, however long-term safety remains a concern, particularly with the more potent formulations. Combination therapy with a corticosteroid and tazarotene may improve psoriasis signs at a lower corticosteroid concentration providing a superior safety profile. OBJECTIVE: To investigate the efficacy and safety of a once-daily application of a fixed combination halobetasol propionate 0.01% and tazarotene 0.045% (HP/TAZ) lotion in comparison with its monads and vehicle in subjects with moderate-to-severe plaque psoriasis. METHODS: Multicenter, randomized, double-blind, vehicle-controlled Phase 2 study in moderate or severe psoriasis (N=212). Subjects randomized (2:2:2:1 ratio) to receive HP/TAZ, individual monads, or vehicle, once-daily for 8 weeks. Efficacy assessments included treatment success (defined as at least a 2-grade improvement from baseline in the IGA score and a score of 'Clear' or 'Almost Clear'), and impact on individual signs of psoriasis (erythema, plaque elevation, and scaling) at the target lesion. Safety and treatment emergent adverse events (TEAEs) were evaluated throughout. RESULTS: HP/TAZ lotion demonstrated statistically significant superiority over vehicle as early as 2 weeks. At week 8, 52.5% of subjects had treatment success compared with 33.3%, 18.6%, and 9.7% in the HP (P=0.033), TAZ (P less than 0.001), and vehicle (P less than 0.001) groups, respectively. HP/TAZ lotion was superior to its monads and vehicle in reducing the psoriasis signs of erythema, plaque elevation, and scaling at the target lesion. At week 8, a 2-grade improvement in IGA was achieved by 54.2% of subjects for erythema, 67.8% for plaque elevation, and 64.4% for scaling. Most frequently reported TEAEs were application site reactions, and were more likely associated with the tazarotene component. Side effects such as skin atrophy were rare. CONCLUSIONS: HP/TAZ lotion was consistently more effective than its monads or vehicle in achieving treatment success and reducing psoriasis signs of erythema, plaque elevation, and scaling at the target lesion. Safety data were consistent with the known safety profile of halobetasol propionate and tazarotene, and did not reveal any new safety concerns with the combination product.

Dermatology
van Geel N, Boniface K, Seneschal J, Jacquemin C, Speeckaert R, Wolkerstorfer A, Bekkenk M, Lommerts JE, **Hamzavi I**, Pandya A, Eleftheriadou V, Ezzedine K, Giannarelli D, Gnarra M, Sperduti I, Prinsen C, Harris J, Taieb A, and Picardo M. Meeting report: Vitiligo Global Issues Consensus Conference (VGICC) Workshop "Outcome measurement instruments" and Vitiligo International Symposium, Rome, Nov 30-Dec 3rd *Pigment Cell Melanoma Res* 2017;PMID: 28379638. Full Text

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The international vitiligo community had last December its first "vitiligo only" research meeting in the Eternal City. Vitiligo is a well-recognized but poorly addressed public health concern worldwide. The Vitiligo International Symposium (VIS) is a strong signal for the medical world of the coming of age of vitiligo as a major research field. Because of the gathering of the majority of world experts, the meeting was preceded by a clinical research methodology workshop held at the San Gallicano Institute. This report gives a combined account of the two parts.

Dermatology
Zabetian S, Jacobson G, **Lim HW**, **Eide MJ**, and **Huggins RH**. Quality of life in a vitiligo support group *J Drugs Dermatol* 2017; 16(4):344-350. PMID: 28403268. Full Text

BACKGROUND: No study has examined the impact of vitiligo support group membership on vitiligo patient quality of life (QoL). OBJECTIVE: We sought to examine the QoL impact of vitiligo support groups by comparing QoL and associated patient characteristics between vitiligo patients who are and are not members of a vitiligo support group. METHODS: Members of a Henry Ford Hospital-sponsored, Southeast Michigan Vitiligo Support Group were compared to non-member vitiligo patients recruited from a previous study cohort.17 Eligible patients were asked to complete the Dermatology Life Quality Index (DLQI) and a study-specific questionnaire designed to collect relevant patient characteristics. RESULTS: The mean DLQI scores for the support group members and non-members were similar (7.1 +/- 5.4 and 6.0 +/- 6.5, respectively; P-value 0.2), despite the support group members reporting more severe overall disease and increased disease severity in exposed portions of the body. The African-American: Caucasian ratio and the prevalence of unemployment were both significantly higher among the support group participants. LIMITATIONS: Small sample size may have limited the study's ability to demonstrate the differences between the support group participants and the controls. CONCLUSIONS: The similar QoL despite an increased prevalence of poorer QoL indicators among the support group participants suggests a protective effect of support group membership.

Diagnostic Radiology
Moriarity AK, Green A, **Klochko C**, **O'Brien M**, and Halabi S. Evaluating the effect of unstructured clinical information on clinical decision support appropriateness ratings *J Am Coll Radiol* 2017;PMID: 28434848. Full Text

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OBJECTIVE: To determine the appropriateness rating (AR) of advanced inpatient imaging requests that were not rated by prospective, point-of-care clinical decision support (CDS) using computerized provider order entry.

MATERIALS AND METHODS: During 30-day baseline and intervention periods, CDS generated an AR for advanced inpatient imaging requests (nuclear medicine, CT, and MRI) using provider-selected structured indications from pull-down menus in the computerized provider order entry portal. The AR was only displayed during the intervention, and providers were required to acknowledge the AR to finalize the request. Subsequently, the unstructured free text information accompanying all requests was reviewed, and the AR was revised when possible. The percentage of unrated requests and the overall AR, before and after radiologist review, were compared between periods and by provider type. RESULTS: CDS software prospectively generated an AR for only 25.4% and 28.4% of baseline and intervention imaging requests, respectively; however, radiologist review generated an AR for 82.4% and 93.6% of the same requests. During the respective periods, the percentage of baseline and intervention imaging requests considered appropriate was 18.7% and 22.9% by prospective CDS software rating and increased to 82.4% and 88.7% with radiologist review. CONCLUSION: Despite limited effective use of CDS software, the percentage of requests containing additional, relevant clinical information increased, and the majority of requests had overall high appropriateness when reviewed by a radiologist. Additional work is needed to improve the amount and quality of clinical information available to CDS software and to facilitate the entry of this information by appropriate end users.

Emergency Medicine

Al-Darzi W, **Nowak R**, **Hudson M**, **Moyer ML**, **Jacobsen G**, and **McCord J**. Ischemicst-segment changes on electrocardiogram in acute myocardial infarction-still common? *J Gen Intern Med* 2017; 32(2):S235-S236. PMID: Not assigned. Abstract

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BACKGROUND: Prior studies report ischemic ST-segment changes on electrocardiogram (ECG) in 40-60% of patients with acute myocardial infarction (AMI) with important diagnostic and prognostic implications. Additionally, 1 to 6% of AMI patients had normal ECG on prior studies. These findings may have changed on the era of more sensitive cardiac troponin (cTn) assays. METHODS: In a single-center we prospectively studied 569 patients who were evaluated for possible AMI in the emergency department from May 2013 to April 2015. Diagnosis of AMI was adjudicated by 2 independent physicians in accordance with the universal definition of AMI using all clinical information and required cTnI > 0.04 ng/ml (Siemens Ultra-cTnI). In situations where there was disagreement between the adjudicators, a third Cardiology adjudicator reviewed the case for final determination. Patients with ECG findings that led to immediate reperfusion therapy were excluded. RESULTS: There were 45 (8%) patients with a diagnosis of AMI. Among AMI patients, the most common ECG findings were T-wave inversion 13 (29%) and normal 13 (29%) while 6 (13%) ECGs demonstrated ST Depression ≥ 1 mm. Comparing patients with and without ST-segment elevation or depression, there was non-significantly higher cTnI levels (13.2 ± 28.3 vs. 5.9 ± 15.6 ng/ml; p = 0.355). CONCLUSIONS: ST-segment changes on ECG are becoming less common in AMI. This may relate to smaller AMIs identified by more sensitive cTn assays which should be verified in larger trials. (Table Presented).

Emergency Medicine

Brown P, **AbdulHamid A**, **Eapen A**, **Elbanna A**, **Greib BJ**, **Vahia A**, and **Miller J**. Severely elevated blood pressure in the emergency department is an independent predictor of 6 and 12 month cardiovascular events *J Gen Intern Med* 2017; 32(2):S315-S316. PMID: Abstract

P. Brown, Henry Ford Health System, Detroit, United States

BACKGROUND: Severely elevated blood pressure (BP) absent acute target organ damage is common in emergency department (ED) patients but the 6 and 12-month risk for such patients is not well described. We tested the hypothesis that severely elevated BP, independent of known cardiovascular risk factors, is associated with 6 and 12 month cardiovascular events. METHODS: We performed a retrospective cohort study using a registry at 8 affiliated hospitals and free-standing EDs. We included all unique adult encounters with recorded BP. We excluded patients that required hospital admission or had an ED systolic BP (SBP) < 110 mmHg. Data extraction included the first recorded ED BP and clinical information with a focus on cardiovascular risk factors. Composite outcomes were obtained from diagnostic coding over a 1-year period following the index visit and included death, myocardial infarction (MI), stroke and acute heart failure (AHF). Logistic and Cox proportional hazards modeling analyzed the association between composite outcomes and increments of HTN above a reference SBP 110-140mmHg. The model adjusted for age, sex, race, a history of HTN, insurance, and 7 core cardiovascular comorbidities. RESULTS: Analysis included 196,244 unique patients over a one year period. The mean age was 46.5 (±19) years, and 56.9% were female. There were 14,887 patients with ED SBP ≥180 mmHg, including 4,379 with a SBP ≥ 200 mmHg. Adjusting for age, sex, race, HTN, insurance and multiple cardiovascular comorbidities, SBP 180-200 mmHg remained an independent predictor of cardiovascular events (OR 1.15, 95% CI 1.1-1.2), as did SBP 200-220 mmHg (OR 1.3, 95% CI 1.2-1.4) and SBP > 220 mmHg (OR 1.7, 95% CI 1.5-2.0). CONCLUSIONS: Among patients

discharged from the ED, severely elevated BP is an independent predictor of 6 and 12 month cardiovascular events, and the magnitude of association increases with higher BP. Further study is needed to evaluate population health strategies that address cardiovascular risks among patients with recent ED visits with extremes of BP elevation.

Emergency Medicine

Harmouche E, **Goyal N**, **Pinawin A**, **Nagarwala J**, and Bhat R. Usmle scores predict success in abem initial certification: A multicenter study *West J Emerg Med* 2017; 18(3):544-549. PMID: 28435509. Full Text

Henry Ford Hospital, Department of Emergency Medicine, Detroit, Michigan.
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INTRODUCTION: There are no existing data on whether performance on the United States Medical Licensing Examination (USMLE) predicts success in American Board of Emergency Medicine (ABEM) certification. The aim of this study was to determine the presence of any association between USMLE scores and first-time success on the ABEM qualifying and oral certification examinations. METHODS: We retrospectively collected USMLE Step 1, Step 2 Clinical Knowledge (CK) scores and pass/fail results from the first attempt at ABEM qualifying and oral examinations from residents graduating between 2009 and 2011 from nine EM programs. A composite score was defined as the sum of USMLE Step 1 and Step 2 CK scores. RESULTS: Sample was composed of 197 residents. Median Step 1, Step 2 CK and composite scores were 218 ([IQR] 207-232), 228 (IQR 217-239) and 444 (IQR 427-468). First-time pass rates were 95% for the qualifying examination and 93% for both parts of the examination. Step 2 CK and composite scores were better predictors of achieving ABEM initial certification compared to Step 1 score (area under the curve 0.800, 0.759 and 0.656). Step 1 score of 227, Step 2 CK score of 225 and composite score of 444 predicted a 95% chance of passing both boards. CONCLUSION: Higher USMLE Step 1, Step 2 CK and composite scores are associated with better performance on ABEM examinations, with Step 2 CK being the strongest predictor. Cutoff scores for USMLE Step 1, Step 2 CK and composite score were established to predict first-time success on ABEM initial certification.

Emergency Medicine

Lipari V, **Mashiba M**, **Mendiratta V**, **Lawler S**, and **Gibbs J**. Observation unit utilization in decompensated heart failure and clinical predictors for appropriate triage *J Gen Intern Med* 2017; 32(2):S256. PMID: Not assigned. Abstract

V. Lipari, Henry Ford Hospital, Detroit, United States

BACKGROUND: Acutely decompensated heart failure (ADHF) represents a significant financial and health burden in the United States with more than 1 million hospitalizations annually and 3% of annual health care expenditure. Currently, 75% of patients presenting to Emergency Departments (ED) are admitted to the hospital, however, estimates suggest as many as 50% may be safely treated in Observation Units (OU). The use of OUs is a cost-effective alternative to inpatient admission for ADHF, however, data to support appropriate triage of patients is sparse. We sought to isolate clinical data indicative of Length of Stay (LOS) greater than 48 hours that is readily available to the ED physician. METHODS: We performed a retrospective cohort study with patients admitted from the ED with ADHF. Patients with end-stage renal disease, heart transplant, or ventricular-assist device were excluded. Demographic and clinical data pertinent to the evaluation of heart failure in the ED were collected. We compared patients with LOS < 48 hours to those with longer stays using Chi-Square analysis, Two-Sample T-Test, Cochran Armitage Trend Test, as well as Wilcoxon Rank Sum Test. RESULTS: Of the 553 patients included in the study, 234 (42%) had LOS > 48 hours. The mean age was 70.3 years (standard deviation, 14.8 years) and 53% were female. Patients were more likely to require >48 hours of care if they had a higher Charlson Comorbidity Index (4.4 vs 3.9, p = 0.014), had systolic pressure <90 mmHg (3.8% vs 0.9%, p = 0.021) or had BNP >200 pg/mL (72.8% vs 60.9%, p = 0.006). Chest x-ray findings of pulmonary vascular congestion (21.6% vs 15.0%), pulmonary edema (6.3% vs 4.1%), or pleural effusion (21.2% vs 14.3%) were likewise associated with increased LOS (p = 0.003). Patients with LOS > 48 hours were also more likely to be anemic (hemoglobin 11.8 vs 12.2, p = 0.005), have a lower lymphocyte percentage count (19.7 vs 22.1, p = 0.009), and have higher troponin (0.07 vs 0.05, p = 0.042). CONCLUSIONS: The Observation Unit is a growing care modality for ADHF. Our study identifies clinical characteristics readily available to the ED physician suggestive of the need for inpatient care. Multivariate analysis and prospective validation will be necessary to further develop our findings into a clinically useful triage tool.

Emergency Medicine
Manthey DE, Hartman ND, **Newmyer A**, Gunalda JC, Hiestand BC, and Askew KL. Erratum: This article corrects: "Trends in nrmp data from 2007-2014 for u.S. Seniors matching into emergency medicine" *West J Emerg Med* 2017; 18(3):550. PMID: 28435510. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5391909/

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[This corrects the article on p. 105 in vol. 18, PMID: 28116018.].

Emergency Medicine
Mashiba M, **Lawler S**, **Mendiratta V**, **Lipari V**, **Georgie F**, **Nona P**, and **Gibbs J**. Overutilization of the observation unit for decompensated heart failure *J Gen Intern Med* 2017; 32(2):S260. PMID: Not assigned. Abstract

M. Mashiba, Henry Ford Hospital, Detroit, United States

BACKGROUND: Acutely decompensated heart failure (ADHF) remains a significant health burden in the United States, with high mortality and cost. To promote quality care, the Centers for Medicare and Medicaid Services have decreased reimbursement for hospital systems with high readmission rates. Observation Units (OU) are a less-costly option for treatment of ADHF, however outcome data beyond 30 days is sparse. We sought to evaluate long-term outcomes and utilization for patients treated in the OU for ADHF. METHODS: We performed a retrospective cohort study with patients admitted from the Emergency Department (ED) with ADHF. Patients with heart transplant, ventricular-assist device, or end-stage renal disease were excluded. Demographic and 12-month outcomes were collected. Patients discharged from the OU were compared with those admitted using Chi-Square Analysis, Fisher Exact Test, and Two-Sample T-Test. OU patients later admitted were also compared with those admitted from the ED. RESULTS: Of the 535 patients included in the study, 427 were triaged to OU. Of these, 156 (37%) had LOS > 48 hours and required admission. The mean age was 71.4 years (standard deviation, 14.9 years) and 52% were female. OU patients converted to admission had higher Charlson Comorbidity Index (4.5 vs 3.9, p = 0.012) and higher 12-month mortality (17.3% vs 9.2%, p = 0.014) compared to those discharged. When converted patients were compared to those admitted from the ED, mortality (17.3% vs 10.3%, p = 0.210) and Charlson (4.3 vs 4.5, p = 0.552) were comparable. Patients triaged to OU showed no difference in readmissions, downstream OU visits, or adverse cardiac events. However, OU patients later admitted had shorter time to death compared to patients triaged directly to inpatient units (137.3 vs 257.9 days, p = 0.023). Patients cared for in the OU were more likely to follow-up outpatient (41.0% vs 25.9%, p = 0.041). CONCLUSIONS: The OU is a venue for high-quality care for ADHF. Our study showed over utilization of the OU, commonly defined as over 15% conversion. A possible difference in time to death exists due to suboptimal triage, but multivariate analysis is needed to confirm. Enhanced risk stratification for patient triage is needed.

Emergency Medicine
Pang PS, Lane KA, Tavares M, Storrow AB, Shen C, Peacock WF, **Nowak R**, Mebazaa A, Laribi S, Hollander JE, Gheorghiade M, and Collins SP. Is there a clinically meaningful difference in patient reported dyspnea in acute heart failure? An analysis from URGENT Dyspnea *Heart Lung* 2017;PMID: 28433323. Full Text

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Department of Anesthesia and Critical Care, Hopitaux Universitaires Saint Louis Lariboisiere, France.
Tours University Hospital, Emergency Department, 37044, France; INSERM, U942, BIOmarkers in CArdioNeuroVAScular diseases, France.
Sidney Kimmel Medical College of Thomas Jefferson University, USA.
Division of Cardiology, Northwestern University Feinberg School of Medicine, USA.

BACKGROUND: Dyspnea is the most common presenting symptom in patients with acute heart failure (AHF), but is difficult to quantify as a research measure. The URGENT Dyspnea study compared 3 scales: (1) 10 cm VAS, (2) 5-point Likert, and (3) a 7-point Likert (both VAS and 5-point Likert were recorded in the upright and supine positions). However, the minimal clinically important difference (MCID) to patients has not been well established. METHODS:

We performed a secondary analysis from URGENT Dyspnea, an observational, multi-center study of AHF patients enrolled within 1 h of first physician assessment in the ED. Using the anchor-based method to determine the MCID, a one-category change in the 7-point Likert was used as the criterion standard ('minimally improved or worse'). The main outcome measures were the change in visual analog scale (VAS) and 5-point Likert scale from baseline to 6-h assessment relative to a 1-category change response in the 7-point Likert scale ('minimally worse', 'no change', or 'minimally better'). RESULTS: Of the 776 patients enrolled, 491 had a final diagnosis of AHF with responses at both time points. A 10.5 mm (SD 1.6 mm) change in VAS was the MCID for improvement in the upright position, and 14.5 mm (SD 2.0 mm) in the supine position. However, there was no MCID for worsening, as few patients reported worse dyspnea. There was also no significant MCID for the 5-point Likert scale. CONCLUSION: A 10.5 mm change is the MCID for improvement in dyspnea over 6 h in ED patients with AHF.

Emergency Medicine

Salem D, and **Delibasic M**. Endovascular approach to treat median arcuate ligament compressing syndrome *Vascular Disease Management* 2017; 14(2):E37-E45. PMID: Not assigned. Article Request Form

D. Salem, Mercy Hospital Medical Center and Wayne State University, Henry Ford Health System, Emergency Medicine, Chicago, United States

Median arcuate ligament compression syndrome (MALS) should be included in the differential diagnosis of chronic abdominal pain, weight loss, and vomiting in a young patient after excluding common etiologies. Definitive radiographic and angiographic findings, along with clinical symptoms, are needed for the accurate diagnosis of MALS. Although laparoscopic resection of the ligament with or without revascularization has been the preferred management strategy, angioplasty with stenting might be undertaken in the treatment of selected patients with this condition, while ensuring adequate long-Term follow-up to assess patency of the stent using either non-invasive (duplex) modalities. The presented case demonstrates the success of angioplasty and stenting and the benefit of avoiding a decompression and revascularization surgery.

Endocrinology and Metabolism

Bergen PM, **Kruger DF**, Taylor AD, Eid WE, **Bhan A**, and Jackson JA. Translating u-500r randomized clinical trial evidence to the practice setting: A diabetes educator/expert prescriber team approach *Diabetes Educ* 2017:145721717701579. PMID: 28427304. Full Text

St Elizabeth Physicians Regional Diabetes Center, Covington, Kentucky (Ms Bergen, Dr Eid).
Henry Ford Health System, Detroit, Michigan (Ms Kruger, Mrs Bhan).
Lilly Diabetes, Lilly USA, LLC, Indianapolis, Indiana (Mrs Taylor, Dr Jackson).
University of Kentucky College of Medicine, Lexington, Kentucky (Dr Eid).
University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota (Dr Eid).
University of Alexandria, Egypt (Dr Eid).

Purpose The purpose of this article is to provide recommendations to the diabetes educator/expert prescriber team for the use of human regular U-500 insulin (U-500R) in patients with severely insulin-resistant type 2 diabetes, including its initiation and titration, by utilizing dosing charts and teaching materials translated from a recent U-500R clinical trial. Conclusions Clinically relevant recommendations and teaching materials for the optimal use and management of U-500R in clinical practice are provided based on the efficacy and safety results of and lessons learned from the U-500R clinical trial by Hood et al, current standards of practice, and the authors' clinical expertise. This trial was the first robustly powered, randomized, titration-to-target trial to compare twice-daily and three-times-daily U-500R dosing regimens. Modifications were made to the initiation and titration dosing algorithms used in this trial to simplify dosing strategies for the clinical setting and align with current glycemic targets recommended by the American Diabetes Association. Leveraging the expertise, resources, and patient interactions of the diabetes educator who can provide diabetes self-management education and support in collaboration with the multidisciplinary diabetes team is strongly recommended to ensure patients treated with U-500R receive the timely and comprehensive care required to safely and effectively use this highly concentrated insulin.

Gastroenterology

Kanwal F, Bacon BR, Beste LA, Brill JV, Gifford AL, **Gordon SC**, Horberg MA, Manthey JG, Reau N, Rustgi VK, and Younossi ZM. Hepatitis c virus infection care pathway-a report from the american gastroenterological association institute hcv care pathway work group *Gastroenterology* 2017; 152(6):1588-1598. PMID: 28442121. Full Text

Baylor College of Medicine and Michael E. DeBakey Veterans Affairs Medical Center, Houston, Texas.

Saint Louis University School of Medicine, St. Louis, Missouri.
VA Puget Sound Health Care System, Seattle, WA and University of Washington School of Medicine.
Predictive Health LLC, Paradise Valley, Arizona.
Boston University and VA Center for Healthcare Organization and Implementation Research, Boston, Massachusetts.
Henry Ford Health System, Detroit, Michigan.
Mid-Atlantic Permanente Research Institute, Kaiser Permanente Mid-Atlantic States, Rockville, Maryland.
American Gastroenterological Association, Bethesda, Maryland.
Rush University Medical Center, Chicago, Illinois.
Robert Wood Johnson School of Medicine, New Brunswick, New Jersey.
Virginia Commonwealth University and Inova Fairfax Hospital, Falls Church, Virginia.

Gastroenterology
Kwo PY, Poordad F, Asatryan A, Wang S, Wyles DL, Hassanein T, Felizarta F, Sulkowski MS, Gane E, Maliakkal B, Scott Overcash J, **Gordon SC**, Muir AJ, Aguilar H, Agarwal K, Dore GJ, Lin CW, Liu R, Lovell SS, Ng TI, Kort J, and Mensa FJ. Glecaprevir and Pibrentasvir Yield High response Rates in Patients with HCV Genotype 1-6 without Cirrhosis *J Hepatol* 2017;PMID: 28412293. Full Text

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Duke University School of Medicine, Durham, NC, USA.
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Kirby Institute, UNSW Sydney, and St. Vincent's Hospital, Sydney, NSW, Australia.

BACKGROUND: and Aims Hepatitis C virus (HCV) therapy that is highly efficacious, pangenotypic, with a high barrier to resistance and short treatment duration is desirable. The efficacy and safety of 8- and 12-week treatments with glecaprevir (ABT-493; NS3/4A protease inhibitor) and pibrentasvir (ABT-530; NS5A inhibitor) was evaluated in non-cirrhotic patients with chronic HCV genotype 1-6 infection. METHODS: SURVEYOR-I and SURVEYOR-II were phase 2, open-label, multicenter, dose-ranging trials including patients with chronic HCV genotype 1-6 infection who were either previously untreated or treated with pegylated interferon plus ribavirin. Patients received once-daily glecaprevir plus pibrentasvir at varying doses with or without ribavirin for 8 or 12 weeks. The primary efficacy endpoint was the percentage of patients with a sustained virologic response at post-treatment week 12 (SVR12). RESULTS: Of the 449 patients who received varying doses of glecaprevir plus pibrentasvir, 25%, 29%, 39%, and 8% had HCV genotype 1, 2, 3, and 4-6 infection, respectively. Twelve-week treatment achieved SVR12 in 97-100%, 96-100%, 83-94%, and 100% in genotypes 1, 2, 3, and 4-6, respectively. Eight-week treatment with 300 mg glecaprevir plus120 mg pibrentasvir in genotype 1-, 2-, or 3-infected patients yielded 97-98% SVR12 with no virologic failures. Three (0.7%) patients discontinued treatment due to adverse events; most events were mild (Grade 1) in severity. No post-nadir alanine aminotransferase elevations were observed. CONCLUSIONS: Glecaprevir plus pibrentasvir was well tolerated and achieved high sustained response rates in HCV genotypes 1-6-infected patients without cirrhosis following 8- or 12-week treatment durations. LAY SUMMARY: The combination of direct-acting antivirals glecaprevir and pibrentasvir comprise a once-daily, all-oral, pangenotypic treatment for HCV genotype 1-6 infection. This article describes results from two Phase 2 trials investigating a range of doses at treatment durations of 8 or 12 weeks in 449 patients without cirrhosis. Efficacy of the optimal dose, as determined by rates of sustained virologic response at post-treatment week 12, ranged from 92%-100%; treatment was well-tolerated and significant laboratory abnormalities were rare.

Gastroenterology
Terrault NA, Berenguer M, Strasser SI, Gadano A, Lilly L, Samuel D, Kwo PY, Agarwal K, Curry MP, Fagiuoli S, Fung JYY, Gane E, **Brown KA**, Burra P, Charlton M, Pessoa MG, and McCaughan GW. International liver transplantation society consensus statement on hepatitis c management in liver transplant recipients *Transplantation* 2017; 101(5):956-967. PMID: 28437388. Full Text

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Gastroenterology
Terrault NA, McCaughan GW, Curry MP, Gane E, Fagiuoli S, Fung JYY, Agarwal K, Lilly L, Strasser SI, **Brown KA**, Gadano A, Kwo PY, Burra P, Samuel D, Charlton M, Pessoa MG, and Berenguer M. International liver transplantation society consensus statement on hepatitis c management in liver transplant candidates *Transplantation* 2017; 101(5):945-955. PMID: 28437387. Full Text

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Global Health Initiative
Parke D, **Plum A**, **Prentiss T**, **Zervos J**, **Dankerlui DN**, and **Kaljee L**. Evaluation of an international trainee exchange program developed by the global health initiative at henry ford health system *Ann Glob Health* 83(1):131. PMID: Not assigned. http://www.annalsofglobalhealth.org/article/S2214-9996(17)30353-3/abstract

The Global Health Initiative (GHI) at Henry Ford Health System (HFHS) in Detroit, Michigan is committed to improving health outcomes and infrastructure in resource-limited countries through collaborative capacity-building models. In collaboration with our international partners, GHI
developed a medical education and research exchange program whereby international trainees (medical and public health students,
residents, and faculty) conduct a one- to two-month observation at HFHS including clinical rotations and lectures, laboratory experience,
and engagement in structured global health research training.

Hematology / Oncology

Abdel-Rahman Z, **Ali H**, **Favazza L**, and **Chitale D**. Poor concordance between 21-gene expression assay recurrence score and all Magee equation recurrence scores in a consecutive cohort of patients treated for hormone receptor positive early breast cancer *Breast* 2017; 32:S87-S87. PMID: Not assigned. Abstract

[Abdel-Rahman, Z.] Henry Ford Hlth Syst, Dept Internal Med, Detroit, MI USA. [Ali, H.] Henry Ford Hlth Syst, Div Hematol & Med Oncol, Detroit, MI USA. [Favazza, L.; Chitale, D.] Henry Ford Hlth Syst, Dept Pathol & Lab Med, Detroit, MI USA.

Hematology / Oncology

Abdel-Rahman Z, **Alkhatib Y**, and **Dabak V**. A mysterious cause of chest pain *J Gen Intern Med* 2017; 32(2):S412. PMID: Not assigned. Abstract

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LEARNING OBJECTIVE #1: Recognize the clinical features of primary cardiac tumors LEARNING OBJECTIVE #2: Manage chest pain by ruling out the most serious and fatal etiologies first CASE: A 42-year-old African American male with a past medical history significant for previously treated non-medullary thyroid carcinoma presented to our hospital with acute onset pleuritic chest pain and dyspnea on exertion. Initial workup revealed a slightly elevated Troponin-I along with a diffuse ST-segment elevation on electrocardiogram. Left sided heart catheterization with coronary angiogram did not show any obstructive lesions. No evidence of pulmonary embolism was seen on computed tomography (CT) angiogram. A transthoracic echocardiogram showed a large right atrial mass, which was further evaluated by a cardiac magnetic resonance imaging (MRI) and found to be involving the right atrial wall and pericardium with evidence of central necrosis on T2 signal. Patient underwent gross total resection of the mass, pathology showed areas of spindle cells and vascular spaces which stained positive for CD31 and CD34 indicating vascular differentiation consistent with angiosarcoma. Staging CT scan of the chest, abdomen and pelvis did not show evidence of distant metastasis. Patient received adjuvant chemotherapy with adriamycin and ifosfamide, postchemotherapy cardiac MRI showed a possible evidence of persistent disease for which he received external beam radiation therapy (EBRT) to the remnant mass. Patient has been stable since then with no evidence of active disease for 2 years. IMPACT: Chest pain is a common presenting complaint in many patients, while the etiology is benign in several occasions, the clinical approach would differ for each particular case depending on several factors which should be incorporated to formulate a specific diagnostic approach and subsequent therapy plan. Younger patients with chest pain should be investigated thoroughly after ruling out deadly cardiac, pulmonary or vascular conditions. DISCUSSION: Primary cardiac tumors are very rare; based upon data from22 large autopsy series the approximate frequency is 0.02%, corresponding to 200 tumors in 1 million autopsies. Malignant tumors constitute around one quarter of these with the majority being sarcomas. Cardiac angiosarcoma typically affects middle aged males and it usually involves the right atrium with pericardial, caval and tricuspid-valve invasion. Metastases are usually found at time of presentation in up to 89% of cases with lungs being the most common site. Presentation is variable depending on the site of involvement. It can be incidentally discovered or might cause symptoms secondary to embolization, direct invasion of adjacent structures or hemodynamic instability due to obstructing cardiac flow. The mainstay of treatment for cardiac tumors remains surgical resection, however chemotherapy and in some occasions radiation therapy are essential adjuvant modalities to achieve cure.

Hematology / Oncology

Apolo AB, Infante JR, Balmanoukian A, Patel MR, **Wang D**, Kelly K, Mega AE, Britten CD, Ravaud A, Mita AC, Safran H, Stinchcombe TE, Srdanov M, Gelb AB, Schlichting M, Chin K, and Gulley JL. Avelumab, an anti-programmed death-ligand 1 antibody, in patients with refractory metastatic urothelial carcinoma: Results from a multicenter, phase ib study *J Clin Oncol* 2017:Jco2016716795. PMID: 28375787. Full Text

Andrea B. Apolo and James L. Gulley, National Institutes of Health, Bethesda, MD; Jeffrey R. Infante, Sarah Cannon Research Institute/Tennessee Oncology, Nashville, TN; Ani Balmanoukian, The Angeles Clinic & Research Institute; Alain C. Mita, Cedars Sinai Medical Center, Los Angeles; Karen Kelly, University of California-Davis, Sacramento; Marko Srdanov, Dako North America, Carpinteria, CA; Manish R. Patel, Florida Cancer Specialists & Research Institute, Sarasota, FL; Ding Wang, Henry Ford Hospital, Detroit, MI; Anthony E. Mega, The Warren Alpert Medical School at Brown University; Howard Safran, The Miriam Hospital, Providence; Howard Safran, Newport Hospital, Newport, RI; Carolyn D. Britten, Medical University of South Carolina, Charleston, SC; Alain Ravaud, CHU de Bordeaux, Bordeaux, France; Thomas E. Stinchcombe, Duke University Medical Center, Durham, NC; Arnold B. Gelb and Kevin Chin, EMD Serono, Billerica, MA; and Michael Schlichting, Merck, Darmstadt, Germany.

Purpose We assessed the safety and antitumor activity of avelumab, a fully human anti-programmed death-ligand 1 (PD-L1) IgG1 antibody, in patients with refractory metastatic urothelial carcinoma. Methods In this phase Ib, multicenter, expansion cohort, patients with urothelial carcinoma progressing after platinum-based chemotherapy and unselected for PD-L1 expression received avelumab 10 mg/kg intravenously every 2 weeks. The primary objectives were safety and tolerability. Secondary objectives included confirmed objective response rate (Response Evaluation Criteria in Solid Tumors [RECIST] version 1.1), progression-free survival, overall survival (OS), and PD-L1-associated clinical activity. PD-L1 positivity was defined as expression by immunohistochemistry on >/= 5% of tumor cells. Results Forty-four patients were treated with avelumab and followed for a median of 16.5 months (interquartile range, 15.8 to 16.7 months). The data cutoff was March 19, 2016. The most frequent treatment-related adverse events of any grade were fatigue/asthenia (31.8%), infusion-related reaction (20.5%), and nausea (11.4%). Grades 3 to 4 treatment-related adverse events occurred in three patients (6.8%) and included asthenia, AST elevation, creatine phosphokinase elevation, and decreased appetite. The confirmed objective response rate by independent central review was 18.2% (95% CI, 8.2% to 32.7%; five complete responses and three partial responses). The median duration of response was not reached (95% CI, 12.1 weeks to not estimable), and responses were ongoing in six patients (75.0%), including four of five complete responses. Seven of eight responding patients had PD-L1-positive tumors. The median progression-free survival was 11.6 weeks (95% CI, 6.1 to 17.4 weeks); the median OS was 13.7 months (95% CI, 8.5 months to not estimable), with a 12-month OS rate of 54.3% (95% CI, 37.9% to 68.1%). Conclusion Avelumab was well tolerated and associated with durable responses and prolonged survival in patients with refractory metastatic UC.

Hematology / Oncology

Garcia-Manero G, Montalban-Bravo G, Berdeja JG, Abaza Y, Jabbour E, Essell J, Lyons RM, Ravandi F, Maris M, Heller B, DeZern AE, Babu S, Wright D, Anz B, Boccia R, Komrokji RS, **Kuriakose P**, Reeves J, Sekeres MA, Kantarjian HM, Ghalie R, and Roboz GJ. Phase 2, randomized, double-blind study of pracinostat in combination with azacitidine in patients with untreated, higher-risk myelodysplastic syndromes *Cancer* 2017; 123(6):994-1002. PMID: 28094841. Full Text

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BACKGROUND: The prognosis of patients with higher-risk myelodysplastic syndromes (MDS) remains poor despite available therapies. Histone deacetylase inhibitors have demonstrated activity in patients with MDS and in vitro synergy with azacitidine. METHODS: A phase 2 randomized, placebo-controlled clinical trial of azacitidine and pracinostat was conducted in patients who had International Prognostic Scoring System intermediate-2-risk or high-risk MDS. The primary endpoint was the complete response (CR) rate by cycle 6 of therapy. RESULTS: Of 102 randomized patients, there were 51 in the pracinostat group and 51 in the placebo group. The median age was 69 years. The CR rate by cycle 6 of therapy was 18% and 33% (P = .07) in the pracinostat and placebo groups, respectively. No significant differences in overall survival (median, 16 vs 19 months, respectively; hazard ratio, 1.21; 95% confidence interval, 0.66-2.23) or progression-free survival (11 vs 9 months, respectively; hazard ratio, 0.82; 95% confidence interval, 0.546-1.46) were observed between groups. Grade >/=3 adverse events occurred more frequently in the pracinostat group (98% vs 74%), leading to more treatment discontinuations (20% vs 10%). CONCLUSIONS: The combination of azacitidine with pracinostat did not improve outcomes in patients with higher-risk MDS. Higher rates of treatment discontinuation may partially explain these results, suggesting alternative dosing and schedules to improve tolerability may be required to determine the potential of the combination. Cancer 2017;123:994-1002. (c) 2016 American Cancer Society.

Hematology / Oncology

Gulley JL, Rajan A, Spigel DR, Iannotti N, Chandler J, Wong DJ, Leach J, Edenfield WJ, **Wang D**, Grote HJ, Heydebreck AV, Chin K, Cuillerot JM, and Kelly K. Avelumab for patients with previously treated metastatic or recurrent non-small-cell lung cancer (JAVELIN Solid Tumor): dose-expansion cohort of a multicentre, open-label, phase 1b trial *Lancet Oncol* 2017;PMID: 28373005. Full Text

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Henry Ford Hospital, Detroit, MI, USA.
Merck KGaA, Darmstadt, Germany.
EMD Serono, Billerica, MA, USA.
University of California-Davis, Comprehensive Cancer Center, Sacramento, CA, USA.

BACKGROUND: Avelumab, a human Ig-G1 monoclonal antibody targeting PD-L1 and approved in the USA for the treatment of metastatic Merkel cell carcinoma, has shown antitumour activity and an acceptable safety profile in patients with advanced solid tumours in a dose-escalation phase 1a trial. In this dose-expansion cohort of that trial, we assess avelumab treatment in a cohort of patients with advanced, platinum-treated non-small-cell lung cancer (NSCLC). METHODS: In this dose-expansion cohort of a multicentre, open-label, phase 1 study, patients with progressive or platinum-resistant metastatic or recurrent NSCLC were enrolled at 58 cancer treatment centres and academic hospitals in the USA. Eligible patients had confirmed stage IIIB or IV NSCLC with squamous or non-squamous histology, measurable disease by Response Evaluation Criteria In Solid Tumors version 1.1 (RECIST v1.1), tumour biopsy or archival sample for biomarker assessment, and Eastern Cooperative Oncology Group performance status 0 or 1, among other criteria. Patient selection was not based on PD-L1 expression or expression of other biomarkers, including EGFR or KRAS mutation or ALK translocation status. Patients received infusional avelumab monotherapy 10 mg/kg every 2 weeks until disease progression or toxicity. The primary objective was to assess safety and tolerability. This trial is registered with ClinicalTrials.gov, number NCT01772004; enrolment in this cohort is closed and the trial is ongoing. FINDINGS: Between Sept 10, 2013, and June 24, 2014, 184 patients were enrolled and initiated treatment with avelumab. Median follow-up duration was 8.8 months (IQR 7.2-11.9). The most common treatment-related adverse events of any grade were fatigue (46 [25%] of 184 patients), infusion-related reaction (38 [21%]), and nausea (23 [13%]). Grade 3 or worse treatment-related adverse events occurred in 23 (13%) of 184 patients; the most common (occurring in more than two patients) were infusion-related reaction (four [2%] patients) and increased lipase level (three [2%]). 16 (9%) of 184 patients had a serious adverse event related to treatment with avelumab, with infusion-related reaction (in four [2%] patients) and dyspnoea (in two [1%]) occurring in more than one patient. Serious adverse events irrespective of cause occurred in 80 (44%) of 184 patients. Those occurring in more than five patients (>/=3%) were dyspnoea (ten patients [5%]), pneumonia (nine [5%]), and chronic obstructive pulmonary disease (six [3%]). Immune-related treatment-related events occurred in 22 patients (12%). Of 184 patients, 22 (12% [95% CI 8-18]) achieved a confirmed objective response, including one complete response and 21 partial responses. 70 (38%) had stable disease. Overall, 92 (50%) of 184 patients achieved disease control (they had a confirmed response or stable disease as their best overall response). One patient was initially thought to have died from grade 5 radiation pneumonitis during the study; however, this adverse event was subsequently regraded to grade 3 and the death was attributed to disease progression. INTERPRETATION: Avelumab showed an acceptable safety profile and antitumour activity in patients with progressive or treatment-resistant NSCLC, providing a rationale for further studies of avelumab in this disease setting. FUNDING: Merck KGaA and Pfizer.

Hematology / Oncology

Naman CB, **Rattan R**, Nikoulina SE, Lee J, Miller BW, Moss NA, Armstrong L, Boudreau PD, Debonsi HM, **Valeriote FA**, Dorrestein PC, and Gerwick WH. Integrating molecular networking and biological assays to target the isolation of a cytotoxic cyclic octapeptide, samoamide a, from an american samoan marine cyanobacterium *J Nat Prod* 2017; 80(3):625-633. PMID: 28055219. Article Request Form

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Integrating LC-MS/MS molecular networking and bioassay-guided fractionation enabled the targeted isolation of a new and bioactive cyclic octapeptide, samoamide A (1), from a sample of cf. Symploca sp. collected in American Samoa. The structure of 1 was established by detailed 1D and 2D NMR experiments, HRESIMS data, and chemical degradation/chromatographic (e.g., Marfey's analysis) studies. Pure compound 1 was shown to have in vitro cytotoxic activity against several human cancer cell lines in both traditional cell culture and zone inhibition bioassays. Although there was no particular selectivity between the cell lines tested for samoamide A, the most potent activity was observed against H460 human non-small-cell lung cancer cells (IC50 = 1.1 muM). Molecular modeling studies suggested that one possible mechanism of action for 1 is the inhibition of the enzyme dipeptidyl peptidase (CD26, DPP4) at a reported allosteric binding site, which could lead to many downstream pharmacological effects. However, this interaction was moderate when tested in vitro at up to 10 muM and only resulted in about 16% peptidase inhibition. Combining bioassay screening with the cheminformatics strategy of LC-MS/MS molecular networking as a discovery tool expedited the targeted isolation of a natural product possessing both a novel chemical structure and a desired biological activity.

Hematology / Oncology

Nemunaitis J, Borghaei H, Akerley W, Gadgeel S, Spira A, **Rybkin I**, Faltaos D, Chen I, Christensen J, Potvin D, Velastegui K, Levisetti M, and Husain H. Phase 2 study of glesatinib or sitravatinib with nivolumab in non-small cell lung cancer (NSCLC) after checkpoint inhibitor therapy *J Thorac Oncol* 2017; 12(1):S1078. PMID: Not assigned. Abstract

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Background: Combination therapy with agents that target the molecular and cellular mechanisms of resistance to checkpoint inhibitor therapy (CIT) is a rational approach to restoring or improving the efficacy of CIT in patients with immunotherapy resistant NSCLC. Glesatinib, a tyrosine kinase inhibitor (TKI), which targets Axl, MER and MET RTKs expressed on macrophages and antigen-presenting-cells within the tumor microenvironment (TME), may reverse the immunosuppressive TME and enhance anti-tumor T and NK cell responses by enhancing antigen presentation and T cell effector function. Sitravatinib, also a TKI, which targets VEGFR2 and KIT as well as Axl, MER and MET, may further enhance anti-tumor activity by VEGFR2 and KIT inhibition mediated reduction of regulatory T cells and myeloid-derived suppressor cells (MDSCs). Given these pleiotropic immune activating effects, the combination of glesatinib or sitravatinib with nivolumab is a rational approach to restoring or enhancing the clinical activity of CIT in patients with immunotherapy resistant NSCLC. Methods: This open-label Phase 2 study evaluates the tolerability and clinical activity of the investigational agents, glesatinib or sitravatinib in combination with nivolumab in separate cohorts of patients with nonsquamous NSCLC who have experienced progression of disease on or after treatment with CIT. The study begins with a limited dose escalation evaluation of each investigational agent in combination with nivolumab to determine the dose levels to be used in Phase 2. The primary objective is to assess the clinical activity of the combination regimens using the Objective Response Rate (ORR) by RECIST 1.1. Other objectives include safety, tolerability, pharmacokinetics and changes in circulating and tumor cell PD-L1, circulating and tumor infiltrating immune cell populations, cytokines and gene expression signatures. Enrollment into each Phase 2 treatment arm is stratified by prior outcome of CIT (e.g., clinical benefit versus progression of disease in ≤ 12 weeks). The investigational agents are administered orally in continuous regimens; nivolumab is administered intravenously, 3 mg/kg every 2 weeks. The sample sizes for the treatment arms are based on two-stage Simon Optimal Designs.

Hematology / Oncology

Thamilselvan V, **Menon M**, Stein GS, **Valeriote F**, and **Thamilselvan S**. Combination of carmustine and selenite Inhibits EGFR mediated growth signaling in androgen-independent prostate cancer cells *J Cell Biochem* 2017;PMID: 28430389. Full Text

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Although aberrant androgen receptor (AR) signaling is a central mechanism for castration resistant prostate cancer (CRPC) progression, AR-independent survival and growth signaling is also present in CRPC. The current therapeutic options for patients with CRPC are limited and new drugs are desperately needed to eliminate these crucial growth signaling pathways. Overexpression of EGFR in CRPC primarily mediates the proliferation of androgen-independent prostate cancer (AIPC) cells. We have previously shown that combination of carmustine and selenite effectively

induces apoptosis and growth inhibition by targeting AR and AR-variants in castration resistant prostate cancer cells. In this study, we investigated whether the combination of carmustine and selenite could inhibit EGFR mediated growth signaling and induce apoptosis in AIPC cells. EGF exposure dose and time dependently increased phospho-EGFR (Tyr845, Tyr1068, and Tyr1045), pAkt (Ser473), and pERK1/2 (Thr204/Tyr202) protein expression levels in AIPC cells. Combination of carmustine and selenite treatment markedly suppressed EGF-stimulated proliferation and survival of AIPC cells and effectively induced apoptosis. The ROS generated by the combination of carmustine and selenite exhibited a strong inhibitory on EGF stimulated EGFR and its downstream signaling molecules such as Akt/NF-kB and ERK1/2/Cyclin D1. Individual agent treatment showed only partial effect. Overall, our findings demonstrated that the combination of carmustine and selenite treatment substantially inhibits EGFR signaling, proliferation and induces apoptosis in AIPC cells. The results of the study further indicate that combination of carmustine and selenite can overcome the obstacles of EGFR mediated AR-independent growth response in castration resistant prostate cancer.

Hematology / Oncology

Werner T, Heist R, Carvajal R, Adkins D, Alva A, Goel S, Hong D, Bazhenova L, Saleh M, Siegel R, Kyriakopoulos C, Blakely C, Eaton K, Lauer R, **Wang D**, Schwartz G, Neuteboom S, Potvin D, Faltaos D, Chen I, Christensen J, Levisetti M, Chao R, and Bauer T. A Study of MGCD516, a receptor tyrosine kinase (RTK) inhibitor, in molecularly selected patients with NSCLC or other advanced solid tumors *J Thorac Oncol* 2017; 12(1):S1068-S1069. PMID: Not assigned. Abstract

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Background: MGCD516 (Sitravatinib), is an oral, potent small molecule inhibitor of a closely related spectrum of RTKs including RET, the split RTKs (VEGFR, PDGFR and KIT), TRK family, DDR2, MET and AXL. RTKs inhibited by sitravatinib are genetically altered in NSCLC and other cancers, where they function as oncogenic drivers, promoting cancer development and progression. Alterations in these RTKs have also been implicated in tumor resistance mechanisms. Sitravatinib has demonstrated antitumor activity in nonclinical cancer models harboring genetic alterations of sitravatinib targets, including rearrangement of RET, NTRK, or CHR4q12 amplification. Phase 1 dose escalation has been completed, showing dose proportional increases in exposure. PK and preliminary PD data indicate inhibition of the targets at the 150 mg dose administered orally once per day. Methods: This phase 1b study includes enrollment of molecularly selected patients (pts) with unresectable or metastatic NSCLC or other advanced solid tumor malignancies in patient cohorts characterized by activating alterations in sitravatinib RTK targets (RET, KDR, PDGFRA, KIT, TRK, DDR2, MET, AXL) or by loss of function mutations in CBL, a negative regulator for MET, AXL and PDGFR/KIT signaling. Pts receive sitravatinib at 150 mg once daily in 21-day cycles. Study endpoints include safety and tolerability, PK/PD, and clinical activity assessed by objective disease response per RECIST 1.1, duration of response and survival. A two stage optimal Simon design of up to 24 pts (8 pts in first stage and 16 pts in second stage) will be applied to those cohorts defined by a specific tumor gene alteration assuming p0=0.15 and p1=0.35, with an additional expansion of a cohort up to a total of 70 pts in order to provide a more precise estimate of ORR. PD biomarkers, including sMET, sVEGFR2, VEGFA and sAXL, are being explored in plasma samples for prognostic potential and possible relationship with clinical outcome. The study is open for enrollment, and recruitment is ongoing.

Hematology / Oncology

Williams A, **Goldberg W**, **Varkas T**, and **Ryan M**. Distress screening for program building: Similarities and differences among patient populations *Psycho-Oncology* 2017; 26:100. PMID: Not assigned. Abstract

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Purpose: The IOM states screening for distress and psychosocial health needs is a critical first step in providing high-quality cancer care. However, high-quality care goes beyond screening and addressing individual patient concerns in that moment. Distress-screening data should also be used to develop patient-centered programs at a health care system level. This study examines similarities and differences in areas of distress across 11 types of cancer based on distress screening data. Methods: Data were obtained from the Cancer Care Assessment (c) patients complete at their first medical oncology appointment, their radiation oncology simulation visit, or at their second post-op appointment with surgical oncology. Chart review was used to abstract demographic and cancer diagnosis. Cancer diagnoses were divided into 11 cancer types: blood/bone, lung, GI, pancreas, breast, head and neck, brain/neurological, urologic, gynecologic, dermatologic, and liver/ kidney. Those areas of distress rated as a “moderate” or “severe” were considered significant areas of distress. Results: The average patient age ranged from 55 years (brain/neurological) to 70 years (dermatologic) (N = 1613). Aside from breast and gynecologic, a majority of patients were male. Areas of common distress were pain, fatigue, sleep, weight loss, and anxiety. Areas of specific

distress varied by cancer type. For example, liver/kidney endorsed concern about end of life decisions while brain/neurological endorsed difficulty coping with treatment side effects. There were also differences in needs both within and across cancer type-based on gender, age, and urban vs suburban residence. Conclusions: While many areas of distress are common across cancer types, there are other areas of distress specific to a particular cancer type. Based on this data, a health care system can develop supportive oncology programs that address both the common and the specific areas of distress to deliver more patient-centered care.

Hematology / Oncology

Yardley D, Coleman R, Conte P, Cortes J, Brufsky A, Shtivelband M, Young R, Bengala C, **Ali H**, Eakel J, Schneeweiss A, Merino LD, Wilks S, O'Shaugnessy J, Gluck S, Li H, Beck R, Barton D, and Harbeck N. nab-paclitaxel plus carboplatin or gemcitabine vs gemcitabine/carboplatin as first-line treatment for patients with triple-negative metastatic breast cancer: Results from the randomized phase 2 portion of the tnAcity trial *Cancer Research* 2017; 77:3. PMID: Not assigned. Abstract

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Hemophilia & Thrombosis Treatment Center

McLaughlin JM, Munn JE, Anderson TL, **Lambing A**, Tortella B, and Witkop ML. Predictors of quality of life among adolescents and young adults with a bleeding disorder *Health Qual Life Outcomes* 2017; 15(1):67. PMID: 28388906. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5383972/

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BACKGROUND: Health-related quality of life (HRQoL) in adolescents and young adults with bleeding disorders is under-researched. We aimed to describe factors related to HRQoL in adolescents and young adults with hemophilia A or B or von Willebrand disease. METHODS: A convenience sample of volunteers aged 13 to 25 years with hemophilia or von Willebrand disease completed a cross-sectional survey that assessed Physical (PCS) and Mental (MCS) Component Summary scores on the SF-36 questionnaire. Quantile regression models were used to assess factors associated with HRQoL. RESULTS: Of 108 respondents, 79, 7, and 14% had hemophilia A, hemophilia B, and von Willebrand disease, respectively. Most had severe disease (71%), had never developed an inhibitor (65%), and were treated prophylactically (68%). Half of patients were aged 13 to 17 years and most were white (80%) and non-Hispanic (89%). Chronic pain was reported as moderate to severe by 31% of respondents. Median PCS and MCS were 81.3 and 75.5, respectively. Quantile regression showed that the median PCS for women (61% with von Willebrand disease) was 13.1 (95% CI: 2.4, 23.8; $p = 0.02$) points lower than men. Ever developing an inhibitor (vs never) was associated with a 13.1-point (95% CI: 4.7, 21.5; $p < 0.01$) PCS reduction. MCS was 10.0 points (95% CI: 0.7, 19.3; $p = 0.04$) higher for prophylactic infusers versus those using on-demand treatment. Compared with patients with no to mild chronic pain, those with moderate to severe chronic pain had 25.5-point (95% CI: 17.2, 33.8; $p < 0.001$) and 10.0-point (95% CI: 0.8, 19.2; $p = 0.03$) reductions in median PCS and MCS, respectively. CONCLUSIONS: Efforts should be made to prevent and manage chronic pain, which was strongly related to physical and mental HRQoL, in adolescents and young adults with hemophilia and von Willebrand disease. Previous research suggests that better clotting factor adherence may be associated with less chronic pain.

Hospital Medicine

Singh Z, and **Gunderson H**. Bacteremia: A noble source *J Gen Intern Med* 2017; 32(2):S454. PMID: Not assigned. Abstract

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LEARNING OBJECTIVE #1: Recognize unusual sources of bacteremia LEARNING OBJECTIVE #2: Educate patients on the use of insulin needles CASE: 57 year old African American male with a PMHx of well-controlled Type-2 DM, on Lantus, presented to the hospital with fevers, chills, and lethargy with abdominal pain and nausea for 2 days duration. He stated that he was in overall good health and denied any sick contacts, cough, sputum production, chest pain, palpitations or shortness of breath. Physical examination was essentially unremarkable except for a group of small painless and pruritic excoriations along the lower half of his abdomen. They were 1-2 mm in size, red in color, and slightly raised, patient stated that they had been there for a little more than 2 weeks. Patient was found to have a temperature of 39.4 deg C, and a heart rate of 115, with a leukocytosis of 17,000. He was admitted for further septic workup. Subsequent blood cultures were positive for MRSA on 2 bottles and he was started on IV antibiotics for bacteremia without any obvious source. Echo was negative for endocarditis. On further questioning, patient stated that he had a remote history of IV drug abuse but quit over 15 years ago and he denied any recent use. He denied any cuts or bruises on his body, and denied recent dental procedures. When asked about his excoriations on his abdomen, he stated that is the location of his insulin shots. Upon further questioning about his insulin needles it was found that the patient was reusing them to inject himself because he was unable to afford more. It was deemed that his insulin needles were the source of his bacteremia. Patient then completed treatment for MRSA bacteremia and his labs improved and he was discharged home. IMPACT: Most cases of bacteremia we see in Detroit are from IV drug abusers or skin and soft tissue infections. In this case, this gentleman was unable to afford new needles and tried to save costs by reusing the old supplies he already had in order to continue to receive his medication. It really changed my thinking because there are many other sources of bacteremia which us physicians usually do not think about right away that may potentially lead to detrimental effects on the human body. DISCUSSION: IV drug abuse is a major worldwide epidemic that affects hundreds of thousands of people and their families. Working in downtown Detroit, we encounter many patients on a daily basis who come in with bacteremia and develop endocarditis or other devastating diseases causing them to be bed bound for the rest of their lives. Physicians have to realize that there are many otherways of becoming bacteremic other than IVdrug users. We also need to learn the cost effectiveness of our therapies. Diabetic supplies can be very expensive for some patients and we need to realize the consequences of this. We should also take time to educate out patients and explain the detrimental effects of reusing medical supplies that are only meant for a single use.

Hypertension Research

Monu SR, **Ren Y**, **Masjoan Juncos JX**, **Kutskill K**, **Wang H**, **Kumar N**, **Peterson EL**, and **Carretero OA**. Connecting tubule glomerular feedback mediates tubuloglomerular feedback resetting post-unilateral nephrectomy *Am J Physiol Renal Physiol* 2017:ajprenal.00619.02016. PMID: 28424211. Full Text

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Unilaterally nephrectomized rats (UNx) have higher glomerular capillary pressure (PGC) that can cause significant glomerular injury in the remnant kidney. PGC is controlled by the ratio of afferent (Af-Art) and efferent arteriole resistance. Af-Art resistance in turn is regulated by two intrinsic feedback mechanisms: 1) Tubuloglomerular feedback (TGF) that causes Af-Art constriction in response to increased NaCl in the macula densa and 2) connecting tubule glomerular feedback (CTGF) that causes Af-Art dilatation in response to an increase in NaCl transport in the connecting tubule via the epithelial sodium channel (ENaC). Resetting of TGF post-UNx can allow systemic pressure to be transmitted to the glomerulus and cause renal damage, but the mechanism behind this resetting is unclear. Since CTGF is an Af-Art dilatory mechanism, we hypothesized that CTGF is increased after UNx, and contributes to TGF resetting. To test this hypothesis, we performed UNx in Sprague Dawley (SD) rats. Twenty-four hours after surgery, we performed micropuncture of individual nephrons and measured stop-flow pressure (PSF). PSF is an indirect measurement of PGC. Maximal TGF response at 40nl/min was 8.9 +/- 1.24 mmHg in sham-UNx rats and 1.39 +/- 1.02 mmHg in UNx rats indicating TGF resetting after UNx. When CTGF was inhibited with the ENaC blocker Benzamil (1muM/L), the TGF response was 12.29 +/- 2.01 mmHg in UNx rats and 13.03 +/- 1.25 mmHg in sham-UNx rats, indicating restoration of the TGF responses in UNx. We conclude that enhanced CTGF contributes to TGF resetting after UNx.

Infectious Diseases

Meighani A, **Hart BR**, Bourgi K, **Miller N**, **John A**, and **Ramesh M**. Outcomes of fecal microbiota transplantation for clostridium difficile infection in patients with inflammatory bowel disease *Dig Dis Sci* 2017;PMID: 28451916. Full Text

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BACKGROUND AND AIMS: Fecal microbiota transplantation (FMT) has recently been shown to be a promising therapy for recurrent and refractory Clostridium difficile infections (CDI) despite lack of protocol standardization. Patients with inflammatory bowel disease (IBD) present a particular challenge to CDI therapy as they are reported to have worse clinical outcomes, including higher colectomy rates and increased mortality. We aimed to assess the outcomes of FMT for recurrent CDI in patients with IBD at our healthcare system. METHODS: We constructed a retrospective cohort of all patients who underwent FMT at our healthcare system between December 2012 and May 2014. Patients with concurrent IBD were identified. We evaluated the differences in demographic and clinical characteristics, along with the outcomes to FMT between patients with IBD as compared to the general population. RESULTS: Over the study period, 201 patients underwent FMT of which 20 patients had concurrent IBD. Patients with IBD were younger but did not differ from the general population in terms of CDI risk factors or disease severity. The response to FMT and rate of CDI relapse in the IBD group were not statistically different compared to the rest of the cohort. The overall response rate in the IBD population was 75% at 12 weeks. Of the patients who failed FMT 4 of 5 patients had active or untreated IBD. CONCLUSION: Fecal microbiota transplantation provides a good alternative treatment option with high success rates for recurrent or refractory Clostridium difficile infection in patients with well-controlled IBD who fail standard antimicrobial therapy.

Internal Medicine
Abdel-Rahman Z, **Ali H**, **Favazza L**, and **Chitale D**. Poor concordance between 21-gene expression assay recurrence score and all Magee equation recurrence scores in a consecutive cohort of patients treated for hormone receptor positive early breast cancer *Breast* 2017; 32:S87-S87. PMID: Not assigned. Abstract

[Abdel-Rahman, Z.] Henry Ford Hlth Syst, Dept Internal Med, Detroit, MI USA. [Ali, H.] Henry Ford Hlth Syst, Div Hematol & Med Oncol, Detroit, MI USA. [Favazza, L.; Chitale, D.] Henry Ford Hlth Syst, Dept Pathol & Lab Med, Detroit, MI USA.

Internal Medicine
Abdel-Rahman Z, **Alkhatib Y**, and **Dabak V**. A mysterious cause of chest pain *J Gen Intern Med* 2017; 32(2):S412. PMID: Not assigned. Abstract

Z. Abdel-Rahman, Henry Ford Health System, Detroit, United States

LEARNING OBJECTIVE #1: Recognize the clinical features of primary cardiac tumors LEARNING OBJECTIVE #2: Manage chest pain by ruling out the most serious and fatal etiologies first CASE: A 42-year-old African American male with a past medical history significant for previously treated non-medullary thyroid carcinoma presented to our hospital with acute onset pleuritic chest pain and dyspnea on exertion. Initial workup revealed a slightly elevated Troponin-I along with a diffuse ST-segment elevation on electrocardiogram. Left sided heart catheterization with coronary angiogram did not show any obstructive lesions. No evidence of pulmonary embolism was seen on computed tomography (CT) angiogram. A transthoracic echocardiogram showed a large right atrial mass, which was further evaluated by a cardiac magnetic resonance imaging (MRI) and found to be involving the right atrial wall and pericardium with evidence of central necrosis on T2 signal. Patient underwent gross total resection of the mass, pathology showed areas of spindle cells and vascular spaces which stained positive for CD31 and CD34 indicating vascular differentiation consistent with angiosarcoma. Staging CT scan of the chest, abdomen and pelvis did not show evidence of distant metastasis. Patient received adjuvant chemotherapy with adriamycin and ifosfamide, postchemotherapy cardiac MRI showed a possible evidence of persistent disease for which he received external beam radiation therapy (EBRT) to the remnant mass. Patient has been stable since then with no evidence of active disease for 2 years. IMPACT: Chest pain is a common presenting complaint in many patients, while the etiology is benign in several occasions, the clinical approach would differ for each particular case depending on several factors which should be incorporated to formulate a specific diagnostic approach and subsequent therapy plan. Younger patients with chest pain should be investigated thoroughly after ruling out deadly cardiac, pulmonary or vascular conditions. DISCUSSION: Primary cardiac tumors are very rare; based upon data from22 large autopsy series the approximate frequency is 0.02%, corresponding to 200 tumors in 1 million autopsies. Malignant tumors constitute around one quarter of these with the majority being sarcomas. Cardiac angiosarcoma typically affects middle aged males and it usually involves the right atrium with pericardial, caval and tricuspid-valve invasion. Metastases are usually found at time of presentation in up to 89% of cases with lungs being the most common site. Presentation is variable depending on the site of involvement. It can be incidentally discovered or might cause symptoms secondary to embolization, direct invasion of adjacent structures or hemodynamic instability due to obstructing cardiac flow. The

mainstay of treatment for cardiac tumors remains surgical resection, however chemotherapy and in some occasions radiation therapy are essential adjuvant modalities to achieve cure.

Internal Medicine
Abdel-Rahman Z, and **Avasarala SK**. Denosumab-induced hypocalcemia *J Gen Intern Med* 2017; 32(2):S483. PMID: Not assigned. Abstract

Z. Abdel-Rahman, Henry Ford Health System, Detroit, United States

LEARNING OBJECTIVE #1: Recognize the increased use of denosumab and the likelihood of developing hypocalcemia LEARNING OBJECTIVE #2: Educate patients on the dire necessity of calcium supplements to prevent the morbidity associated with denosumabinduced hypocalcemia CASE: An 83-year-old male with chronic kidney disease (CKD), early Alzheimer's dementia presents with worsening back pain. Magnetic resonance imaging showed vertebral lesions, labs showed a high prostate-specific antigen (PSA) and he was eventually diagnosed with metastatic prostate cancer based on bone biopsy results. Treatment was initiated with bicalutamide followed by leuprorelin and radiation therapy to the vertebral lesions. Five months after starting therapy, he developed castration resistance and his PSA started to rise so he was started on docetaxel followed by cabazitaxel. He received additional radiotherapy sessions for cauda equine syndrome in addition to a denosumab injection for his bony metastases. Before administering denosumab, his baseline ionized calcium (iCa) was 1.1 mmol/l (1.00 - 1.35 mmol/L) and vitamin D and calcium supplements were prescribed. Six days after the injection he presented to the emergency department with generalized weakness and muscle twitches, his iCa was found to be 0.61 mmol/L requiring an intensive care unit (ICU) admission where he was started on an intravenous calciumdrip while his QTintervals were closely monitored. After normalization of his calciumlevels, he was switched to oral supplements and discharged on 500 mg of calcium citrate three times daily and 2000 units of vitamin D daily. Twenty eight days after the injection, he presented with similar complaints and his iCa was found to be 0.62 mmol/L. This necessitated another ICU admission for IV calcium replacement and monitoring. He was then discharged on the same supplements as last time with the addition of calcitriol 1 mcg twice daily. His serum calcium levels were followed on outpatient basis by his oncologist. Fifty days after the denosumab injection, he had a third ICU admission for severe hypocalcemia IMPACT: Many factors played a role in this patient's course, most importantly; he was not taking his calcium and vitamin D supplements thinking that these are just non-essential vitamins rather than a key component of his treatment, in addition to CKD and social factors like not getting prescriptions filled because of transportation issues. Keeping these issues in mind can decrease the burden and morbidity of a preventable complication. DISCUSSION: Hypocalcemia can be a serious electrolyte abnormality that can result in cardiac arrhythmias, coronary vasospasmand even sudden cardiac death. Denosumab-induced hypocalcemia has an incidence of 2-5 and as the use of denosumab is increasing among cancer and non-cancer patients (e.g., osteoporosis), all physicians should be aware of this adverse effect and should monitor patients by frequently checking their calcium levels before and after treatment and making sure they are taking their supplements as prescribed.

Internal Medicine
Al-Abid B, **Sohaney R**, **Alamiri K**, **Kumbar L**, **Soi V**, and **Yee J**. Dementia and catheter dysfunction as under identified and documented risk factors for catheter related blood stream infections *Am J Kidney Dis* 2017; 69(4):A19-A19. PMID: Not assigned. Abstract

[Al-Abid, Baha; Sohaney, Ryann; Alamiri, Khalid; Kumbar, Lalathaksha; Soi, Vivek; Yee, Jerry] Henry Ford Hosp, Detroit, MI 48202 USA.

Internal Medicine
Al-Darzi W, Rahman M, Sandhu S, **Philip J**, and **Shah V**. Rare case of olanzapine induced hypoglycemia, bradycardia, and hypothermia *J Gen Intern Med* 2017; 32(2):S576-S577. PMID: Not assigned. Abstract

W. Al-Darzi, Henry Ford Hospital, Detroit, United States

LEARNING OBJECTIVE #1: Recognizing that Olanzapine can induce hypoglycemia. Although Olanzapine is known to cause hyperglycemia and new onset diabetes, there are few case reports of Olanzapine induced hypoglycemia. CASE: 65 year old female with history of schizophrenia, hypertension and hyperlipidemia presented for dizziness. She has had multiple ER evaluations for similar complaints with a largely negative evaluation including normal orthostatic vitals and lack of events on implanted loop monitor. During this presentation she was noted to be in sinus bradycardia, hypothermic at 35.3 C and hypoglycemic at 49 mg/dl. Initial symptoms subsided with supplemental glucose, device interrogation of her loop recorder demonstrated sinus bradycardia with multiple PAC's and sinus

pauses. Intracranial imaging with CTand MRI did not reveal acute pathology and EEG was negative for epileptiform activity. She had repeat neuroglycopenic episodes with altered mentation during her hospitalization with blood glucose levels repeatedly in the 50's mg/dl despite appropriate dietary intake. Endocrinology was consulted with extensive evaluation yielding negative results for potential etiologies including hypothyroidism, adrenal insufficiency, insulinoma, sulfonylurea toxicity. Abdominal CT did not show evidence of adrenal or pancreaticmass. On review of her medications, Olanzapine was identified as the iatrogenic cause of her symptoms. After discontinuation of the drug, patient had gradual improvement remaining normothermic and with normal blood glucose levels throughout the rest of her inpatient visit. IMPACT: Olanzapine can cause glucose dysregulationwhether hypoglycemia or hyperglycemia. Hypoglycemia can produce bradycardia and hypothermia. DISCUSSION: Olanzapine is a commonly used atypical antipsychotic medication. It has well documented side effects of dyslipidemia and hyperglycemia, often resulting in new onset diabetes in patients. However, there are very rare reported cases of hypoglycemia with this medication. The mechanism for glucose dysregulation in general is poorly understood. Hypoglycemia is proposed to be a result of insulin hypersecretion due to systemic increases in insulin resistance. In patients with prior risk factors for hypoglycemia, previous episodes of unexplained syncope, obesity or pre-existing diabetes, prescribing physician to re-evaluate the role of Olanzapine over another agent with similar efficacy in treatment as an antipsychotic.

Internal Medicine

Al-Darzi W, Zlatopolsky M, **Abu Sayf A**, and **Awdish RL**. To close or not to close a patent foramen ovale: That is the question *J Gen Intern Med* 2017; 32(2):S624-S625. PMID: Not assigned. Abstract

W. Al-Darzi, Henry Ford Hospital, Detroit, United States

LEARNING OBJECTIVE #1: Recognizing that cardiac shunting often occur in setting of severe pulmonary hypertension (PH) and serves to relieve the severe increase in the right sided pressures. LEARNING OBJECTIVE #2: Recognizing one of the contraindications to patent foramen ovale (PFO) closure. CASE: A 65-year old female presented to Heart Failure clinic after a follow up transthoracic echocardiography (TTE). She complained of dyspnea, bilateral lower extremity edema, and right 4th digit pain. On physical exam, patient was noted to have darkening of her right 4th digits. She had hypoxia with higher oxygen requirement than baseline. Past medical history is significant for Interstitial Lung Disease (ILD), Pulmonary Hypertension (PH) groups (2 and 3), coronary artery disease with three prior stents, and chronic diastolic dysfunction. Her TTE showed EF of 50%, pulmonary artery systolic pressure of 60 mmHg, and large (greater than 20 bubbles) PFO, that is new, with predominantly right to left shunting across the atrial septum. Patient was hospitalized due to concern for paradoxical emboli and for her hypoxia. Right heart catheterization (RHC) was done that showedmean Pulmonary arterial pressure of 45 mmHg, wedge pressure of 8 mmHg, cardiac index of 2.13 L/min/m2, pulmonary vascular resistance of 840 dynes.sec.cm-5 (10.5 Wood units), and systemic vascular resistance (SVR) of 797.84 dynes.sec.cm-5 at rest. CT angiography was done that showed acute pulmonary embolus (PE) to segmental branches of right lower lobe and demonstrated stable ILD. An upper extremity arterial study demonstrated reduced perfusion to the right 4th digit attributable to a possible embolic event. High intensity heparin was initiated. Risks and Benefits of PFO closure were discussed at a multi-disciplinary meeting. Given that patient's PVR > 2/3 of SVR in the RHC, PFO closure was deferred. The patient was ultimately discharged on warfarin. IMPACT: Careful decision making in PFO closure should be pursued for PH patients, even in presence of a known indication for closure. One of the contraindications to PFO closure is the irreversible pulmonary hypertension (PVR >2/3 SVR or pulmonary artery pressure > 2/3 systemic arterial pressure). It is important to recognize that closure of PFO in those situations could precipitate decompensation of right ventricular (RV) function and sudden drop in cardiac output which could be fatal. DISCUSSION: While PFO closure may be pursued in cases of paradoxical emboli, a risk/benefit analysis, especially looking at PH, is necessary. In this case, acute PE is the likely cause of acute rise in the right sided cardiac pressures. Eventually, the acute PFO provided a necessary outflow tract for right sided pressure overload.

Internal Medicine

Brown P, **AbdulHamid A**, **Eapen A**, **Elbanna A**, **Greib BJ**, **Vahia A**, and **Miller J**. Severely elevated blood pressure in the emergency department is an independent predictor of 6 and 12 month cardiovascular events *J Gen Intern Med* 2017; 32(2):S315-S316. PMID: Abstract

P. Brown, Henry Ford Health System, Detroit, United States

BACKGROUND: Severely elevated blood pressure (BP) absent acute target organ damage is common in emergency department (ED) patients but the 6 and 12-month risk for such patients is not well described. We tested the hypothesis that severely elevated BP, independent of known cardiovascular risk factors, is associated with 6 and 12 month cardiovascular events. METHODS: We performed a retrospective cohort study using a registry at 8 affiliated hospitals and free-standing EDs. We included all unique adult encounters with recorded BP. We excluded patients

that required hospital admission or had an ED systolic BP (SBP) < 110 mmHg. Data extraction included the first recorded ED BP and clinical information with a focus on cardiovascular risk factors. Composite outcomes were obtained from diagnostic coding over a 1-year period following the index visit and included death, myocardial infarction (MI), stroke and acute heart failure (AHF). Logistic and Cox proportional hazards modeling analyzed the association between composite outcomes and increments of HTN above a reference SBP 110-140mmHg. The model adjusted for age, sex, race, a history of HTN, insurance, and 7 core cardiovascular comorbidities. RESULTS: Analysis included 196,244 unique patients over a one year period. The mean age was 46.5 (±19) years, and 56.9% were female. There were 14,887 patients with ED SBP ≥180 mmHg, including 4,379 with a SBP ≥ 200 mmHg. Adjusting for age, sex, race, HTN, insurance and multiple cardiovascular comorbidities, SBP 180-200 mmHg remained an independent predictor of cardiovascular events (OR 1.15, 95% CI 1.1-1.2), as did SBP 200-220 mmHg (OR 1.3, 95% CI 1.2-1.4) and SBP > 220 mmHg (OR 1.7, 95% CI 1.5-2.0). CONCLUSIONS: Among patients discharged from the ED, severely elevated BP is an independent predictor of 6 and 12 month cardiovascular events, and the magnitude of association increases with higher BP. Further study is needed to evaluate population health strategies that address cardiovascular risks among patients with recent ED visits with extremes of BP elevation.

Internal Medicine

Coniglio B, **Drake S**, and **Meysami A**. Musculoskeletal ultrasound training for the internal medicine resident: Development and assessment of a teaching curriculum for elective rotation *J Gen Intern Med* 2017; 32(2):S694-S695. PMID: Not assigned. Abstract

B. Coniglio, Henry Ford Hospital, Detroit, United States

NEEDS AND OBJECTIVES: Ultrasound has become increasingly utilized throughout internal medicine and its subspecialties. Musculoskeletal ultrasound is a vital tool for assessing patients with tendon and joint abnormalities, and is employed for diagnostic as well as therapeutic purposes. Internal medicine residents would benefit from using musculoskeletal ultrasound as musculoskeletal problems are among the most frequently encountered complaints in ambulatory clinic. Formal training in musculoskeletal ultrasound is largely absent from internal medicine residency programs. We sought to establish an elective rotation in musculoskeletal ultrasound for the internal medicine resident, and develop an effective teaching curriculum that could be easily implemented at other internal medicine residencies. SETTING AND PARTICIPANTS: The course took place as part of a month-long elective rotation at an outpatient rheumatology musculoskeletal ultrasound clinic. A senior staff rheumatologist who was board certified in musculoskeletal ultrasound by the American College of Rheumatology assisted with curriculum development and led the course. Internal medicine residents from a large academic teaching hospital and from all training levels took part, including some interested in pursuing rheumatology fellowship training. DESCRIPTION: Goals and objectives were created to reflect the six core competencies for residents in graduate medical education. A structured curriculum was developed using units with modules that incorporated book chapters, online videos, and hands-on workshops with the ultrasound, which were broken down by joint system. Residents spent time reading, observing, and practicing with the ultrasound before performing supervised examinations and interventions on their own. EVALUATION: A pre- and post-test was administered to the residents. It consisted of multiple choice questions and ultrasound-captured images covering principles of ultrasound as well as basic musculoskeletal anatomy and pathology. An opportunity to provide course feedback was given on the posttest evaluation. DISCUSSION/REFLECTION/LESSONS LEARNED: Feedback was very positive from the six internal medicine residents who took part in the course, and pre- to post-test scores improved by over fifty percent. Residents felt the course was a good learning experience and that its strengths were a clear curriculum, the amount of teaching and the opportunity to become comfortable using ultrasound to both understand musculoskeletal anatomy and pathology as well as perform joint aspirations and injections. Overall, everyone indicated that the course had very good utility for the internal medicine resident. Based on our positive results and feedback, we felt the course and its curriculum were an effective means to teach musculoskeletal ultrasound to internal medicine residents.

Internal Medicine

Evans KL, Wirtz H, Li J, **She RC**, Maya J, Depre C, Hamer A, and **Lanfear D**. Genetics of heart rate observational study (genhrate) *J Am Coll Cardiol* 2017; 69(11):685-685. PMID: Not assigned. Abstract

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Internal Medicine
Garza N, **Georgie F**, **Horbal A**, **Willens DE**, and **Haftka-George AC**. Does physician gender effect ordering practice *J Gen Intern Med* 2017; 32(2):S169. PMID: Not assigned. Abstract

N. Garza, Henry Ford Hospital, Detroit, United States

BACKGROUND: Breast cancer cases represent 14.6% of all new cancer diagnosis in the United States. However, medical societies disagree when, and how often, we should be screening. The United States Preventative Service Task Force recommends starting at 50 years of age and screening biennially, while others recommend starting at 40 years of age, or screening annually. This has created an environment where physicians must decide which guideline is best for their patients. We sought to find out what factors influence this decision, specifically if the gender of the ordering physician was associated with different screening practices in women aged 40-49. METHODS: We examined every office visit for female patients age 40-49 with an internal medicine (IM), family medicine (FM) or gynecology (Gyn) provider in our health system between July 1, 2015 to May 30, 2016. Patients with a history of breast cancer or other malignant neoplasm were excluded. The association between physician gender and mammogram ordering rates was assessed via chi-squared testing. Other factors, such as comparison between specialties, were assessed via multivariable binary logistic regression. RESULTS: In female patients aged 40-49, female physicians are more likely to order mammograms than male physicians overall. This disparity between genders was largest in internal medicine. Gynecology physicians order mammograms at a higher rate than internal medicine or family medicine physicians. Women aged 45-49 were more likely to receive a mammogram order than women aged 40-44. Also, black patients were less likely to receive a mammogram order compared to white patients. CONCLUSIONS: Physician ordering practices do appear to vary by gender, however, this pattern is also influenced by specialty. The decision also seems to be effected by the age and/or race of the patient. The results of this study support the need for more research in factors contributing to preventive healthcare disparities.

Internal Medicine
Gordish KL, **Kassem KM**, **Ortiz PA**, and **Beierwaltes WH**. Moderate (20%) fructose-enriched diet stimulates salt-sensitive hypertension with increased salt retention and decreased renal nitric oxide *Physiol Rep* 2017; 5(7)PMID: 28408634. Full Text

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Previously, we reported that 20% fructose diet causes salt-sensitive hypertension. In this study, we hypothesized that a high salt diet supplemented with 20% fructose (in drinking water) stimulates salt-sensitive hypertension by increasing salt retention through decreasing renal nitric oxide. Rats in metabolic cages consumed normal rat chow for 5 days (baseline), then either: (1) normal salt for 2 weeks, (2) 20% fructose in drinking water for 2 weeks, (3) 20% fructose for 1 week, then fructose + high salt (4% NaCl) for 1 week, (4) normal chow for 1 week, then high salt for 1 week, (5) 20% glucose for 1 week, then glucose + high salt for 1 week. Blood pressure, sodium excretion, and cumulative sodium balance were measured. Systolic blood pressure was unchanged by 20% fructose or high salt diet. 20% fructose + high salt increased systolic blood pressure from 125 +/- 1 to 140 +/- 2 mmHg ($P < 0.001$). Cumulative sodium balance was greater in rats consuming fructose + high salt than either high salt, or glucose + high salt (114.2 +/- 4.4 vs. 103.6 +/- 2.2 and 98.6 +/- 5.6 mEq/Day19; $P < 0.05$). Sodium excretion was lower in fructose + high salt group compared to high salt only: 5.33 +/- 0.21 versus 7.67 +/- 0.31 mmol/24 h; $P < 0.001$). Nitric oxide excretion was 2935 +/- 256 mumol/24 h in high salt-fed rats, but reduced by 40% in the 20% fructose + high salt group (2139 +/- 178 mumol /24 hrs $P < 0.01$). Our results suggest that fructose predisposes rats to salt-sensitivity and, combined with a high salt diet, leads to sodium retention, increased blood pressure, and impaired renal nitric oxide availability.

Internal Medicine
Iqbal U, **Siddiqui MA**, Chaudhary A, and Anwar H. Gangrenous gastritis: Unusual cause of upper GI bleeding *J Gen Intern Med* 2017; 32(2):S503. PMID: Not assigned. Abstract

U. Iqbal, Bassett Medical Center, Cooperstown, United States

LEARNING OBJECTIVE #1: Mesenteric ischemia can present without abdominal pain especially if chronic due to formation of collateral vessels LEARNING OBJECTIVE #2: Weight loss in elderly can be the only sign of chronic mesenteric ischemia CASE: A 67 year old male with history of COPD and coronary artery disease presented with

hematemesis and black stools for a day. He denied any abdominal pain, loss of appetite, or weight loss. No prior history of GI bleeding or postparandial abdominal pain. He was a current smoker with 50-year smoking history. On presentation he had BP of 146/94, pulse 83 and afebrile. Abdominal exam was unremarkable for tenderness. Bowel sounds were present. Rectal exam revealed black stools. Labs showed hemoglobin of 16. g/dl1, hematocrit 45%, WBC of 34,000 with 83% neutrophils, bicarbonate 20 mmol/L and INR of 1.7. EGD revealed inflamed gangrenous-appearing gastritis throughout with multiple clean ulcers, raising suspicion for ischemia. Cardia revealed extensive gastric ulcer; 5-6 cmin greatest dimension, with a large visible vessel. CTangiographyof abdomen showed proximal occlusion of Superior mesenteric artery (SMA), near complete occlusion of celiac artery and hypertrophic Inferior mesenteric artery which is likely the supply of much of his GI tract. Patient underwent successful SMA bypass from left iliac to mid. He was discharged home on aspirin daily. IMPACT: Clinicians should have a high index of suspicion in diagnosing intestinal ischemia in elderly patients with risk factors for atherosclerosis as clinical presentation can be misleading. Early diagnosis can prevent morbidity and mortality associated with this serious disease by decreasing the dreadful complication of bowel gangrene as developed in our patient. DISCUSSION: Patients with chronic mesenteric ischemia (CMI) typically present with recurrent abdominal pain after meals, resulting in fear of eating and weight loss. In a survey of 270 patients, weight loss, postprandial pain, adapted eating pattern, and diarrhea are associated with CMI. Probability of diagnosis increases to 60%with all four symptoms, and reduces to 13% if none are present. Few patients present with non-specific symptoms of nausea, vomiting and/or GI bleeding. This patient was unique in that he had no abdominal pain even with a total occlusion SMA, possibly due to well-formed collaterals which were seen in his CT abdomen. His upper GI bleeding as a result of gangrenous gastritis resulted from ischemic bowel from total occlusion. Review of literature shows delay in diagnosis ranges from 10.7 months to 15 months in diagnosing CMI, resulting in more complications. CT angiography abdomen is more than 90 sensitive and specific in diagnosing it. Endovascular therapy with stenting is the preferred method of revascularization in these patients and has widely replaced open surgical management. The non-specific symptoms and unremarkable physical exam in our patient demonstrate how silently intestinal ischemia can present.

Internal Medicine

Iqbal U, **Siddiqui MA**, Chaudhary A, Anwar H, and Alvi M. Severe hypertriglyceridemia induced acute pancreatitis: Management strategy in a rural setup *J Gen Intern Med* 2017; 32(2):S387. PMID: Not assigned. Abstract

U. Iqbal, Bassett Medical Center, Cooperstown, United States

LEARNING OBJECTIVE #1: Intravenous Insulin has similar efficacy to plasmapheresis in emergent management of HTG induced AP LEARNING OBJECTIVE #2: Patients with TG > 500 mg/dl are recommended to undergo genetic testing to rule out disorders associated with lipid metabolism. CASE: 44 year old male with history of diabetes mellitus and hypertension presented with severe epigastric abdominal pain radiated to the back associated with several episodes of vomiting for past 24 h. He denies fever, chills, diarrhea, black tarry stools and weight loss. He denied history of excessive alcohol use. His medications included metformin and insulin glargine. On presentation he was vitally stable and had generalized abdominal tenderness, audible bowel sounds with no palpable hepatosplenomegaly. Labs revealed lipase of 5006 U/L (50-290 U/L), amylase of 299 U/L (30-110 U/L). CT abdomen revealed moderate peri-pancreatic edema concerning for acute pancreatitis (AP). Triglycerides levels (TG) were severely elevated to 6672 mg/dl (55-150 mg/dl). He was started on conventional treatment of AP with IV hydration and analgesia. Given our rural setup and absence of availability of plasmapheresis (PP) for rapid correction of HTG, patient was started on insulin infusion 0.1 units/kg/hr along with D5W to maintain euglycemia. He was continued on that regimen with hourly blood glucosemonitoring until TG were <500 mg/dl which was achieved on day 8. He was discharged on atorvastatin and fenofibrate with a referral to a lipidologist to rule out genetic causes of hypertriglyceridemia (HTG). IMPACT: In a clinical setup where PP is not readily available for acute management of HTG induced AP, use of IV insulin with IV dextrose is an effective alternative treatment strategy. Rapid reduction in TG levels to <500 mg/dl is associated with improved clinical outcomes. DISCUSSION: HTG is the third most common cause and is responsible for almost 1-4% of AP. The incidence of AP in patients with TG > 2000 up to 20. In patients who developed an episode of AP secondary to severeHTG, the goal is to bring the TGless than 500 as early as possible because it is associated with improved clinical outcome. PP is usually considered first-line therapy for severe HTG with many studies supporting its clinical utility. In a case series of 7 patient, 41% decrease in TG was reported with single plasma exchange. In absence of availability of PP, alternate treatment modalities with intravenous (IV) insulin should be considered. Standard approach is 0.1-0.3 units/kg/hr of regular insulin IValong with dextrose saline to maintain euglycemia until TG come down to <500. There are no randomized controlled trials which compare efficacy of insulin with PP in treatment of severe HTG. Therefore, treatment is usually based on availability and preference. Long-term goal for patients who had episodes of AP secondary to HTG, is to prevent further episodes by optimizing lipid lowering therapy and lifestyle modification. Non-compliant patients may need periodic PP to prevent episodes of AP.

Internal Medicine

Lipari V, **Mashiba M**, **Mendiratta V**, **Lawler S**, and **Gibbs J**. Observation unit utilization in decompensated heart failure and clinical predictors for appropriate triage *J Gen Intern Med* 2017; 32(2):S256. PMID: Not assigned. Abstract

V. Lipari, Henry Ford Hospital, Detroit, United States

BACKGROUND: Acutely decompensated heart failure (ADHF) represents a significant financial and health burden in the United States with more than 1 million hospitalizations annually and 3% of annual health care expenditure. Currently, 75% of patients presenting to Emergency Departments (ED) are admitted to the hospital, however, estimates suggest as many as 50% may be safely treated in Observation Units (OU). The use of OUs is a cost-effective alternative to inpatient admission for ADHF, however, data to support appropriate triage of patients is sparse. We sought to isolate clinical data indicative of Length of Stay (LOS) greater than 48 hours that is readily available to the ED physician. METHODS: We performed a retrospective cohort study with patients admitted from the ED with ADHF. Patients with end-stage renal disease, heart transplant, or ventricular-assist device were excluded. Demographic and clinical data pertinent to the evaluation of heart failure in the ED were collected. We compared patients with LOS < 48 hours to those with longer stays using Chi-Square analysis, Two-Sample T-Test, Cochran Armitage Trend Test, as well as Wilcoxon Rank Sum Test. RESULTS: Of the 553 patients included in the study, 234 (42%) had LOS > 48 hours. The mean age was 70.3 years (standard deviation, 14.8 years) and 53% were female. Patients were more likely to require >48 hours of care if they had a higher Charlson Comorbidity Index (4.4 vs 3.9, p = 0.014), had systolic pressure <90 mmHg (3.8% vs 0.9%, p = 0.021) or had BNP >200 pg/mL (72.8% vs 60.9%, p = 0.006). Chest x-ray findings of pulmonary vascular congestion (21.6% vs 15.0%), pulmonary edema (6.3% vs 4.1%), or pleural effusion (21.2% vs 14.3%) were likewise associated with increased LOS (p = 0.003). Patients with LOS > 48 hours were also more likely to be anemic (hemoglobin 11.8 vs 12.2, p = 0.005), have a lower lymphocyte percentage count (19.7 vs 22.1, p = 0.009), and have higher troponin (0.07 vs 0.05, p = 0.042). CONCLUSIONS: The Observation Unit is a growing care modality for ADHF. Our study identifies clinical characteristics readily available to the ED physician suggestive of the need for inpatient care. Multivariate analysis and prospective validation will be necessary to further develop our findings into a clinically useful triage tool.

Internal Medicine

Mashiba M, **Lawler S**, **Mendiratta V**, **Lipari V**, **Georgie F**, **Nona P**, and **Gibbs J**. Overutilization of the observation unit for decompensated heart failure *J Gen Intern Med* 2017; 32(2):S260. PMID: Not assigned. Abstract

M. Mashiba, Henry Ford Hospital, Detroit, United States

BACKGROUND: Acutely decompensated heart failure (ADHF) remains a significant health burden in the United States, with high mortality and cost. To promote quality care, the Centers for Medicare and Medicaid Services have decreased reimbursement for hospital systems with high readmission rates. Observation Units (OU) are a less-costly option for treatment of ADHF, however outcome data beyond 30 days is sparse. We sought to evaluate long-term outcomes and utilization for patients treated in the OU for ADHF. METHODS: We performed a retrospective cohort study with patients admitted from the Emergency Department (ED) with ADHF. Patients with heart transplant, ventricular-assist device, or end-stage renal disease were excluded. Demographic and 12-month outcomes were collected. Patients discharged from the OU were compared with those admitted using Chi-Square Analysis, Fisher Exact Test, and Two-Sample T-Test. OU patients later admitted were also compared with those admitted from the ED. RESULTS: Of the 535 patients included in the study, 427 were triaged to OU. Of these, 156 (37%) had LOS > 48 hours and required admission. The mean age was 71.4 years (standard deviation, 14.9 years) and 52% were female. OU patients converted to admission had higher Charlson Comorbidity Index (4.5 vs 3.9, p = 0.012) and higher 12-month mortality (17.3% vs 9.2%, p = 0.014) compared to those discharged. When converted patients were compared to those admitted from the ED, mortality (17.3% vs 10.3%, p = 0.210) and Charlson (4.3 vs 4.5, p = 0.552) were comparable. Patients triaged to OU showed no difference in readmissions, downstream OU visits, or adverse cardiac events. However, OU patients later admitted had shorter time to death compared to patients triaged directly to inpatient units (137.3 vs 257.9 days, p = 0.023). Patients cared for in the OU were more likely to follow-up outpatient (41.0% vs 25.9%, p = 0.041). CONCLUSIONS: The OU is a venue for high-quality care for ADHF. Our study showed over utilization of the OU, commonly defined as over 15% conversion. A possible difference in time to death exists due to suboptimal triage, but multivariate analysis is needed to confirm. Enhanced risk stratification for patient triage is needed.

Internal Medicine

Meighani A, **Hart BR**, Bourgi K, **Miller N**, **John A**, and **Ramesh M**. Outcomes of fecal microbiota transplantation for clostridium difficile infection in patients with inflammatory bowel disease *Dig Dis Sci* 2017;PMID: 28451916. Full Text

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BACKGROUND AND AIMS: Fecal microbiota transplantation (FMT) has recently been shown to be a promising therapy for recurrent and refractory Clostridium difficile infections (CDI) despite lack of protocol standardization. Patients with inflammatory bowel disease (IBD) present a particular challenge to CDI therapy as they are reported to have worse clinical outcomes, including higher colectomy rates and increased mortality. We aimed to assess the outcomes of FMT for recurrent CDI in patients with IBD at our healthcare system. METHODS: We constructed a retrospective cohort of all patients who underwent FMT at our healthcare system between December 2012 and May 2014. Patients with concurrent IBD were identified. We evaluated the differences in demographic and clinical characteristics, along with the outcomes to FMT between patients with IBD as compared to the general population. RESULTS: Over the study period, 201 patients underwent FMT of which 20 patients had concurrent IBD. Patients with IBD were younger but did not differ from the general population in terms of CDI risk factors or disease severity. The response to FMT and rate of CDI relapse in the IBD group were not statistically different compared to the rest of the cohort. The overall response rate in the IBD population was 75% at 12 weeks. Of the patients who failed FMT 4 of 5 patients had active or untreated IBD. CONCLUSION: Fecal microbiota transplantation provides a good alternative treatment option with high success rates for recurrent or refractory Clostridium difficile infection in patients with well-controlled IBD who fail standard antimicrobial therapy.

Internal Medicine

Omar J, **Heidemann DL**, **Blum-Alexandar B**, **Uju-Eke C**, **Alam Z**, **Willens DE**, and **Wisdom K**. Fresh prescription: Improving nutrition education and access to fresh produce in detroit *J Gen Intern Med* 2017; 32(2):S752. PMID: Not assigned. Abstract

J. Omar, Henry Ford Hospital, Macomb, United States

STATEMENT OF PROBLEM OR QUESTION (ONE SENTENCE): Lack of basic knowledge of nutrition and limited access to fresh produce contribute to difficulty in controlling chronic diseases like obesity, diabetes, and cardiovascular disease among underserved adults in Detroit. OBJECTIVES OF PROGRAM/INTERVENTION (NO MORE THAN THREE OBJECTIVES): To improve patient's knowledge of nutrition and confidence in their ability to eat healthy. To improve access to fresh produce by 1) providing financial support, 2) introducing patients to new local Detroit farmer's markets. DESCRIPTION OF PROGRAM/INTERVENTION, INCLUDING ORGANIZATIONAL CONTEXT (E.G. INPATIENT VS. OUTPATIENT, PRACTICE OR COMMUNITY CHARACTERISTICS): Fresh Prescription is a program that serves patients at several different sites in the Detroit area. We implemented Fresh Prescription at our tertiary-care academic institution in the outpatient Internal Medicine clinic. Eligible participants with body mass index >25 and motivation to learn healthy eating habits were enrolled by their primary care physician from July- September 2016. Participants were given a $10 reward on a rechargeable debit card for completing a nutrition educational counseling session, which could include tele-counseling, cooking demonstrations, and other events. They were able to redeem their reward at local farmer's markets or with boxed food deliveries to receive a maximum total of $40 in fresh produce. Patients underwent a total of 4 counseling sessions over 6 weeks and received an additional $20 boxed food delivery for returning for a 12 week follow up. MEASURES OF SUCCESS (DISCUSS QUALITATIVE AND/OR QUANTITATIVE METRICS WHICH WILL BE USED TO EVALUATE PROGRAM/INTERVENTION): Success was measured through comparison of pre- and post-survey responses. FINDINGS TODATE (IT IS NOT SUFFICIENT TOSTATE FINDINGS WILL BEDISCUSSED):Atotal of 149 patients were referred to the program by their primary care physician. 39 of these patients were enrolled, and 28 patients completed the program (72% completion rate). Post-survey responses are available for 27 of the 39 patients enrolled in the program. 96% of participants reported they were better able to manage their health and their chronic conditions. 78% of participants reported an increase in their daily intake for fresh fruits and vegetables, with an average increase of 2 cups/day. 48% of participants reported a decrease in their intake of unhealthy food items, with an average decrease of 1 item/day. There was an increase in measures of knowledge base, which included ability to select, prepare, and store fresh produce. 85% of participants reported better knowledge of where to buy fresh produce. Price, access, and transportation were still noted to be barriers for many participants. Of the 39 patients who completed the program, 16 returned for follow up on biometrics, including weight and blood pressure. 5 of 16 participants had weight loss, and 5

of 16 had improvement in blood pressure. KEYLESSONS FORDISSEMINATION(WHATCAN OTHERS TAKE AWAY FOR IMPLEMENTATION TO THEIR PRACTICE OR COMMUNITY?): Increasing general nutrition knowledge base among participants led to an increase in the amount of fresh produce consumed, a decrease in unhealthy food items consumed, and increase in ability to manage chronic health conditions. Providing financial resources and improving access to fresh produce are important in supporting patients in an underserved population while encouraging healthy eating habits.

Internal Medicine

Robbins-Ong M, **Chasteen KA**, and **Cerasale MT**. Palliative medicine consultation triggers on the general practice unit *J Gen Intern Med* 2017; 32(2):S780-S781. PMID: Not assigned. Abstract

M. Robbins-Ong, Henry Ford Hospital, Detroit, United States

STATEMENT OF PROBLEM OR QUESTION (ONE SENTENCE): Identifying patients on general practice units who could benefit from a palliativemedicine consultation can be difficult and there is little available literature to help guide selection. OBJECTIVES OF PROGRAM/INTERVENTION (NO MORE THAN THREE OBJECTIVES): 1. Develop evidence-based criteria for identification of patients who would benefit from a palliative medicine consultation. 2. Integrate the criteria into a sustainable workflow, such that the volume of triggered consultations is manageable to be seen daily. DESCRIPTION OF PROGRAM/INTERVENTION, INCLUDING ORGANIZATIONAL CONTEXT (E.G. INPATIENT VS. OUTPATIENT, PRACTICE OR COMMUNITY CHARACTERISTICS): The development of criteria to trigger a palliative medicine consultation began with a review of the available literature. Multiple studies have created consultation criteria for the intensive care unit. Features of these studies were selected that could be applied on general practice units. An initial list of patient characteristics was developed and included potentially life-threatening condition plus positive “surprise” question, ≥2 hospitalizations for the same condition in 3 months, admission for difficult to control physical or psychological symptoms, metastatic or incurable cancer, advanced dementia, failure to thrive, or admission from advanced care facility, which was to be applied upon admission. Secondary criteria were developed to increase specificity of patients who would benefit from consultation. These criteria included ongoing distressing physical or psychological symptoms, social or spiritual concerns affecting daily life, lack of understanding of current illness, goals or care unidentified, uncertainly of decision maker, or treatment options do not match patientcentered goals, which would be applied on the second day of hospitalization and only to patients who met the initial criteria. MEASURES OF SUCCESS (DISCUSS QUALITATIVE AND/OR QUANTITATIVE METRICS WHICH WILL BE USED TO EVALUATE PROGRAM/INTERVENTION): The primary outcomemeasure of the project is the number of consultations that would be generated daily. Initial process measures include the number of patients triaged and the number of patients whomeet the first set of criteria. Qualitative feedback from the general practice unit teams on the aid from the completed consultations would also be reviewed. FINDINGS TODATE (IT IS NOT SUFFICIENT TOSTATE FINDINGS WILL BE DISCUSSED): Two PDSA cycles using consultation trigger criteria were completed on a single general practice unit with largely qualitative data collection. The first cycle found the single-step criteria was easily applied in daily rounds, but there was initially discrepancy amongst the providers regarding criteria definitions. Nearly 50% of new admissions met the initial criteria. During the second PDSA cycle, fewer patients met the initial trigger criteria and even fewer met the second step. The volume of potential new consultations averaged less than one per day. The project lead felt the criteria were easy to apply, but had to help guide the other members of the team on criteria application. KEYLESSONS FORDISSEMINATION(WHATCAN OTHERS TAKE AWAY FOR IMPLEMENTATION TO THEIR PRACTICE OR COMMUNITY?): A two-step, evidence-based, criteria for recommendation of a palliative medicine consultation was able to generate a sustainable volume of potential new patients on general practice units who would be highly likely to see benefit from a consultation.

Internal Medicine

Selim R, **Gorgis SA**, **Al-Darzi W**, **Abdelrahim E**, and **Digiovine B**. A case of isolated acquired factor VIII inhibitor *J Gen Intern Med* 2017; 32(2):S394-S395. PMID: Not assigned. Abstract

R. Selim, Henry Ford Hospital, Detroit, United States

LEARNING OBJECTIVE #1: Diagnose and manage the presence of factor VIII inhibitor. CASE: We present the case of a 76-year-old lady with a history of breast cancer post mastectomy who was transferred to our Intensive Care Unit (ICU) for acute blood loss anemia. The patient had initially presented 3 weeks prior to an outside hospital (OSH) after a fall with a hemoglobin of 4.7 g/dL (from 11.7 g/dL), PTT at 73, creatinine at 3.8 mg/dL, and BUN at 55 mg/dL. CT demonstrated a large intramuscular hematoma anterior to the right femur and a retroperitoneal hematoma. She was given several units of blood, and hemoglobin remained stable. Femoral dialysis catheter placement was then attempted due to worsening renal function with resultant profuse bleeding. Given her persistent bleeding of unknown etiology, she was transferred for escalation of care. On arrival to the ICU, the patient required suturing of the femoral

site. Workup of her elevated PPT was initiated. Monoclonal protein evaluation, cardiolipin antibodies, beta 2 glycoprotein were all within normal limits. ANA was mildly positive. Her Factor VIII levels were <1% with elevated inhibitor level. Mixing study was consistent with presence of an inhibitor. She was believed to have acquired factor VIII inhibitor. CT was done to rule out an associated malignancy and was negative. She was given 4 days of high dose decadron, followed by daily cyclophosphamide and prednisone, as well as intermittent doses of Novoseven (factor VII), Obizur (factor VIII), and later Feiba (longer acting factor VII). She did not require further doses as her hemoglobin remained stable with resolution of bleeding. She was discharged on low dose oral prednisone maintenance therapy. IMPACT: Our case highlights the importance of consideration of other etiologies for coagulopathy, especially in patients with no known coagulopathic disorders. Though factor VIII inhibitor is uncommon, it could be an aqcuired disorder in adults with otherwise unexplained elevation in PTT. DISCUSSION: Acquired Factor VIII inhibitor is a rare disorder that may present with severe bleeding episodes that may be life-threatening, with mortality rates up to 22%. The most commonly associated illnesses reported in the literature include autoimmune disorders and malignancy/pre-malignant states. Diagnosis is made both clinically and based on laboratory evaluation; an isolated prolonged PTT (normal PT and platelets), and a mixing study consistent with the presence of an inhibitor, in the absence of heparin contamination and lupus anticoagulant. Factor VIII activity should be measured, and the strength of inhibitor quantified. Acute bleeding episodes with low-titer inhibitors can be treated using human factor VIII concentrates, whereas factor VIII bypassing agents (prothrombin complex concentrates or recombinant activated factor VII) are effective in the presence of high-titer inhibitors. The first-line treatment for the eradication of factor VIII autoantibodies is a combination of steroids and cyclophosphamide.

Internal Medicine

Sherenian MG, Cho SH, **Levin AM**, Min JY, Sen S, Oh S, Huntsman S, Eng C, Farber HJ, Rodriguez-Cintron W, Rodriguez-Santana JR, Serebrisky D, Borrell L, **Williams LK**, Thyne S, Seibold MA, Burchard E, and Kumar R. PAI-1 gain of function genotype and airway obstruction in asthma *J Allergy Clin Immunol* 2017; 139(2):AB171. PMID: Not assigned. Abstract

M.G. Sherenian, Division of Allergy and Immunology, Ann and Robert H. Lurie Children's Hospital of Chicago, Chicago, United States

RATIONALE: A gain of function promoter polymorphism in Plasminogen Activator Inhibitor -1 (PAI-1) modulates airway remodeling. We sought to determine if this polymorphism is associated with greater airway obstruction in children with asthma. METHODS: We studied 2070 Latino children (8-21y) from the GALA II cohort with genotypic and pulmonary function data. The rs2227631 snp was categorized as wild-type (AA) or any risk allele (AG, GG). We examined the association of the polymorphism with asthma and airway obstruction within asthmatics (FEV1/FVC <80%) via multivariate logistic regression. We estimated the relationship of the PAI-1 risk allele with FEV1/FVC by multivariate linear regression, stratified by asthma status. We replicated associations in the SAPPHIRE cohort of African American adults (n=1056). RESULTS: There was an interaction between asthma and the PAI-1 polymorphism on FEV1/FVC (p=0.03). The genotype was associated with lower FEV1/FVC in subjects with asthma (β=-1.25, SE50.45, p=0.006), but not in normal controls (β=-0.38, SE50.69, p=0.58). Compared to nonasthmatic subjects without the polymorphism, subjects with asthma and the genotype had an approximately 5% decrease in FEV1/FVC (β= -5.18, SE50.79, p=0.000). The presence of the polymorphism in asthmatics was associated with a 75% increase in risk of clinical obstruction defined as FEV1/FVC < 80%-predicted (OR=1.76, SE50.45, p=0.03). All findings were replicated in the SAPPHIRE cohort. CONCLUSIONS: The PAI-1 gain of function mutation is only associated with decreased FEV1/FVC ratio in asthmatics, with a 75% increased odds of airway obstruction. Further research is needed to determine if PAI-1 modifies the progression of airway obstruction in asthmatic subjects.

Internal Medicine

Singh Z, and **Gunderson H**. Bacteremia: A noble source *J Gen Intern Med* 2017; 32(2):S454. PMID: Not assigned. Abstract

Z. Singh, Henry Ford Hospital, Detroit, United States

LEARNING OBJECTIVE #1: Recognize unusual sources of bacteremia LEARNING OBJECTIVE #2: Educate patients on the use of insulin needles CASE: 57 year old African American male with a PMHx of well-controlled Type-2 DM, on Lantus, presented to the hospital with fevers, chills, and lethargy with abdominal pain and nausea for 2 days duration. He stated that he was in overall good health and denied any sick contacts, cough, sputum production, chest pain, palpitations or shortness of breath. Physical examination was essentially unremarkable except for a group of small painless and pruritic excoriations along the lower half of his abdomen. They were 1-2 mm in size, red in color, and slightly raised, patient stated that they had been there for a little more than 2 weeks. Patient was found to have a temperature of 39.4 deg C, and a heart rate of 115, with a leukocytosis of 17,000. He was admitted for further

septic workup. Subsequent blood cultures were positive for MRSA on 2 bottles and he was started on IV antibiotics for bacteremia without any obvious source. Echo was negative for endocarditis. On further questioning, patient stated that he had a remote history of IV drug abuse but quit over 15 years ago and he denied any recent use. He denied any cuts or bruises on his body, and denied recent dental procedures. When asked about his excoriations on his abdomen, he stated that is the location of his insulin shots. Upon further questioning about his insulin needles it was found that the patient was reusing them to inject himself because he was unable to afford more. It was deemed that his insulin needles were the source of his bacteremia. Patient then completed treatment for MRSA bacteremia and his labs improved and he was discharged home. IMPACT: Most cases of bacteremia we see in Detroit are from IV drug abusers or skin and soft tissue infections. In this case, this gentleman was unable to afford new needles and tried to save costs by reusing the old supplies he already had in order to continue to receive his medication. It really changed my thinking because there are many other sources of bacteremia which us physicians usually do not think about right away that may potentially lead to detrimental effects on the human body. DISCUSSION: IV drug abuse is a major worldwide epidemic that affects hundreds of thousands of people and their families. Working in downtown Detroit, we encounter many patients on a daily basis who come in with bacteremia and develop endocarditis or other devastating diseases causing them to be bed bound for the rest of their lives. Physicians have to realize that there are many otherways of becoming bacteremic other than IVdrug users. We also need to learn the cost effectiveness of our therapies. Diabetic supplies can be very expensive for some patients and we need to realize the consequences of this. We should also take time to educate out patients and explain the detrimental effects of reusing medical supplies that are only meant for a single use.

Internal Medicine

Solomon R, **Nowak R**, **Hudson M**, **Moyer M**, and **McCord J**. Is duration of symptoms predictive of acute myocardial infarction? *J Am Coll Cardiol* 2017; 69(11):247-247. PMID: Not assigned. Abstract

[Solomon, Robert; Nowak, Richard; Hudson, Michael; Moyer, Michele; McCord, James] Henry Ford Hosp, Detroit, MI 48202 USA.

Internal Medicine

Ting C, **Singh A**, **Solomon R**, **Murad A**, **Woolley R**, and **Michaels A**. No maggic in predicting heart failure readmissions *J Am Coll Cardiol* 2017; 69(11):788-788. PMID: Not assigned. Abstract

[Ting, Christopher; Singh, Aditya; Solomon, Robert; Murad, Ahmad; Woolley, Ryan; Michaels, Alexander] Henry Ford Hosp, Detroit, MI 48202 USA.

Background: Readmission for acute decompensated heart failure represents a significant burden to healthcare in the United States with nearly a quarter of patients being readmitted by 30 days. Here, we evaluate the ability of two robust risk tools derived from ambulatory cohorts, the MAGGIC score and Seattle Heart Failure Model (SHFM), to predict 30-day readmission in an urban heart failure population. Methods: This single center retrospective cohort study analyzed a total of 1172 patients admitted for acute systolic or combined systolic-diastolic heart failure. All patients were assigned a discharge NYHA class 2 status. The primary endpoint was readmission with primary diagnosis of decompensated heart failure. Patients with end-stage renal disease, isolated diastolic heart failure, history of or awaiting heart transplant, and ventricular assist devices were excluded. Data from all variables identified in the MAGICC and SHFM risk scores were abstracted from this cohort, as well as BNP and renal function. The association of SHFM or MAGICC variables and 30-day readmission risk was evaluated with univariate binary logistic regression models. Results: Of 1172 patients included in the study, there were 245 readmissions. 43 patients who expired or placed in hospice at the index encounter were removed prior to analysis, leaving 1129 in the final analysis. The average age was 69.3 years, with 43% female and 49% white. Neither risk tool, SHFM (OR 0.96, 95% CI 0.79-1.17, p=0.7) or MAGGIC (OR 1.0, 95% CI 0.98-1.02, p = 0.892), demonstrated utility in stratifying hospitalized patients at discharge for risk of readmission. Conclusions: The MAGGIC and Seattle Heart Failure Model are two robust risk models of all-cause mortality in ambulatory heart failure patients but fail to predict 30-day readmission in acute decompensated heart failure. Assessing readmission risk in a heart failure patient is complex and likely dependent on many patient-level factors that are not readily quantifiable in current risk-prediction tools. Traditional risk factors identified for mortality may not be sufficient in predicting readmission risk and future endeavors may benefit from evaluating socioeconomic influences.

Nephrology
Al-Abid B, **Sohaney R**, **Alamiri K**, **Kumbar L**, **Soi V**, and **Yee J**. Dementia and catheter dysfunction as under identified and documented risk factors for catheter related blood stream infections *Am J Kidney Dis* 2017; 69(4):A19-A19. PMID: Not assigned. Abstract

[Al-Abid, Baha; Sohaney, Ryann; Alamiri, Khalid; Kumbar, Lalathaksha; Soi, Vivek; Yee, Jerry] Henry Ford Hosp, Detroit, MI 48202 USA.

Nephrology
Jasinski MJ, Lumley MA, **Soman S**, **Yee J**, and **Ketterer MW**. Indicators of cognitive impairment from a medical record review: Correlations with early (30-d) readmissions among hospitalized patients in a nephrology unit *Psychosomatics* 2017; 58(2):173-179. PMID: 28104336. Full Text

M.J. Jasinski, Department of Psychology, Wayne State University, Detroit, United States

Background Patients with end-stage renal disease have the highest 30-day hospital readmission rates of any medical condition. Previous research suggests that cognitive impairment contributes to readmission. It is important to identify patients at risk for early readmission, and this might be accomplished efficiently using medical record data. Method We reviewed the medical records of 100 patients with kidney disease (57 women, mean age = 61.2) who were hospitalized in the nephrology unit at an urban U.S. hospital. For each patient, we recorded easily available indicators of cognitive impairment along with other potential risk factors, and also recorded the number of 30-day readmissions over the past year. Results Half of the sample (n = 50) had at least 1 readmission (median = 0.5, range: 0–20). A lifetime history of delirium, which is a known marker of chronic cognitive impairment, was significantly related to readmissions, and several other impairment indicators (positive head imaging, history of seizures, and history of hypoxia) showed similar trends. A “cognitive impairment index” (positive for one or more variables possibly reflecting impaired central nervous system) was significantly related to the presence of a 30-day readmission, beyond the effects of a number of behavioral and medical covariates. Conclusions Easily accessible cognitive impairment markers, especially a known history of delirium, may be useful to identify patients in nephrology units who are at increased risk for early hospital readmissions. Interventions can be targeted to these patients with the goal of reducing the likelihood of readmissions and improving health care outcomes.

Nephrology
Kumbar L, **Zasuwa G**, **Zaborowicz M**, **Taylor A**, and **Yee J**. Post-angioplasty changes in venous access pressure ratio is a novel diagnostic tool predicting access failure *Am J Kidney Dis* 2017; 69(4):A60-A60. PMID: Not assigned. Abstract

[Kumbar, Lalathaksha; Zasuwa, Gerard; Zaborowicz, Mathew; Taylor, Andrew; Yee, Jerry] Henry Ford Hosp, Detroit, MI 48202 USA.

Nephrology
Sonalika A, **Muhammad F**, Vini S, and **Snigdha R**. Lvad-a cause of cola-colored urine *Am J Kidney Dis* 2017; 69(4):A18-A18. PMID: Not assigned. Abstract

[Sonalika, Agarwal; Muhammad, Farooq; Snigdha, Reddy] Henry Ford Hosp, Detroit, MI 48202 USA. [Vini, Singh] Mercy St Vincent Med Ctr, Toledo, OH USA.

Nephrology
Thaxton S, Rouen P, Groh C, **Li J**, and **Peterson E**. Practice standards and health-related quality of life in kidney disease *Am J Kidney Dis* 2017; 69(4):A97-A97. PMID: Not assigned. Abstract

[Thaxton, Schawana; Li, Jung; Peterson, Edward] Henry Ford Hlth Syst, Detroit, MI USA. [Rouen, Patricia; Groh, Carla] Univ Detroit Mercy, Detroit, MI 48221 USA.

Nephrology
Umanath K, Greco B, Jalal DI, McFadden M, Sika M, Koury MJ, Niecestro R, Hunsicker LG, Greene T, Lewis JB, and Dwyer JP. The safety of achieved iron stores and their effect on IV iron and ESA use: post-hoc results from a randomized trial of ferric citrate as a phosphate binder in dialysis *Clin Nephrol* 2017; 87 (2017)(3):124-133. PMID: 28128726. Full Text

Iron stores assuring optimal efficacy/safety for erythropoiesis are unknown in the dialysis population. Using multicenter trial data, we related safety profiles, erythropoiesis-stimulating agent (ESA), and intravenous iron dosing to achieved iron stores in 441 subjects randomized 2 : 1 to ferric citrate or active control as their phosphate binder over 52 weeks. Intravenous iron was given at each site's discretion if ferritin </= 1,000 ng/mL and transferrin saturation </= 30%. Multivariable time-dependent Cox regression jointly related the primary safety outcome (composite of cardiac, infection, gastrointestinal, and hepatobiliary serious adverse events) to moving averages of ferritin and transferrin saturation over the preceding 90 days with covariate adjustment. Multivariable generalized estimating equations related elevated ESA and intravenous iron doses to trailing 90-day averages of ferritin and transferrin saturation with covariate adjustment. The adjusted hazard ratio for the safety composite per 10% increase in transferrin saturation was 0.84 (95% confidence interval 0.68 - 1.02, p = 0.08) and 1.09 (0.86 - 1.35, p = 0.48) per 400 ng/mL increase in ferritin. The adjusted hazard ratio for the safety composite was 0.50 (0.29 - 0.88, p = 0.016) for the highest transferrin saturation tertile vs. the lowest. Adjusted odds ratios for higher intravenous iron dose were lower in the highest (0.23 [0.16 - 0.35], p < 0.001) and middle transferrin saturation tertile (0.42 [0.31 - 0.57], p < 0.001) vs. lowest. Incidence of elevated ESA dose was lower in the highest transferrin saturation tertile (p = 0.01). Ferritin did not predict clinical events or ESA dose. Transferrin saturation may be a better marker than serum ferritin to judge optimal iron stores in dialysis patients. Transferrin saturations > 34% are safe and provide maximal efficacy..

Nephrology
Winkelmayer W, Block G, Chertow G, Fishbane S, Komatsu Y, McCullough P, Pergola P, Rosenberger C, Williamson D, **Yee J**, Collins A, Khawaja Z, Sharma A, Zuraw Q, and Maroni B. The inno(2)vate phase 3 program of vadadustat for treatment of anemia in dialysis-dependent ckd: Rationale and study design *Am J Kidney Dis* 2017; 69(4):A102-A102. PMID: Not assigned. Abstract

[Winkelmayer, W.] Baylor Coll Med, Houston, TX 77030 USA. [Block, G.] Denver Nephrol, Denver, CO USA. [Chertow, G.] Stanford Univ, Palo Alto, CA 94304 USA. [Fishbane, S.] Hofstra Northwell Hlth, Hempstead, NY USA. [Komatsu, Y.] St Lukes Int Hosp, Tokyo, Japan. [McCullough, P.] Baylor Univ, Med Ctr, Dallas, TX USA. [Pergola, P.] Renal Associates PA, San Antonio, TX USA. [Rosenberger, C.] Charite, Berlin, Germany. [Williamson, D.] Nephrol Associates PC, Augusta, GA USA. [Yee, J.] Henry Ford Hosp, Detroit, MI 48202 USA. [Collins, A.] Chron Dis Res Grp, Minneapolis, MN USA. [Khawaja, Z.; Sharma, A.; Zuraw, Q.; Maroni, B.] Akebia Therapeut Inc, Cambridge, MA USA.

Neurology
Cerghet M, **Poisson L**, **Dutta I**, **Suhil H**, **Elias SB**, **Giri S**, and Mangalam A. A blood-based, six metabolite signature for relapsing-remitting multiple sclerosis *Mult Scler J* 2017; 23(1):14-14. PMID: Not assigned. Abstract

[Cerghet, Mirela; Poisson, Laila; Dutta, Indrani; Suhil, Hamid; Elias, Stanton B.; Giri, Shailendra] Henry Ford Hlth Syst, Detroit, MI USA. [Cerghet, Mirela] Wayne State Univ, Detroit, MI USA. [Mangalam, Ashutosh] Univ Iowa, Iowa City, IA USA.

Neurology
Dangayach NS, Caridi J, Bederson J, and **Mayer SA**. Enhanced recovery after neurosurgery: Paradigm shift and call to arms *World Neurosurg* 2017; 100:683-685. PMID: 28254597. Full Text

Mount Sinai Hospital, New York, New York, USA.
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Neurology
Geller EB, Skarpaas TL, Gross RE, Goodman RR, **Barkley GL**, Bazil CW, Berg MJ, Bergey GK, Cash SS, Cole AJ, Duckrow RB, Edwards JC, Eisenschenk S, Fessler J, Fountain NB, Goldman AM, Gwinn RP, Heck C, Herekar A, Hirsch LJ, Jobst BC, King-Stephens D, Labar DR, Leiphart JW, Marsh WR, Meador KJ, Mizrahi EM, Murro AM, Nair DR, Noe KH, Park YD, Rutecki PA, Salanova V, Sheth RD, Shields DC, Skidmore C, Smith MC, Spencer DC,

Srinivasan S, Tatum W, Van Ness PC, Vossler DG, Wharen RE, Jr., Worrell GA, Yoshor D, Zimmerman RS, Cicora K, Sun FT, and Morrell MJ. Brain-responsive neurostimulation in patients with medically intractable mesial temporal lobe epilepsy *Epilepsia* 2017;PMID: 28398014. Full Text

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OBJECTIVE: Evaluate the seizure-reduction response and safety of mesial temporal lobe (MTL) brain-responsive stimulation in adults with medically intractable partial-onset seizures of mesial temporal lobe origin. METHODS: Subjects with mesial temporal lobe epilepsy (MTLE) were identified from prospective clinical trials of a brain-responsive neurostimulator (RNS System, NeuroPace). The seizure reduction over years 2-6 postimplantation was calculated by assessing the seizure frequency compared to a preimplantation baseline. Safety was assessed based on reported adverse events. RESULTS: There were 111 subjects with MTLE; 72% of subjects had bilateral MTL onsets and 28% had unilateral onsets. Subjects had one to four leads placed; only two leads could be connected to the device. Seventy-six subjects had depth leads only, 29 had both depth and strip leads, and 6 had only strip leads. The mean follow-up was 6.1 +/- (standard deviation) 2.2 years. The median percent seizure reduction was 70% (last observation carried forward). Twenty-nine percent of subjects experienced at least one seizure-free period of 6 months or longer, and 15% experienced at least one seizure-free period of 1 year or longer. There was no difference in seizure reduction in subjects with and without mesial temporal sclerosis (MTS), bilateral MTL onsets, prior resection, prior intracranial monitoring, and prior vagus nerve stimulation. In addition, seizure reduction was not dependent on the location of depth leads relative to the hippocampus. The most frequent serious device-related adverse event was soft tissue implant-site infection (overall rate, including events categorized as device-related, uncertain, or not device-related: 0.03 per implant year, which is not greater than with other neurostimulation devices). SIGNIFICANCE: Brain-responsive stimulation represents a safe and effective treatment option for patients with medically intractable epilepsy, including patients with unilateral or bilateral MTLE who are not candidates for temporal lobectomy or who have failed a prior MTL resection.

Neurology

Girotra T, **Mahajan A**, and Sidiropoulos C. Levodopa responsive parkinsonism in patients with hemochromatosis: Case presentation and literature review *Case Rep Neurol Med* 2017; 2017:5146723. PMID: 28424751. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5382304/

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Hemochromatosis is an autosomal recessive disorder which leads to abnormal iron deposition in the parenchyma of multiple organs causing tissue damage. Accumulation of iron in the brain has been postulated to be associated with several neurodegenerative diseases including Parkinson's disease. The excess iron promotes Parkin and alpha-synuclein aggregation in the neurons. Excess iron has also been noted in substantia nigra on MRI especially using susceptibility weighted imaging in patients with Parkinson's disease. We present a case of a young male with alleles for both C282Y and H63D who presented with signs of Parkinsonism and demonstrated significant improvement with levodopa treatment.

Neurology

Jobst BC, Kapur R, **Barkley GL**, Bazil CW, Berg MJ, Bergey GK, Boggs JG, Cash SS, Cole AJ, Duchowny MS, Duckrow RB, Edwards JC, Eisenschenk S, Fessler AJ, Fountain NB, Geller EB, Goldman AM, Goodman RR, Gross RE, Gwinn RP, Heck C, Herekar AA, Hirsch LJ, King-Stephens D, Labar DR, Marsh WR, Meador KJ, Miller I, Mizrahi EM, Murro AM, Nair DR, Noe KH, Olejniczak PW, Park YD, Rutecki P, Salanova V, Sheth RD, Skidmore C, Smith MC, Spencer DC, Srinivasan S, Tatum W, Van Ness P, Vossler DG, Wharen RE, Jr., Worrell GA, Yoshor D, Zimmerman RS, Skarpaas TL, and Morrell MJ. Brain-responsive neurostimulation in patients with medically intractable seizures arising from eloquent and other neocortical areas *Epilepsia* 2017;PMID: 28387951. Full Text

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OBJECTIVE: Evaluate the seizure-reduction response and safety of brain-responsive stimulation in adults with medically intractable partial-onset seizures of neocortical origin. METHODS: Patients with partial seizures of neocortical origin were identified from prospective clinical trials of a brain-responsive neurostimulator (RNS System, NeuroPace). The seizure reduction over years 2-6 postimplantation was calculated by assessing the seizure frequency compared to a preimplantation baseline. Safety was assessed based on reported adverse events. Additional analyses considered safety and seizure reduction according to lobe and functional area (e.g., eloquent cortex) of seizure onset. RESULTS: There were 126 patients with seizures of neocortical onset. The average follow-up was 6.1 implant years. The median percent seizure reduction was 70% in patients with frontal and parietal seizure onsets, 58% in those with temporal neocortical onsets, and 51% in those with multilobar onsets (last observation carried forward [LOCF] analysis). Twenty-six percent of patients experienced at least one seizure-free period of 6 months or longer and 14% experienced at least one seizure-free period of 1 year or longer. Patients with lesions on magnetic resonance imaging (MRI; 77% reduction, LOCF) and those with normal MRI findings (45% reduction, LOCF) benefitted, although the treatment response was more robust in patients with an MRI lesion ($p = 0.02$, generalized estimating equation [GEE]). There were no differences in the seizure reduction in patients with and without prior epilepsy surgery or vagus nerve stimulation. Stimulation parameters used for treatment did not cause acute or chronic neurologic deficits, even in eloquent cortical areas. The rates of infection (0.017 per patient implant year) and perioperative hemorrhage (0.8%) were not greater than with other neurostimulation devices. SIGNIFICANCE: Brain-responsive stimulation represents a safe and effective treatment option for patients with medically intractable epilepsy, including adults with seizures of neocortical onset, and those with onsets from eloquent cortex.

Neurology

Kolpakova J, Li L, Hatcher JT, Gu H, **Zhang X**, Chen J, and Cheng ZJ. Responses of Nucleus Tractus Solitarius (NTS) early and late neurons to blood pressure changes in anesthetized F344 rats *PLoS One* 2017; 12(4):e0169529. PMID: 28384162. Full Text

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Previously, many different types of NTS barosensitive neurons were identified. However, the time course of NTS barosensitive neuronal activity (NA) in response to arterial pressure (AP) changes, and the relationship of NA-AP changes, have not yet been fully quantified. In this study, we made extracellular recordings of single NTS neurons firing in response to AP elevation induced by occlusion of the descending aorta in anesthetized rats. Our findings were that: 1) Thirty-five neurons (from 46 neurons) increased firing, whereas others neurons either decreased firing upon AP elevation, or were biphasic: first decreased firing upon AP elevation and then increased firing during AP decrease. 2) Fourteen neurons with excitatory responses were activated and rapidly increased their firing during the early phase of AP increase (early neurons); whereas 21 neurons did not increase firing until the mean arterial pressure changes (DeltaMAP) reached near/after the peak (late neurons). 3) The early neurons had a significantly higher firing rate than late neurons during AP elevation at a similar rate. 4) Early neuron NA-DeltaMAP relationship could be well fitted and characterized by the sigmoid logistic function with the maximal gain of 29.3. 5) The increase of early NA correlated linearly with the initial heart rate (HR) reduction. 6) The late neurons did not contribute to the initial HR reduction. However, the late NA could be well correlated with HR reduction during the late phase. Altogether, our study demonstrated that the NTS excitatory neurons could be grouped into early and late neurons based on their firing patterns. The early neurons could be characterized by the sigmoid logistic function, and different neurons may differently contribute to HR regulation. Importantly, the grouping and quantitative methods used in this study may provide a useful tool for future assessment of functional changes of early and late neurons in disease models.

Neurology

Konnai R, Scherer RC, Peplinski A, and Ryan K. Whisper and phonation: Aerodynamic comparisons across adduction and loudness *J Voice* 2017;PMID: 28366247. Full Text

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INTRODUCTION: Whisper is known to be produced by different speakers differently, especially with respect to glottal configuration that influences glottal aerodynamics. Differences in whisper production and phonation types imply important linguistic information in many languages, are identified in vocal pathologies, are used to communicate mood and emotion, and are used in vocal performance. OBJECTIVE: The present study focused on investigating the aerodynamic differences between whisper and phonation at different loudness and adduction levels. METHODS: Three men and five women between 20 and 40 years of age participated in the study. Smooth syllable strings of the syllable /baep:/ were whispered and phonated at three different loudness levels (soft, medium, and loud) and three voice qualities (breathy, normal, and pressed). The voice qualities are associated with different adduction levels. This resulted in 18 treatment combinations (three adduction levels x three loudness levels x two sexes). RESULTS: A regression analysis was performed using a PROC MIXED procedure with SAS statistical software. Under similar production conditions, subglottal pressure was significantly lower in whisper than in phonation in 10 of 18 combinations, mean glottal airflow was significantly higher in whisper than in phonation in 13 of 18 combinations, and flow resistance was significantly lower in whisper than in phonation in 14 of 18 combinations, with the female subjects demonstrating these trends more frequently than the male subjects do. Of importance, in general, compared with phonation under similar production conditions, whisper is not always accompanied by lower subglottal pressure and higher airflows. CONCLUSION: Results from this study suggest that the typical finding of lower subglottal pressure, higher glottal airflow, and decreased flow resistance in whisper compared with phonation cannot be generalized to all individuals and depends on the "whisper type." The nine basic production conditions (three loudness levels and three adduction levels) resulted in data that may help explain the wide range of variation of whisper production reported in earlier studies.

Neurology

Loeffler DA, Klaver AC, Coffey MP, Aasly JO, and **LeWitt PA**. Increased oxidative stress markers in cerebrospinal fluid from healthy subjects with parkinson's disease-associated lrrk2 gene mutations *Front Aging Neurosci* 2017; 9:89. PMID: 28420983. Full Text

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Mutations in the leucine-rich repeat kinase 2 (LRRK2) gene are the most frequent cause of inherited Parkinson's disease (PD). The most common PD-associated LRRK2 mutation, G2019S, induces increased production of reactive oxygen species in vitro. We therefore hypothesized that individuals with PD-associated LRRK2 mutations might have increased concentrations of oxidative stress markers and/or decreased total antioxidant capacity (TAC) in their cerebrospinal fluid (CSF). We measured two oxidative stress markers, namely 8-hydroxy-2'-deoxyguanosine (8-OHdG) and 8-isoprostane (8-ISO), and TAC in CSF from LRRK2 mutation-bearing PD patients (LRRK2 PD = 19), sporadic PD patients (sPD = 31), and healthy control subjects with or without these mutations (LRRK2 CTL = 30, CTL = 27). 8-OHdG and 8-ISO levels were increased in LRRK2 CTL subjects, while TAC was similar between groups. 8-ISO was negatively correlated, and TAC was positively correlated, with Montreal Cognitive Assessment scores in LRRK2 PD, LRRK2 CTL, and CTL subjects. Correlations in both groups of PD patients between the two oxidative stress markers and Unified Parkinson Disease Rating Scale Total scores were weak, while TAC was negatively correlated with these scores. These findings suggest that oxidative stress may be increased in the CNS in healthy individuals with PD-associated LRRK2 mutations. Further, TAC may decrease in the CNS with the progression of PD, and when cognitive impairment is present regardless of the presence or absence of PD.

Neurology

Mahajan A, Deal JA, and Carlson M. Interventions in Parkinson's disease: Role of executive function *Front Biosci (Landmark Ed)* 2017; 22:416-427. PMID: 27814622. Article Request Form

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The cortico-striatal network plays a major role in executive functions (EF), and is believed to play a role in the pathophysiology of Parkinson's disease (PD). However, the tools to assess EF are limited. This review assesses the impact of all PD interventions, namely, pharmacotherapy, physical exercise and Deep Brain Stimulation (DBS) surgery on EF. The effect of PD pharmacotherapy varies with the drug class, neuropsychological test used and the affected dopamine receptor family. There appears to be a benefit of aerobic exercise on EF, including judgment and attention. The effect of Deep Brain Stimulation on EF might vary with site of brain stimulation, the neuropsychological

test performed and the pre-operative cognitive state. The effect of EF on underlying manifestations and as a factor in the pathway to the motor benefit needs to be better assessed with more accurate tests that focus on motor component of EF.

Neurology
Mahajan A, and **Sidiropoulos C**. TPK1 mutation induced childhood onset idiopathic generalized dystonia: Report of a rare mutation and effect of deep brain stimulation *J Neurol Sci* 2017; 376:42-43. PMID: 28431625. Full Text

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Neurology
Niethammer M, Tang CC, **LeWitt PA**, Rezai AR, Leehey MA, Ojemann SG, Flaherty AW, Eskandar EN, Kostyk SK, Sarkar A, Siddiqui MS, Tatter SB, **Schwalb JM**, Poston KL, Henderson JM, Kurlan RM, Richard IH, Sapan CV, Eidelberg D, During MJ, Kaplitt MG, and Feigin A. Long-term follow-up of a randomized AAV2-GAD gene therapy trial for Parkinson's disease *JCI Insight* 2017; 2(7):e90133. PMID: 28405611. Full Text

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BACKGROUND. We report the 12-month clinical and imaging data on the effects of bilateral delivery of the glutamic acid decarboxylase gene into the subthalamic nuclei (STN) of advanced Parkinson's disease (PD) patients. METHODS. 45 PD patients were enrolled in a 6-month double-blind randomized trial of bilateral AAV2-GAD delivery into the STN compared with sham surgery and were followed for 12 months in open-label fashion. Subjects were assessed with clinical outcome measures and 18F-fluorodeoxyglucose (FDG) PET imaging. RESULTS. Improvements under the blind in Unified Parkinson's Disease Rating Scale (UPDRS) motor scores in the AAV2-GAD group compared with the sham group continued at 12 months [time effect: $F(4,138) = 11.55$, $P < 0.001$; group effect: $F(1,35) = 5.45$, $P < 0.03$; repeated-measures ANOVA (RMANOVA)]. Daily duration of levodopa-induced dyskinesias significantly declined at 12 months in the AAV2-GAD group ($P = 0.03$; post-hoc Bonferroni test), while the sham group was unchanged. Analysis of all FDG PET images over 12 months revealed significant metabolic declines ($P < 0.001$; statistical parametric mapping RMANOVA) in the thalamus, striatum, and prefrontal, anterior cingulate, and orbitofrontal cortices in the AAV2-GAD group compared with the sham group. Across all time points, changes in regional metabolism differed for the two groups in all areas, with significant declines only in the AAV2-GAD group ($P < 0.005$; post-hoc Bonferroni tests). Furthermore, baseline metabolism in the prefrontal cortex (PFC) correlated with changes in motor UPDRS scores; the higher the baseline PFC metabolism, the better the clinical outcome. CONCLUSION. These findings show that clinical benefits after gene therapy with STN AAV2-GAD in PD patients persist at 12 months. TRIAL REGISTRATION. ClinicalTrials.gov NCT00643890. FUNDING. Neurologix Inc.

Neurology
Trosch RM, Espay AJ, Truong D, Gil R, Singer C, **LeWitt PA**, Lew MF, Tagliati M, Adler CH, Chen JJ, Marchese D, and Comella CL. Multicenter observational study of abobotulinumtoxinA neurotoxin in cervical dystonia: The ANCHOR-CD registry *J Neurol Sci* 2017; 376:84-90. PMID: 28431634. Full Text

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BACKGROUND: The ANCHOR-CD prospective observational registry study evaluated the effectiveness of abobotulinumtoxinA in adult idiopathic cervical dystonia (CD) in clinical practice. METHODS: Adults with CD were eligible. Treating physicians determined abobotulinumtoxinA dose and treatment interval. The primary endpoint was patient response rate (Toronto Western Spasmodic Torticollis Rating Scale [TWSTRS] score reduction>/=25% and Patient Global Impression of Change [PGIC] score of +2 or +3 at Week 4 of Cycle 1). RESULTS: 350 patients enrolled (75% women; mean age 59+/-13.6years; 27.4% botulinum neurotoxin-naive) and 347 received at least 1 treatment. The median abobotulinumtoxinA dose for Cycle 1 was 500 Units. At Week 4, the responder rate was 30.6% (n=304) and the TWSTRS total score decreased 27.4% from baseline. PGIC of at least "Much improved" was documented in 43.6% of patients and maintained in Cycles 2 through 4 (43.3%, 48.9%, and 52.8%, respectively). A total of 39 adverse events (31 study drug-related) were reported in 17 patients (5%); the most common were dysphagia (n=6), muscle weakness (n=4), and neck pain (n=3). CONCLUSION: This study confirmed the beneficial effect of abobotulinumtoxinA on CD in routine clinical practice as measured by improvements in TWSTRS and PGIC. No new safety concerns were identified.

Neurology
Wang L, **Chopp M**, and **Zhang ZG**. PDE5 inhibitors promote recovery of peripheral neuropathy in diabetic mice *Neural Regen Res* 2017; 12(2):218-219. PMID: 28400802. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5361504/

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Neurology
Zhang L, **Chopp M**, **Lu M**, **Zhang T**, **Li C**, Winter S, Brandstaetter H, Doppler E, Meier D, **Pabla P**, and **Zhang ZG**. Demonstration of therapeutic window of Cerebrolysin in embolic stroke: A prospective, randomized, blinded, and placebo-controlled study *Int J Stroke* 2017:1747493017702665. PMID: 28382851. Article Request Form

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Background and aims In an effort to characterize the effects of Cerebrolysin for treatment of stroke that are essential for successful clinical translation, we have demonstrated that Cerebrolysin dose dependently enhanced neurological functional recovery in experimental stroke. Here, we conduct a prospective, randomized, placebo-controlled, blinded study to examine the therapeutic window of Cerebrolysin treatment of rats subjected to embolic stroke. Methods Male Wistar rats age 3-4 months (n = 100) were subjected to embolic middle cerebral artery occlusion. Animals were randomized to receive saline or Cerebrolysin daily for 10 consecutive days starting 4, 24, 48, and 72 h after middle cerebral artery occlusion. Neurological outcome was measured weekly with a battery of behavioral tests (adhesive removal test, modified neurological severity score (mNSS), and foot-fault test). Global test was employed to assess Cerebrolysin effect on neurological recovery with estimation of mean difference between Cerebrolysin and control-treated groups and its 95% confidence interval in the intent-to-treat population, where a negative value of the mean difference and 95% confidence interval < 0 indicated a significant treatment effect. All rats were sacrificed 28 days after middle cerebral artery occlusion and infarct volume was measured. Results Cerebrolysin treatment initiated within 48 h after middle cerebral artery occlusion onset significantly improved functional outcome; mean differences and 95% confidence interval were -11.6 (-17.7, -5.4) at 4 h, -7.1 (-13.5, -0.8) at 24 h, -8.4 (-14.2, -8.6) at 48 h, and -4.9 (-11.4, 1.5) at 72 h. There were no differences on infarct volume and mortality rate among groups. Conclusions With a clinically relevant rigorous experimental design, our data demonstrate that Cerebrolysin treatment effectively improves stroke recovery when administered up to 48 h after middle cerebral artery occlusion.

Neurosurgery

Figueroa JM, Skog J, Akers J, Li H, Komotar R, Jensen R, Ringel F, Yang I, **Kalkanis S**, Thompson R, LoGuidice L, Berghoff E, Parsa A, Liau L, Curry W, Cahill D, Bettegowda C, Lang FF, Chiocca EA, Henson J, Kim R, Breakefield X, Chen C, Messer K, Hochberg F, and Carter BS. Detection of wtEGFR Amplification and EGFRvIII Mutation in CSF-Derived Extracellular Vesicles of Glioblastoma Patients *Neuro Oncol* 2017;PMID: 28453784. Full Text

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Background: RNA within extracellular vesicles (EVs) have potential as diagnostic biomarkers for patients with cancer, and are identified in a variety of biofluids. Glioblastomas (GBMs) release EVs containing RNA into cerebrospinal fluid (CSF). Here we describe a multi-institutional study of RNA extracted from CSF-derived EVs of GBM patients, for the presence of tumor-associated amplifications and mutations in the epidermal growth factor receptor (EGFR). Methods: CSF and matching tumor tissue were obtained from patients undergoing resection of GBMs. We determined wild-type EGFR (wtEGFR) DNA copy number amplification, as well as wtEGFR and EGFRvIII RNA expression, in tumor samples. We also characterized wtEGFR and EGFRvIII RNA expression in CSF-derived EVs. Results: EGFRvIII positive tumors had significantly greater wtEGFR DNA amplification (p=0.02) and RNA expression (p=0.03), and EGFRvIII positive CSF-derived EVs had significantly more wtEGFR RNA expression (p=0.004). EGFRvIII was detected in CSF-derived EVs for 14 of the 23 EGFRvIII tissue-positive GBM patients. Conversely, only one of the 48 EGFRvIII tissue-negative patients had the EGFRvIII mutation detected in their CSF-derived EVs. These results yield a sensitivity of 61% and a specificity of 98% for the utility of CSF-derived EVs to detect an EGFRvIII-positive GBM. Conclusions: Our results demonstrate CSF-derived EVs contain RNA signatures reflective of the underlying molecular genetic status of GBMs in terms of wtEGFR expression and EGFRvIII status. The high specificity of the CSF-derived EV diagnostic test gives us an accurate determination of positive EGFRvIII tumor status, and is essentially a less-invasive 'liquid biopsy' that might direct mutation-specific therapies for GBMs.

Neurosurgery

Holdhoff M, Ye X, Supko JG, Nabors LB, Desai AS, **Walbert T**, Lesser GJ, Read WL, Lieberman FS, Lodge MA, Leal J, Fisher JD, Desideri S, Grossman SA, Wahl RL, and Schiff D. Timed sequential therapy of the selective T-type calcium channel blocker mibefradil and temozolomide in patients with recurrent high-grade gliomas *Neuro Oncol* 2017;PMID: 28371832. Full Text

The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins, Baltimore, Maryland (M.H., X.Y., J.D.F., S.D., S.A.G.); Massachusetts General Hospital, Boston, Massachusetts (J.G.S.); University of Alabama at Birmingham Comprehensive Cancer Center, Birmingham, Alabama (L.B.N.); University of Pennsylvania, Philadelphia, Pennsylvania (A.S.D.); Henry Ford Health System, Detroit, Michigan (T.W.); Wake Forest University, School of Medicine, Winston-Salem, North Carolina (G.J.L.); Emory University, Atlanta, Georgia (W.L.R.); University of Pittsburgh, Pittsburgh, Pennsylvania (F.S.L.); The Johns Hopkins University School of Medicine, Baltimore, Maryland (M.A.L., J.L.); Washington University School of Medicine, St. Louis, Missouri (R.L.W.); University of Virginia Medical Center, Charlottesville, Virginia (D.S.).

Background.: Mibefradil (MIB), previously approved for treatment of hypertension, is a selective T-type calcium channel blocker with preclinical activity in high-grade gliomas (HGGs). To exploit its presumed mechanism of impacting cell cycle activity (G1 arrest), we designed a phase I study to determine safety and the maximum tolerated dose (MTD) of MIB when given sequentially with temozolomide (TMZ) in recurrent (r)HGG. Methods.: Adult patients with rHGG >/=3 months from TMZ for initial therapy received MIB in 4 daily doses (q.i.d.) for 7 days followed by standard TMZ at 150-200 mg/m2 for 5 days per 28-day cycle. MIB dose escalation followed a modified 3 + 3 design, with an extension cohort of 10 patients at MTD who underwent 3'-deoxy-3'-18F-fluorothymidine (18F-FLT) PET imaging, to image proliferation before and after 7 days of MIB. Results.: Twenty-seven patients were enrolled (20 World Health Organization grade IV, 7 grade III; median age 50 y; median KPS 90). The MTD of MIB was 87.5 mg p.o. q.i.d. Dose-limiting toxicities were elevation of alanine aminotransferase/aspartate aminotransferase (grade 3) and sinus bradycardia. The steady-state maximum plasma concentration of MIB at the MTD was 1693 +/- 287 ng/mL (mean +/- SD). 18F-FLT PET imaging showed a significant decline in standardized uptake value (SUV) signal in 2 of 10 patients after 7 days of treatment with MIB. Conclusions.: MIB followed by TMZ was well tolerated in rHGG patients at the MTD. The lack of toxicity and presence of some responses in this selected patient population suggest that this regimen warrants further investigation.

Neurosurgery

Lim S, Kesavabhotla K, Cybulski GR, Dahdaleh NS, and Smith ZA. Predictors for airway complications following single- and multilevel anterior cervical discectomy and fusion *Spine (Phila Pa 1976)* 2017; 42(6):379-384. PMID: 27310025. Full Text

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STUDY DESIGN: A retrospective, multivariate analyses of a prospectively collected multicenter database. OBJECTIVE: The aim of this study was to evaluate the risk factors for postoperative airway complications following single- and multilevel anterior cervical discectomy and fusion (ACDF). SUMMARY OF BACKGROUND DATA: Airway compromise following ACDF may result in catastrophic outcome. However, its predictors have not been identified by a multi-institutional study. METHODS: Patients who underwent ACDF between 2011 and 2013 were selected from the American College of Surgeons National Surgical Quality Improvement Program database. Multiple logistic regression analysis was performed to identify the risk factors for airway compromise following ACDF. RESULTS: Twelve thousand one hundred eighty-five patients were analyzed in this study. Our multivariate analysis identified older age, male gender, dependent functional status, chronic obstructive pulmonary disease, bleeding disorder, American Society of Anesthesiology class >2, Wound Class >2, and prolonged operative durations as significant predictors of postoperative airway compromise following ACDF. Surprisingly, multilevel and corpectomy procedures were not significant risk factors for airway complication following ACDF. CONCLUSION: We identified significant risk factors for airway compromise following ACDF procedures. While ACDF is considered a safe procedure, postoperative airway complication can lead to disastrous outcome. Continued efforts to elucidate preoperative risk factors and subsequent optimization are warranted to improve outcomes in ACDF. LEVEL OF EVIDENCE: 3.

Neurosurgery

Migliara G, Mueller M, Piermattei A, **Brodie C**, Paidas MJ, Barnea ER, and Ria F. PIF* promotes brain re-myelination locally while regulating systemic inflammation- clinically relevant multiple sclerosis M.smegmatis model *Oncotarget* 2017; 8(13):21834-21851. PMID: 28423529. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5400627/

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Neurologic disease diagnosis and treatment is challenging. Multiple Sclerosis (MS) is a demyelinating autoimmune disease with few clinical forms and uncertain etiology. Current studies suggest that it is likely caused by infection(s) triggering a systemic immune response resulting in antigen/non-antigen-related autoimmune response in central nervous system (CNS). New therapeutic approaches are needed. Secreted by viable embryos, PreImplantation Factor (PIF) possesses a local and systemic immunity regulatory role. Synthetic PIF (PIF) duplicates endogenous peptide's protective effect in pre-clinical autoimmune and transplantation models. PIF protects against brain hypoxia-ischemia by directly targeting microglia and neurons. In chronic experimental autoimmune encephalitis (EAE) model PIF reverses paralysis while promoting neural repair. Herein we report that PIF directly promotes brain re-myelination and reverses paralysis in relapsing remitting EAE MS model. PIF crosses the blood-brain barrier targeting microglia. Systemically, PIF decreases pro-inflammatory IL23/IL17 cytokines, while preserving CNS-specific T-cell repertoire. Global brain gene analysis revealed that PIF regulates critical Na+/K+/Ca++ ions, amino acid and glucose transport genes expression. Further, PIF modulates oxidative stress, DNA methylation, cell cycle regulation, and protein ubiquitination while regulating multiple genes. In cultured astrocytes, PIF promotes BDNF-myelin synthesis promoter and SLC2A1 (glucose transport) while reducing deleterious E2F5, and HSP90ab1 (oxidative stress) genes expression. In cultured microglia, PIF increases anti-inflammatory IL10 while reducing pro-inflammatory IFNgamma expression. Collectively, PIF promotes brain re-myelination and neuroprotection in relapsing remitting EAE MS model. Coupled with ongoing, Fast-Track FDA approved clinical trial, NCT#02239562 (immune disorder), current data supports PIF's translation for neurodegenerative disorders therapy.

Neurosurgery

Snyder J, **Schultz L**, and **Walbert T**. The role of tumor board conferences in neuro-oncology: a nationwide provider survey *J Neurooncol* 2017;PMID: 28421461. Full Text

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The tumor board or multidisciplinary cancer meeting (MCM) is the foundation of high value multidisciplinary oncology care, coordinating teams of specialists. Little is known on how these meetings are implemented in Neuro-oncology. Benefits of MCMs include coordination, direction for complicated cases, education, and a forum for communication, emerging technology, and clinical trials. This study identifies participation and utilization of neuro-oncology MCMs. A cross-sectional descriptive survey was dispersed through an internet questionnaire. The Society of Neuro-Oncology and the American Brain Tumor Association provided a list of dedicated neuro-oncology centers. All National Cancer Institute designated centers, and participants in the Adult Brain Tumor Consortium or the Brain Tumor Trials Collaborative were included, identifying 85 centers. Discussion included primary brain tumors (100%), challenging cases (98%), recurrent disease (96%), neoplastic spine disease (93%), metastatic brain lesions (89%), pre-surgical cases (82%), pathology (76%), and paraneoplastic disease (40%). MCMs were composed of neuro-oncologists, neurosurgeons, and radiation oncologists (100%), radiologists (98%), pathologists (96%), and clinical trial participants (64%). Individual preparation ranged from 15 to 300 min. MCMs were valued for clinical decision making (94%), education (89%), and access to clinical trials (69%). 13% documented MCMs in the medical record. 38% of centers used a molecular tumor board; however, many commented with uncertainty as to how this is defined. Neuro-oncology MCMs at leading U.S. institutions demonstrate congruity of core disciplines, cases discussed, and perceived value. We identified variability in preparation time and implementation of MCM recommendations. There is high uncertainty as to the definition and application of a molecular tumor board.

Neurosurgery

Wharen RE, Jr., Okun MS, Guthrie BL, Uitti RJ, Larson P, Foote K, Walker H, Marshall FJ, **Schwalb J**, Ford B, Jankovic J, Simpson R, Dashtipour K, Phibbs F, Neimat JS, Stewart RM, Peichel D, Pahwa R, and Ostrem JL. Thalamic DBS with a constant-current device in essential tremor: A controlled clinical trial *Parkinsonism Relat Disord* 2017;PMID: 28400200. Full Text

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INTRODUCTION: This study of thalamic deep brain stimulation (DBS) investigated whether a novel constant-current device improves tremor and activities of daily living (ADL) in patients with essential tremor (ET). METHODS: A prospective, controlled, multicenter study was conducted at 12 academic centers. We investigated the safety and efficacy of unilateral and bilateral constant-current DBS of the ventralis intermedius (VIM) nucleus of the thalamus in patients with essential tremor whose tremor was inadequately controlled by medications. The primary outcome measure was a rater-blinded assessment of the change in the target limb tremor score in the stimulation-on versus stimulation-off state six months following surgery. Multiple secondary outcomes were assessed at one-year follow-up, including motor, mood, and quality-of-life measures. RESULTS: 127 patients were implanted with VIM DBS. The blinded, primary outcome variable (n = 76) revealed a mean improvement of 1.25 +/- 1.26 points in the target limb tremor rating scale (TRS) score in the arm contralateral to DBS ($p < 0.001$). Secondary outcome variables at one year revealed significant improvements ($p </= 0.001$) in quality of life, depression symptoms, and ADL scores. Forty-seven patients had a second contralateral VIM-DBS, and this group demonstrated reduction in second-sided tremor at 180 days ($p < 0.001$). Serious adverse events related to the surgery included infection (n = 3), intracranial

hemorrhage (n = 3), and device explantation (n = 3). CONCLUSION: Unilateral and bilateral constant-current VIM DBS significantly improves upper extremity tremor, ADL, quality of life, and depression in patients with severe ET.

Obstetrics, Gynecology and Women's Health Services

Elshaikh MA, **Vance S**, **Kamal M**, **Burmeister C**, **Hanna RK**, **Rasool N**, and **Siddiqui F**. Influence of comorbidity on the risk of death: A single institution study of 1132 women with early-stage uterine cancer *Am J Clin Oncol* 2017; 40(2):183-188. PMID: 25222075. Full Text

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PURPOSE/OBJECTIVE(S): The impact of competing medical comorbidity on survival endpoints in women with early stage endometrial carcinoma (EC) is not well studied. The study goal was to utilize a validated comorbidity scoring system to determine its impact on all-cause mortality as well as on recurrence-free survival (RFS), disease-specific survival (DSS), and overall survival (OS) in patients with early-stage EC. MATERIALS AND METHODS: For this IRB-approved study, we reviewed our prospectively maintained uterine cancer database of 1720 patients. We identified 1132 patients with EC FIGO stages I-II who underwent hysterectomy from 1984 to 2011. Age-adjusted Charlson Comorbidity Index (AACCI) at time of hysterectomy was retrospectively calculated by physician chart review. The cause of death (uterine cancer-related and unrelated) was correlated with AACCI. Univariate and multivariate modeling with Cox regression analysis was used to determine significant predictors of OS, DSS, and RFS. The Kaplan-Meier and the log-rank test methods were used to evaluate survival outcomes. RESULTS: After a median follow-up of 51 months, 262 deaths were recorded (42 from EC [16%], and 220 [84%] from other causes). Median AACCI score for the study cohort was 3 (range, 0 to 15). On the basis of AACCI, patients were grouped as follows: 0 to 2 (group 1, n=379), 3 to 4 (group 2, n=532), and >/=5 (group 3, n=221). By AACCI grouping, the 5-year RFS, DSS, and OS were 95%, 98%, and 97% for group 1, 89%, 95%, and 87% for group 2, and 86%, 95% and 72% for group 3 (P<0.0001). The cause of death in the first 10 years after hysterectomy in our study was mainly non-uterine cancer-related (78% vs. 22% for uterine cancer-related) causes. On multivariate analyses, higher AACCI, lymphovascular space invasion (LVSI), higher tumor grade, age, and involvement of the lower uterine segment were significant predictors of shorter OS. On multivariate analysis for DSS and RFS, only high tumor grade and LVSI were significant predictors. CONCLUSIONS: The cause of death for women with early stage EC is mainly nonuterine cancer-related. Comorbidity score is a significant predictor of OS in our study cohort. Comorbidity scores may be useful as a stratification factor in any prospective clinical trial for women with early-stage EC.

Obstetrics, Gynecology and Women's Health Services

Naman CB, **Rattan R**, Nikoulina SE, Lee J, Miller BW, Moss NA, Armstrong L, Boudreau PD, Debonsi HM, **Valeriote FA**, Dorrestein PC, and Gerwick WH. Integrating molecular networking and biological assays to target the isolation of a cytotoxic cyclic octapeptide, samoamide a, from an american samoan marine cyanobacterium *J Nat Prod* 2017; 80(3):625-633. PMID: 28055219. Article Request Form

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Integrating LC-MS/MS molecular networking and bioassay-guided fractionation enabled the targeted isolation of a new and bioactive cyclic octapeptide, samoamide A (1), from a sample of cf. Symploca sp. collected in American Samoa. The structure of 1 was established by detailed 1D and 2D NMR experiments, HRESIMS data, and chemical degradation/chromatographic (e.g., Marfey's analysis) studies. Pure compound 1 was shown to have in vitro cytotoxic activity against several human cancer cell lines in both traditional cell culture and zone inhibition bioassays. Although there was no particular selectivity between the cell lines tested for samoamide A, the most potent activity was observed against H460 human non-small-cell lung cancer cells (IC50 = 1.1 muM). Molecular modeling studies suggested that one possible mechanism of action for 1 is the inhibition of the enzyme dipeptidyl peptidase (CD26, DPP4) at a reported allosteric binding site, which could lead to many downstream pharmacological effects. However, this interaction was moderate when tested in vitro at up to 10 muM and only resulted in about 16% peptidase inhibition. Combining bioassay screening with the cheminformatics strategy of LC-MS/MS molecular networking as a discovery tool expedited the targeted isolation of a natural product possessing both a novel chemical structure and a desired biological activity.

Obstetrics, Gynecology and Women's Health Services

Tsafrir Z, **Aoun J**, Papalekas E, **Taylor A**, Schiff L, **Theoharis E**, and **Eisenstein D**. Risk factors for trachelectomy following supracervical hysterectomy *Acta Obstet Gynecol Scand* 2017; 96(4):421-425. PMID: 28107774. Full Text

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INTRODUCTION: We identified risk factors for trachelectomy after supracervical hysterectomy (SCH) due to persistence of symptoms. MATERIAL AND METHODS: A retrospective case-control study in a university-affiliated hospital. Seventeen women who underwent a trachelectomy following SCH for nonmalignant indications between June 2002 and October 2014 were compared with 68 randomly selected women (controls) who underwent a SCH within the same time period. Demographics and clinical characteristics were compared between the study and control groups. Univariate analysis identified potential risk factors for trachelectomy following SCH. Univariate logistic regression models predicted which patients would have a trachelectomy following SCH. RESULTS: The occurrence of trachelectomy following SCH during the study period was 0.9% (17/1892). The study group was younger than the control group (mean age 38 +/- 6 years vs. 44 +/- 5 years; $p < 0.001$). Patients who had a history of endometriosis [odds ratio (OR) 6.23, 95% CI 1.11-40.5, $p = 0.038$] had increased risk for trachelectomy. Pathology diagnosed endometriosis only among women in the study group. Preoperative diagnosis of abnormal uterine bleeding (OR 0.22, 95% CI 0.06-0.075, $p = 0.016$), anemia (OR 0.12, 95% CI 0.01-0.53; $p = 0.003$), and fibroid uterus (OR 0.24, 95% CI 0.07-0.82, $p = 0.024$) reduced the risk for future trachelectomy. CONCLUSION: Young age and endometriosis are significant risk factors for trachelectomy following SCH.

Orthopaedics

Burnham JM, **Meta F**, **Lizzio V**, **Makhni EC**, and Bozic KJ. Technology assessment and cost-effectiveness in orthopedics: how to measure outcomes and deliver value in a constantly changing healthcare environment *Curr Rev Musculoskelet Med* 2017;PMID: 28421386. Full Text

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PURPOSE OF REVIEW: The purpose of this study is to review the basic concepts of healthcare value, patient outcome measurement, and cost-effectiveness analyses as they relate to the introduction of new surgical techniques and technologies in the field of orthopedic surgery. RECENT FINDINGS: An increased focus on financial stewardship in healthcare has resulted in a plethora of cost-effectiveness and patient outcome research. Recent research has made great progress in identifying orthopedic technologies that provide exceptional value and those that do not meet adequate standards for widespread adoption. As the pace of technological innovation advances in lockstep with an increased focus on value, orthopedic surgeons will need to have a working knowledge of value-based healthcare decision-making. Value-based healthcare and cost-effectiveness analyses can aid orthopedic surgeons in making ethical and fiscally responsible treatment choices for their patients.

Orthopaedics

Frisch NB, **Nahm NJ**, **Khalil JG**, **Les CM**, **Guthrie ST**, and **Charters MA**. Short versus long cephalomedullary nails for pertrochanteric hip fracture *Orthopedics* 2017; 40(2):83-88. PMID: 27874910. Article Request Form

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This study compared patients who underwent treatment with short or long cephalomedullary nails with integrated cephalocervical screws and linear compression. Patients with AO/OTA 31-A2 or A3 pertrochanteric fractures treated with either short (n=72) or long (n=97) InterTAN (Smith & Nephew, Memphis, Tennessee) cephalomedullary nails were reviewed. Information on perioperative measures (estimated blood loss, surgical time, and fluoroscopy time) and postoperative orthopedic complications (infection, implant failure, screw cutout, and periprosthetic femur fracture) was included. Estimated blood loss (short nail, 161 mL; long nail, 208 mL; P=.002) and surgical time (short nail, 64 minutes; long nail, 83 minutes; P=.001) were lower in the short nail group. There were no differences in fluoroscopy

time (short nail, 90 seconds; long nail, 142 seconds; P=.071) or rates of infection (short nail, 1.4%; long nail, 3.1%; P=.637) or overall orthopedic complications (short nail, 11.1%; long nail, 9.3%; P=.798) between the 2 groups. The long nail group had a trend toward more screw cutouts (long nail, 5.2%; short nail, 0.0%; P=.134) but fewer periprosthetic femur fractures (short nail, 8.3%; long nail, 0.0%; P=.013). This study found a similar overall rate of orthopedic complications between short and long nails with integrated cephalocervical screws and linear compression. These results confirm the suspected advantages of short nails, including faster surgery and less blood loss; however, the rate of periprosthetic femur fracture remains high, despite changes to implant design.

Orthopaedics

Jacobs CA, Burnham JM, **Makhni E**, Malempati CS, Swart E, and Johnson DL. Allograft augmentation of hamstring autograft for younger patients undergoing anterior cruciate ligament reconstruction *Am J Sports Med* 2017; 45(4):892-899. PMID: 28298052. Full Text

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BACKGROUND: Younger patients and those with smaller hamstring autograft diameters have been shown to be at significantly greater risk of graft failure after anterior cruciate ligament (ACL) reconstruction. To date, there is no information in the literature about the clinical success and/or cost-effectiveness of increasing graft diameter by augmenting with semitendinosus allograft tissue for younger patients. HYPOTHESIS: Hybrid hamstring grafts are a cost-effective treatment option because of a reduced rate of graft failure. STUDY DESIGN: Cohort study (economic and decision analysis); Level of evidence, 3. METHODS: We retrospectively identified patients younger than 18 years who had undergone ACL reconstruction by a single surgeon between 2010 and 2015. During this period, the operating surgeon's graft selection algorithm included the use of bone-patellar tendon-bone (BTB) autografts for the majority of patients younger than 18 years. However, hamstring autografts (hamstring) or hybrid hamstring autografts with allograft augment (hybrid) were used in skeletally immature patients and in those whom the surgeon felt might have greater difficulty with postoperative rehabilitation after BTB graft harvest. Patient demographics, graft type, graft diameter, the time the patient was cleared to return to activity, and the need for secondary surgical procedures were compared between the hamstring and hybrid groups. The clinical results were then used to assess the potential cost-effectiveness of hybrid grafts in this select group of young patients with an ACL injury or reconstruction. RESULTS: This study comprised 88 patients (hamstring group, n = 46; hybrid group, n = 42). The 2 groups did not differ in terms of age, sex, timing of return to activity, or prevalence of skeletally immature patients. Graft diameters were significantly smaller in the hamstring group (7.8 vs 9.9 mm; P < .001), which corresponded with a significantly greater rate of graft failure (13 of 46 [28.3%] vs 5 of 42 [11.9%]; P = .049). As a result of the reduced revision rate, the hybrid graft demonstrated incremental cost savings of US$2765 compared with the hamstring graft, and the hybrid graft was the preferred strategy in 89% of cases. CONCLUSION: Driven by increased graft diameters and the reduced risk of revision, hybrid grafts appear to be a more cost-effective treatment option in a subset of younger patients with an ACL injury.

Orthopaedics

Makhni EC, Hamamoto JT, Higgins JD, Patterson T, Griffin JW, Romeo AA, and Verma NN. How comprehensive and efficient are patient-reported outcomes for rotator cuff tears? *Orthop J Sports Med* 2017; 5(3):2325967117693223. PMID: 28451596. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5400217/

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BACKGROUND: Increasing emphasis is placed on patient-reported outcomes (PROs) after common orthopaedic procedures as a measure of quality. When considering PRO utilization in patients with rotator cuff tears, several different PROs exist with varying levels of accuracy and utilization. HYPOTHESIS/PURPOSE: Understanding which disease-specific PRO may be most efficiently administered in patients after rotator cuff repair may assist in promoting increased patient and physician adoption of these useful scores. Using a novel assessment criterion, this study assessed all commonly used rotator cuff PROs. We hypothesize that surveys with fewer numbers of questions may remain comparable (with regard to comprehensiveness) to longer surveys. STUDY DESIGN: Systematic review. METHODS: Commonly utilized rotator cuff PROs were analyzed with regard to number of survey components, comprehensiveness, and efficiency. Comprehensiveness (maximum score, 11) was scored as the total number of pain (at rest/baseline, night/sleep, activities of daily living [ADLs], sport, and work) and functional (strength, motion/stiffness, and ability to perform ADLs, sport, and work) metrics included, along with inclusion of quality of

life/satisfaction metrics. Efficiency was calculated as comprehensiveness divided by the number of survey components. RESULTS: Sixteen different PROs were studied. Number of components ranged from 5 (University of California at Los Angeles score [UCLA]) to 36 (Short Form-36 [SF-36], Japanese Orthopaedic Association score [JOA]). The Quality of Life Outcome Measure for Rotator Cuff Disease (RC-QoL) included all 5 pain components, while 7 PROs contained all 5 functional components. Ten PROs included a quality of life/satisfaction component. The most comprehensive scores were the RC-QoL (score, 11) and Penn (score, 10), and the least comprehensive score was the Marx (score, 3). The most efficient PROs were the UCLA, the Quick Disabilities of the Arm, Shoulder, and Hand score (QuickDASH), and Constant scores. The least efficient scores were the JOA and SF-36 scores. CONCLUSION: Many commonly utilized PROs for rotator cuff tears are lacking in comprehensiveness and efficiency. Continued critical assessment of PRO quality may help practitioners identify the most comprehensive and efficient PRO to incorporate into daily clinical practice.

Orthopaedics

Newman JM, George J, **North WT**, Navale SM, Klika AK, Barsoum WK, and Higuera CA. Hematologic malignancies are associated with adverse perioperative outcomes after total hip arthroplasty *J Arthroplasty* 2017;PMID: 28372919. Full Text

Department of Orthopaedic Surgery, Cleveland Clinic, Cleveland, Ohio.
Department of Orthopaedic Surgery, Henry Ford Hospital, Detroit, Michigan.
Department of Epidemiology and Biostatistics, Case Western Reserve University, Cleveland, Ohio.

BACKGROUND: Advancements in treating hematologic malignancies have improved survival, and these patients may be part of the growing population undergoing total hip arthroplasty (THA). Therefore, the purpose of this study was to evaluate the perioperative outcomes of THA in patients with hematologic malignancies. METHODS: The Nationwide Inpatient Sample identified patients who underwent THA from 2000 to 2011 (n = 2,864,412). Patients diagnosed with any hematologic malignancy (n = 18,012) were further stratified into Hodgkin disease (n = 786), non-Hodgkin lymphoma (n = 5062), plasma cell dyscrasias (n = 2067), leukemia (n = 5644), myeloproliferative neoplasms (n = 3552), and myelodysplastic syndromes (n = 1082). Propensity matching for demographics, hospital characteristics, and comorbidities identified 17,810 patients with any hematologic malignancy and 17,888 controls; additional matching was performed to compare hematologic malignancy subtypes with controls. Multivariate regression was used to analyze surgical and medical complications, length of stay (LOS), and costs. RESULTS: Compared to controls, hematologic malignancies increased the risk of any surgery-related complication (odds ratio [OR], 1.4; P < .0001) and any general medical complication (OR, 1.47; P < .0001). Additionally, hematologic malignancies were associated with an increase in LOS (0.16 days; P = .004) and increased costs ($1,101; P < .0001). CONCLUSION: Patients with hematologic malignancies undergoing THA have an increased risk of perioperative complications, longer LOS, and higher costs. The risk quantification for adverse perioperative outcomes in association with increased cost may help to design different risk stratification and reimbursement methods in such populations.

Orthopaedics

Okoroha KR, **Kadri O**, **Keller RA**, **Marshall N**, Cizmic Z, and **Moutzouros V**. Return to play after revision anterior cruciate ligament reconstruction in national football league players *Orthop J Sports Med* 2017; 5(4):2325967117698788. PMID: 28451611. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5400221/

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School of Medicine, Wayne State University, Detroit, Michigan, USA.

BACKGROUND: National Football League (NFL) players who undergo anterior cruciate ligament (ACL) reconstruction have been shown to have a lower return to play (RTP) than previously expected. However, RTP in the NFL after revision ACL reconstruction (RACLR) is not well defined. PURPOSE/HYPOTHESIS: The purpose of this study is to determine the RTP of NFL players after RACLR and evaluate factors that predict RTP. Our hypothesis was that more experienced and established players would be more likely to RTP after RACLR. STUDY DESIGN: Cohort study; Level of evidence, 3. METHODS: A total of 24 NFL players who underwent RACLR between 2007 and 2014 were reviewed and evaluated. Return to NFL play, time to return, seasons and games played prior to and after revision surgery, draft status, and demographic data were collected. Overall RTP was determined, and players who did RTP were compared with those unable to RTP. Data were also compared with control players matched for age, position, size, and experience. RESULTS: After RACLR, 79% (19/24) of NFL players returned to NFL regular-season play at an average of 12.6 months. All players who were drafted in the first 4 rounds, played in at least 55 games, or played 4 seasons of NFL play prior to injury were able to RTP. Players drafted in the first 4 rounds of the NFL draft were more likely to RTP than those who were not (odds ratio, 0.1; 95% CI, 0.01-1.00; P = .05). Those who returned to

NFL play played in significantly less games and seasons after their injury than before (P = .01 and P = .01, respectively). However, these values did not differ when compared with matched controls (P = .67 and P = .33). CONCLUSION: NFL players who RTP after RACLR do so at a similar rate but prolonged time period compared with after primary ACL reconstruction. Athletes who were drafted in earlier rounds were more likely to RTP than those who were not. Additionally, player experience prior to injury is an important factor when predicting RTP after RACLR.

Orthopaedics

Shukla M, **Keller R**, **Marshall N**, Ahmed H, **Scher C**, **Moutzouros VB**, and **van Holsbeeck M**. Ultrasound evaluation of the ulnar collateral ligament of the elbow: Which method is most reproducible? *Skeletal Radiol* 2017;PMID: 28424849. Full Text

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Division Head and Senior Staff Radiologist, Musculoskeletal Radiology, Henry Ford Health System, 2799 West Grand Boulevard, E-328, Detroit, MI, 48202-2689, USA.

INTRODUCTION: The ulnar collateral ligament (UCL) is an important medial stabilizer of the elbow, particularly in overhead-throwing athletes. However, there is no universally accepted method for evaluating UCL thickness with ultrasound (US). OBJECTIVE: To assess reproducibility of previously published methods, as well as a modified technique, for evaluating the UCL via US. We hypothesize that a modified technique would show greater reproducibility. MATERIAL AND METHODS: Using US, the thickness of the UCL in 50 volunteers was measured by two musculoskeletal trained radiologists using two different measurement techniques. The techniques utilized were as described by Nazarian and Jacobson/Ward (JW). Technique measurements were evaluated using interclass correlation coefficients (ICC) to determine the reproducibility of each method. Twenty-eight of the subjects also underwent measurement via a modified JW technique, measured perpendicular to the ligament rather than the frame of imaging. This technique was also evaluated with ICC values. RESULTS: The ICC value for the Nazarian technique was 0.82 (very good) and 0.51 (moderate) for the JW technique. When using the modified JW technique, we found an ICC value of 0.84 (very good). Mean ligament thickness was greatest with the Nazarian technique, 6.41 mm, with the JW technique measuring 1.86 mm and the modified technique measuring 1.38 mm. CONCLUSION: US assessment of UCL thickness by all three measurement techniques are reproducible. The JW technique had less interobserver agreement when compared to the Nazarian method, whereas the modified JW technique had greater reproducibility compared to the JW technique and similar to the Nazarian technique.

Orthopaedics

Young NM, Roach NT, Herfat S, Rainbow M, Marmor M, Feeley B, **Baum T**, and **Bey M**. Anatomical determinants of dysfunction inform the evolution of the human shoulder *Am J Phys Anthropol* 2017; 162:418. PMID: Not assigned. Abstract

N.M. Young, Orthopaedic Surgery, University of California San Francisco, United States

We previously demonstrated that fossil hominins support a scenario in which the lateralized shoulder joint configuration found in modern humans evolved from the more cranial organization seen in African apes. This trajectory is consistent with selection against overhead functions (e.g., climbing) and for more human-specific behaviors (e.g., tool use). Human populations retain remarkable variability in the skeletal shape and configuration of the shoulder, which may reflect both functional tradeoffs and weak costs associated with more primitive shape configurations. We predicted these configurations experience higher shear forces during lateralized behaviors leading to a higher lifetime incidence of rotator cuff injury (RCI). To test the second of these predictions, we compared computed tomography (CT) data of the scapula from individuals diagnosed with a rotator cuff tear and age-matched controls (n=48). To characterize shape, we collected three-dimensional landmark data, performed Procrustes superimposition to remove the effect of orientation and scale, a Canonical Variates Analysis (CVA) to identify shape differences that maximize between group variation, and ANOVA to test for significance of mean shape differences. RCI and control populations exhibit a significant difference in mean shape ($F=1.77$, $df=77$, $p<0.0001$), the former having a more cranial orientation of the glenoid and scapular spine, a reduced supraspinatus attachment area, and a

smaller attachment area and altered orientation of the teres major. These results are consistent with a direct role of selection in the hypothesized LCA-hominin evolutionary trajectory and help explain the observed variability of scapular shape in modern human populations.

Otolaryngology – Head and Neck Surgery
Williams A, **Ghanem T**, **Siddiqui F**, and **Chang S**. Clinical assessment of cognitive function in head and neck cancer *Psycho-Oncology* 2017; 26:74-74. PMID: Not assigned. Abstract

[Williams, Amy; Ghanem, Tamer; Siddiqui, Farzan; Chang, Steven] Henry Ford Hlth Syst, Detroit, MI USA.

Otolaryngology – Head and Neck Surgery
Worsham MJ, **Chen KM**, **Datta I**, **Stephen JK**, **Chitale D**, and **Divine G**. Network integration of epigenomic data: Leveraging the concept of master regulators in ER negative breast cancer *Cancer Research* 2017; 77:1. PMID: Not assigned. Abstract

[Worsham, M. J.; Chen, K. M.; Datta, I.; Stephen, J. K.; Chitale, D.; Divine, G.] Henry Ford Hlth Syst, Detroit, MI USA.

Palliative Care
Robbins-Ong M, **Chasteen KA**, and **Cerasale MT**. Palliative medicine consultation triggers on the general practice unit *J Gen Intern Med* 2017; 32(2):S780-S781. PMID: Not assigned. Abstract

M. Robbins-Ong, Henry Ford Hospital, Detroit, United States

STATEMENT OF PROBLEM OR QUESTION (ONE SENTENCE): Identifying patients on general practice units who could benefit from a palliativemedicine consultation can be difficult and there is little available literature to help guide selection. OBJECTIVES OF PROGRAM/INTERVENTION (NO MORE THAN THREE OBJECTIVES): 1. Develop evidence-based criteria for identification of patients who would benefit from a palliative medicine consultation. 2. Integrate the criteria into a sustainable workflow, such that the volume of triggered consultations is manageable to be seen daily. DESCRIPTION OF PROGRAM/INTERVENTION, INCLUDING ORGANIZATIONAL CONTEXT (E.G. INPATIENT VS. OUTPATIENT, PRACTICE OR COMMUNITY CHARACTERISTICS): The development of criteria to trigger a palliative medicine consultation began with a review of the available literature. Multiple studies have created consultation criteria for the intensive care unit. Features of these studies were selected that could be applied on general practice units. An initial list of patient characteristics was developed and included potentially life-threatening condition plus positive “surprise” question, ≥2 hospitalizations for the same condition in 3 months, admission for difficult to control physical or psychological symptoms, metastatic or incurable cancer, advanced dementia, failure to thrive, or admission from advanced care facility, which was to be applied upon admission. Secondary criteria were developed to increase specificity of patients who would benefit from consultation. These criteria included ongoing distressing physical or psychological symptoms, social or spiritual concerns affecting daily life, lack of understanding of current illness, goals or care unidentified, uncertainly of decision maker, or treatment options do not match patientcentered goals, which would be applied on the second day of hospitalization and only to patients who met the initial criteria. MEASURES OF SUCCESS (DISCUSS QUALITATIVE AND/OR QUANTITATIVE METRICS WHICH WILL BE USED TO EVALUATE PROGRAM/INTERVENTION): The primary outcomemeasure of the project is the number of consultations that would be generated daily. Initial process measures include the number of patients triaged and the number of patients whomeet the first set of criteria. Qualitative feedback from the general practice unit teams on the aid from the completed consultations would also be reviewed. FINDINGS TODATE (IT IS NOT SUFFICIENT TOSTATE FINDINGS WILL BE DISCUSSED): Two PDSA cycles using consultation trigger criteria were completed on a single general practice unit with largely qualitative data collection. The first cycle found the single-step criteria was easily applied in daily rounds, but there was initially discrepancy amongst the providers regarding criteria definitions. Nearly 50% of new admissions met the initial criteria. During the second PDSA cycle, fewer patients met the initial trigger criteria and even fewer met the second step. The volume of potential new consultations averaged less than one per day. The project lead felt the criteria were easy to apply, but had to help guide the other members of the team on criteria application. KEYLESSONS FORDISSEMINATION(WHATCAN OTHERS TAKE AWAY FOR IMPLEMENTATION TO THEIR PRACTICE OR COMMUNITY?): A two-step, evidence-based, criteria for recommendation of a palliative medicine consultation was able to generate a sustainable volume of potential new patients on general practice units who would be highly likely to see benefit from a consultation.

Pathology

Abdel-Rahman Z, **Ali H**, **Favazza L**, and **Chitale D**. Poor concordance between 21-gene expression assay recurrence score and all Magee equation recurrence scores in a consecutive cohort of patients treated for hormone receptor positive early breast cancer *Breast* 2017; 32:S87-S87. PMID: Not assigned. Abstract

[Abdel-Rahman, Z.] Henry Ford Hlth Syst, Dept Internal Med, Detroit, MI USA. [Ali, H.] Henry Ford Hlth Syst, Div Hematol & Med Oncol, Detroit, MI USA. [Favazza, L.; Chitale, D.] Henry Ford Hlth Syst, Dept Pathol & Lab Med, Detroit, MI USA.

Pathology

Datta L, and **Menon MP**. Plasmacytoid lymphocytes: a clue to dengue diagnosis *Blood* 2017; 129(15):2202. PMID: 28408424. Full Text

Henry Ford Health System.

Pathology

Gulati R, **Carey JL**, **Chitale D**, and **Sharma G**. An effective and multidisciplinary utilization framework for esoteric/ referred tests in molecular pathology *Lab Invest* 2017; 97:507A. PMID: Not assigned. Abstract

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Background: In the emerging Value-Based Payment healthcare model, Pathology's governance of referral (send-out) testing is a prime opportunity to demonstrate domain expertise and reduce costs. However, in the absence of an institutional governance mechanism, pathologists have limited influence on utilization of novel, expensive, and esoteric molecular genetic tests. This unchecked utilization may place undue financial burden on the laboratory. To overcome these challenges, we designed and deployed a multidisciplinary and collaborative framework to ensure cost-effective and medically relevant utilization. Design: We approached our institutional apex governance council and chartered an executive-level Medical Laboratory Formulary (MLFC) to govern the laboratory utilization framework for the entire health system. Clinical Evaluation and Technical Assessment Committee (CETAC), an MLFC subcommittee, is led by Pathology's Vice-Chair. It comprises of pathologists, clinical scientist, laboratory administrators, and representatives from billing and specimen handling. A specified workflow was developed to perform an exhaustive medical, scientific and operational analysis including (1) FDA Clearance (2) National Guidelines (3) Impact on diagnosis/treatment (4) Test cost (5) Coverage by insurance carriers. Subsequently, CETAC invited clinician experts. Based on their input and (1-5), utilization parameters were defined as (a) No restrictions (b) Available after medical review and (c) Off-formulary (i.e. not available through laboratory's referral channels). Results: In total, 14 germline and nine somatic testing requests were reviewed over 33 CETAC meetings. The final utilization parameters were: No restriction (n=0), Available after medical review by CETAC expert (n=8), and Off-formulary (n=15). For individual tests within the medical review category, utilization was limited to four medical specialties (Genetics, Transplant, Neurology and Oncology). The prices of these requests ranged from $50- $5800. A distinct Off-formulary ordering pathway was created for patients or providers still wishing to access such tests. MLFC endorsed 22/23 CETAC determinations and revised only one. Conclusions: CETAC has been successful because of its inclusive nature, well-defined pathways and deriving its legitimacy under system-level MLFC. We have managed to deploy an objective and cost-effective utilization framework. Through its work, it has provided an effective and visible role to pathologists. Based on our experience, we highly recommend deploying similar frameworks at other Pathology departments.

Pathology

Sharma G, and Carter A. Artificial intelligence and the pathologist: Future frenemies? *Arch Pathol Lab Med* 2017; 141(5):622-623. PMID: 28447905. Full Text

From the Department of Pathology & Laboratory Medicine, Henry Ford Health System, Detroit, Michigan (Dr Sharma); and the Department of Pathology and Laboratory Medicine, Children's Healthcare of Atlanta, Atlanta, Georgia (Dr Carter).

Pathology

Sirohi D, Smith SC, Epstein JI, Balzer BL, Simko JP, Balitzer D, Benhamida J, Kryvenko ON, **Gupta NS**, Paluru S, da Cunha IW, Leal DN, Williamson SR, de Peralta-Venturina M, and Amin MB. Pericytic tumors of the kidney - a clinicopathologic analysis of 17 cases *Hum Pathol* 2017;PMID: 28438616. Full Text

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Department of Pathology and Laboratory Medicine, Department of Urology, Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, FL, USA.
Department of Pathology, Henry Ford Health System, Detroit, MI, USA.
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The pericytic (perivascular myoid cell) family of tumors is a distinctive group of mesenchymal neoplasms encountered in superficial sites and only rarely seen in viscera. The pericytic family subtends a spectrum of lesions, namely, glomus tumors and variants; myopericytoma, including myofibroma; and angioleiomyoma. In light of the contemporary classification of pericytic lesions, we identified and reviewed 17 cases of renal pericytic tumors from the files of 6 referral centers. These tumors presented over an age range of 17 to 76years (mean 46.7, median 53), with essentially equal male: female ratio. History of hypertension (available in 11 patients) was noted in 7 (64%), which persisted even after surgical resection, including in 2 younger patients (17 and 30years). The tumors (1.7-11.0cm) included: glomus tumors (n=11); glomangiomyoma (n=1); glomus tumor with atypical features (n=1); and angioleiomyoma (n=1), as well as tumors showing features overlapping pericytic tumor subtypes (n=3). The histomorphology observed in these renal examples closely resembled that of their soft tissue counterparts, a subset with symplastic changes and atypical features, and pericytic immunophenotype. Despite large size and deep site, no progression was identified during a median of 7months follow-up (1-62months). In context of prior reported experience, our series identifies a wide morphologic spectrum, including lesions presenting composite morphologies. Taken with the experience of others, our series further corroborates that malignant behavior is rare, and that criteria associated with aggression among soft tissue pericytic tumors may not be predictive for those in the kidney.

Pathology

Takahashi K, **Go P**, **Stone CH**, **Safwan M**, **Putchakayala KG**, **Kane WJ**, **Malinzak LE**, **Kim DY**, and **Denny JE**. Mycophenolate mofetil and pulmonary fibrosis after kidney transplantation: A case report *Am J Case Rep* 2017; 18:399-404. PMID: 28408734. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5398249/

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Department of Pathology, Henry Ford Hospital, Detroit, MI, USA.

BACKGROUND Mycophenolate mofetil (MMF) induced lung disease has been described in only a few isolated reports. We report a case of fatal respiratory failure associated with MMF after kidney transplantation. CASE REPORT A 50-year-old Hispanic male with a history of end-stage renal disease secondary to hypertension underwent deceased donor kidney transplantation. His preoperative evaluations were normal except for a chest x-ray which showed bilateral interstitial opacities. Tacrolimus and MMF were started on the day of surgery. His postoperative course was uneventful and he was discharged on postoperative day 5. One month later, he presented with shortness of breath and a cough with blood-tinged sputum. His respiratory condition deteriorated rapidly, requiring intubation. Chest computer tomography (CT) demonstrated patchy ground-glass opacities with interlobular septal thickening. Comprehensive pulmonary, cardiac, infectious, and immunological evaluations were all negative. Open lung biopsy revealed extensive pulmonary fibrosis with no evidence of infection. He temporarily improved after discontinuation of tacrolimus and MMF, however, on resuming MMF his respiratory status deteriorated again and he subsequently died from hypoxic respiratory failure. CONCLUSIONS An awareness of pulmonary lung disease due to MMF is important to prevent adverse outcomes after organ transplantation. MMF must be used with utmost care in recipients with underlying lung disease as their pulmonary condition might make them more susceptible to any harmful effects of MMF.

Pathology

Williamson SR. Renal splenosis: Renal mass biopsy diagnosis of a tumor clinically mimicking renal cell carcinoma *Appl Immunohistochem Mol Morphol* 2016;PMID: 27028241. Full Text

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Renal mass biopsy is increasingly used to guide conservative tumor management, placing increasing importance on pathologists' ability to diagnose small tumor samples. A 66-year-old man with a history of prior splenectomy for trauma presented for urologic evaluation after identification of a left 5.8 cm renal mass. Partial envelopment of the mass by renal parenchyma and equivocal enhancement on computed tomography raised concern for renal cell carcinoma. Needle-core biopsy revealed blood, subtle vasculature, few aggregates of lymphocytes, and rare renal tubules. Immunohistochemical staining revealed CD8-positive sinusoids but negative reactivity for epithelial antigens (PAX8, keratin, epithelial membrane antigen, carbonic anhydrase IX), supporting diagnosis of renal splenosis. Renal splenosis is a rare phenomenon that can form a sizeable intrarenal mass, mimicking renal cell carcinoma. Pathologists' awareness of this uncommon occurrence may avoid unnecessary surgery. CD8-positive sinusoids and negative epithelial markers are helpful confirmatory features in the biopsy setting.

Pathology

Worsham MJ, **Chen KM**, **Datta I**, **Stephen JK**, **Chitale D**, and **Divine G**. Network integration of epigenomic data: Leveraging the concept of master regulators in ER negative breast cancer *Cancer Research* 2017; 77:1. PMID: Not assigned. Abstract

[Worsham, M. J.; Chen, K. M.; Datta, I.; Stephen, J. K.; Chitale, D.; Divine, G.] Henry Ford Hlth Syst, Detroit, MI USA.

Pharmacy

Zhang L, **Chopp M**, **Lu M**, **Zhang T**, **Li C**, Winter S, Brandstaetter H, Doppler E, Meier D, **Pabla P**, and **Zhang ZG**. Demonstration of therapeutic window of Cerebrolysin in embolic stroke: A prospective, randomized, blinded, and placebo-controlled study *Int J Stroke* 2017:1747493017702665. PMID: 28382851. Article Request Form

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5 Department of Pharmacology, Henry Ford Hospital, Detroit, USA.

Background and aims In an effort to characterize the effects of Cerebrolysin for treatment of stroke that are essential for successful clinical translation, we have demonstrated that Cerebrolysin dose dependently enhanced neurological functional recovery in experimental stroke. Here, we conduct a prospective, randomized, placebo-controlled, blinded study to examine the therapeutic window of Cerebrolysin treatment of rats subjected to embolic stroke. Methods Male Wistar rats age 3-4 months (n = 100) were subjected to embolic middle cerebral artery occlusion. Animals were randomized to receive saline or Cerebrolysin daily for 10 consecutive days starting 4, 24, 48, and 72 h after middle cerebral artery occlusion. Neurological outcome was measured weekly with a battery of behavioral tests (adhesive removal test, modified neurological severity score (mNSS), and foot-fault test). Global test was employed to assess Cerebrolysin effect on neurological recovery with estimation of mean difference between Cerebrolysin and control-treated groups and its 95% confidence interval in the intent-to-treat population, where a negative value of the mean difference and 95% confidence interval < 0 indicated a significant treatment effect. All rats were sacrificed 28 days after middle cerebral artery occlusion and infarct volume was measured. Results Cerebrolysin treatment initiated within 48 h after middle cerebral artery occlusion onset significantly improved functional outcome; mean differences and 95% confidence interval were -11.6 (-17.7, -5.4) at 4 h, -7.1 (-13.5, -0.8) at 24 h, -8.4 (-14.2, -8.6) at 48 h, and -4.9 (-11.4, 1.5) at 72 h. There were no differences on infarct volume and mortality rate among groups. Conclusions With a clinically relevant rigorous experimental design, our data demonstrate that Cerebrolysin treatment effectively improves stroke recovery when administered up to 48 h after middle cerebral artery occlusion.

Psychiatry

Ghaziuddin N, **Hendriks M**, Patel P, Wachtel LE, and Dhossche DM. Neuroleptic malignant syndrome/malignant catatonia in child psychiatry: Literature review and a case series *J Child Adolesc Psychopharmacol* 2017;PMID: 28398818. Article Request Form

1 Department of Psychiatry, University of Michigan , Ann Arbor, Michigan.
2 Henry Ford Health System , Detroit, Michigan.
3 Kennedy Kreiger Institute, Baltimore, Maryland.
4 Department of Psychiatry, University of Mississippi Medical Center , Jackson, Mississippi.

OBJECTIVE: To describe the presentation of neuroleptic malignant syndrome (NMS) and malignant catatonia (MC) in children and adolescents. BACKGROUND: NMS and MC are life-threatening, neuropsychiatric syndromes,

associated with considerable morbidity and mortality. NMS is diagnosed when there is a recent history of treatment with an antipsychotic (AP) medication, while MC is diagnosed when the symptoms resemble NMS but without a history of exposure to an AP agent. Some authorities believe that apart from the history of exposure to an AP medication, the two conditions are identical. The symptoms of NMS/MC include severe agitation, behavior disregulation, motor and speech changes, self-injury and aggression, autonomic instability, and a range of psychiatric symptoms (affective, anxiety, or psychotic symptoms). Patients may be misdiagnosed with another disorder leading to extensive tests and a delay in treatment. Untreated, the condition may be fatal in 10%-20% of patients, with death sometimes occurring within days of disease onset. METHOD: We describe the presentation and management of five children and adolescents with NMS/MC. CONCLUSION: MC and NMS are life-threatening medical emergencies, which if diagnosed promptly, can be successfully treated with known effective treatments (benzodiazepines and/or electroconvulsive therapy).

Psychiatry
Toledo T, and **Akinyemi E**. Caregiver burnout: Application of dialectal behavioral therapy *Am J Geriatr Psychiatry* 2017; 25(3):S88-S89. PMID: Not assigned. Abstract

[Toledo, Theresa] Henry Ford Hosp, Residency Program, Detroit, MI 48202 USA. [Akinyemi, Esther] Henry Ford Hlth Syst, Detroit, MI USA.

Psychology
Ryan M. Leveraging electronic distress screening: Building equity and high-value psychosocial care *Psycho-Oncology* 2017; 26:21-22. PMID: Not assigned. Abstract

M. Ryan, Henry Ford Health System, United States

Henry Ford Cancer Institute, an oncology care model, serves 5000 new/15 000 follow-up patients annually across greater than 25 clinics dispersed geographically. One-third of patients are underserved minorities, many with limited literacy. Automated distress screening was implemented to systematically assess patient distress, provide real-time triage and referrals, and deliver high-value, equitable, psychosocial care. This study describes using e-health to identify high-distress concerns, better understand unmet needs, and remediate psychosocial care gaps. Methods: New patients to medical/radiation/surgical oncology completed a 31-item automated distress screening (DS) survey. Patients screened January 2015 to May 2016 were included. Distress screening responses were automatically populated to an internal database, and retrospective chart review provided additional demographic variables (ie, gender, age, ethnicity, race, zip code, cancer diagnosis, psychiatric diagnosis, and medications). Staff also completed a brief survey following a supplemental education seminar. Descriptive, frequency, and univariate analyses were conducted. Results: Most frequent concerns: pain, fatigue, sleep, and weight-loss -urban patients most often requested to speak with medical providers about concerns-Urban patients reported severe/very severe concerns understanding treatment options, side effects of treatments, transportation, questions/fear about end-of-life, becoming too ill to communicate medical choices, needing help finding community resources, needing help coordinating medical care-non-white urban patients endorsed more tobacco and substance use concerns -non-whites reported more pain, sleep, and side effects of treatment as severe/very severe-Whites endorsed more irritability, difficulty managing emotions, depressed mood, concerns about becoming too ill to communicate choices, and transportation to medical appointments-patients younger than 40 years old endorsed concerns about family coping and difficulty managing work/home/ school. Conclusions: Leveraging electronic distress screening can inform clinical practice, guide program development, enhance employee engagement in patient care, and promote equitable care among disparate patient populations. Additional work is needed to further examine disparities in cancer care. Study variables should not be limited to race, but include SES, education, location of residence, and social support.

Psychology
Williams A, **Ghanem T**, **Siddiqui F**, and **Chang S**. Clinical assessment of cognitive function in head and neck cancer *Psycho-Oncology* 2017; 26:74-74. PMID: Not assigned. Abstract

[Williams, Amy; Ghanem, Tamer; Siddiqui, Farzan; Chang, Steven] Henry Ford Hlth Syst, Detroit, MI USA.

Psychology
Williams A, **Goldberg W**, **Varkas T**, and **Ryan M**. Distress screening for program building: Similarities and differences among patient populations *Psycho-Oncology* 2017; 26:100. PMID: Not assigned. Abstract

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Purpose: The IOM states screening for distress and psychosocial health needs is a critical first step in providing high-quality cancer care. However, high-quality care goes beyond screening and addressing individual patient concerns in that moment. Distress-screening data should also be used to develop patient-centered programs at a health care system level. This study examines similarities and differences in areas of distress across 11 types of cancer based on distress screening data. Methods: Data were obtained from the Cancer Care Assessment (c) patients complete at their first medical oncology appointment, their radiation oncology simulation visit, or at their second post-op appointment with surgical oncology. Chart review was used to abstract demographic and cancer diagnosis. Cancer diagnoses were divided into 11 cancer types: blood/bone, lung, GI, pancreas, breast, head and neck, brain/neurological, urologic, gynecologic, dermatologic, and liver/ kidney. Those areas of distress rated as a "moderate" or "severe" were considered significant areas of distress. Results: The average patient age ranged from 55 years (brain/neurological) to 70 years (dermatologic) (N = 1613). Aside from breast and gynecologic, a majority of patients were male. Areas of common distress were pain, fatigue, sleep, weight loss, and anxiety. Areas of specific distress varied by cancer type. For example, liver/kidney endorsed concern about end of life decisions while brain/neurological endorsed difficulty coping with treatment side effects. There were also differences in needs both within and across cancer type-based on gender, age, and urban vs suburban residence. Conclusions: While many areas of distress are common across cancer types, there are other areas of distress specific to a particular cancer type. Based on this data, a health care system can develop supportive oncology programs that address both the common and the specific areas of distress to deliver more patient-centered care.

Public Health Sciences

Al-Darzi W, **Nowak R**, **Hudson M**, **Moyer ML**, **Jacobsen G**, and **McCord J**. Ischemicst-segment changes on electrocardiogram in acute myocardial infarction-still common? *J Gen Intern Med* 2017; 32(2):S235-S236. PMID: Not assigned. Abstract

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BACKGROUND: Prior studies report ischemic ST-segment changes on electrocardiogram (ECG) in 40-60% of patients with acute myocardial infarction (AMI) with important diagnostic and prognostic implications. Additionally, 1 to 6% of AMI patients had normal ECG on prior studies. These findings may have changed on the era of more sensitive cardiac troponin (cTn) assays. METHODS: In a single-center we prospectively studied 569 patients who were evaluated for possible AMI in the emergency department from May 2013 to April 2015. Diagnosis of AMI was adjudicated by 2 independent physicians in accordance with the universal definition of AMI using all clinical information and required cTnI > 0.04 ng/ml (Siemens Ultra-cTnI). In situations where there was disagreement between the adjudicators, a third Cardiology adjudicator reviewed the case for final determination. Patients with ECG findings that led to immediate reperfusion therapy were excluded. RESULTS: There were 45 (8%) patients with a diagnosis of AMI. Among AMI patients, the most common ECG findings were T-wave inversion 13 (29%) and normal 13 (29%) while 6 (13%) ECGs demonstrated ST Depression ≥ 1 mm. Comparing patients with and without ST-segment elevation or depression, there was non-significantly higher cTnI levels (13.2 ± 28.3 vs. 5.9 ± 15.6 ng/ml; p = 0.355). CONCLUSIONS: ST-segment changes on ECG are becoming less common in AMI. This may relate to smaller AMIs identified by more sensitive cTn assays which should be verified in larger trials. (Table Presented).

Public Health Sciences

Brodie S, Kyung Lee H, Jiang W, Cazacu S, Xiang C, **Poisson LM**, **Datta I**, Kalkanis S, Ginsberg D, and Brodie C. The novel long non-coding RNA TALNEC2, regulates tumor cell growth and the stemness and radiation response of glioma stem cells *Oncotarget* 2017;PMID: 28423669.
http://www.impactjournals.com/oncotarget/index.php?journal=oncotarget&page=article&op=view&path[]=15991&pubmed-linkout=1

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Despite advances in novel therapeutic approaches for the treatment of glioblastoma (GBM), the median survival of 12-14 months has not changed significantly. Therefore, there is an imperative need to identify molecular mechanisms that play a role in patient survival. Here, we analyzed the expression and functions of a novel lncRNA, TALNEC2 that was identified using RNA seq of E2F1-regulated lncRNAs. TALNEC2 was localized to the cytosol and its expression was E2F1-regulated and cell-cycle dependent. TALNEC2 was highly expressed in GBM with poor prognosis, in GBM

specimens derived from short-term survivors and in glioma cells and glioma stem cells (GSCs). Silencing of TALNEC2 inhibited cell proliferation and arrested the cells in the G1\S phase of the cell cycle in various cancer cell lines. In addition, silencing of TALNEC2 decreased the self-renewal and mesenchymal transformation of GSCs, increased sensitivity of these cells to radiation and prolonged survival of mice bearing GSC-derived xenografts. Using miRNA array analysis, we identified specific miRNAs that were altered in the silenced cells that were associated with cell-cycle progression, proliferation and mesenchymal transformation. Two of the downregulated miRNAs, miR-21 and miR-191, mediated some of TALNEC2 effects on the stemness and mesenchymal transformation of GSCs. In conclusion, we identified a novel E2F1-regulated lncRNA that is highly expressed in GBM and in tumors from patients of short-term survival. The expression of TALNEC2 is associated with the increased tumorigenic potential of GSCs and their resistance to radiation. We conclude that TALNEC2 is an attractive therapeutic target for the treatment of GBM.

Public Health Sciences

Casso D, Phillips S, **Woodcroft K**, Sidovar M, Oliveria S, Trudeau J, and Sidovar M. Assessment of cognitive impairment, treatment adherence, and healthcare resource utilization among treated schizophrenia patients *Schizophrenia Bulletin* 2017; 43:S127-S127. PMID: Not assigned. Abstract

[Casso, Deborah; Phillips, Syd; Oliveria, Susan] QuintilesIMS, Denver, CO USA. [Woodcroft, Kimberley] Henry Ford Hlth Syst, Detroit, MI USA.

Public Health Sciences

Cerghet M, **Poisson L**, **Dutta I**, **Suhil H**, **Elias SB**, **Giri S**, and Mangalam A. A blood-based, six metabolite signature for relapsing-remitting multiple sclerosis *Mult Scler J* 2017; 23(1):14-14. PMID: Not assigned. Abstract

[Cerghet, Mirela; Poisson, Laila; Dutta, Indrani; Suhil, Hamid; Elias, Stanton B.; Giri, Shailendra] Henry Ford Hlth Syst, Detroit, MI USA. [Cerghet, Mirela] Wayne State Univ, Detroit, MI USA. [Mangalam, Ashutosh] Univ Iowa, Iowa City, IA USA.

Public Health Sciences

Elshaikh MA, **Vance S**, **Kamal M**, **Burmeister C**, **Hanna RK**, **Rasool N**, and **Siddiqui F**. Influence of comorbidity on the risk of death: A single institution study of 1132 women with early-stage uterine cancer *Am J Clin Oncol* 2017; 40(2):183-188. PMID: 25222075. Full Text

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PURPOSE/OBJECTIVE(S): The impact of competing medical comorbidity on survival endpoints in women with early stage endometrial carcinoma (EC) is not well studied. The study goal was to utilize a validated comorbidity scoring system to determine its impact on all-cause mortality as well as on recurrence-free survival (RFS), disease-specific survival (DSS), and overall survival (OS) in patients with early-stage EC. MATERIALS AND METHODS: For this IRB-approved study, we reviewed our prospectively maintained uterine cancer database of 1720 patients. We identified 1132 patients with EC FIGO stages I-II who underwent hysterectomy from 1984 to 2011. Age-adjusted Charlson Comorbidity Index (AACCI) at time of hysterectomy was retrospectively calculated by physician chart review. The cause of death (uterine cancer-related and unrelated) was correlated with AACCI. Univariate and multivariate modeling with Cox regression analysis was used to determine significant predictors of OS, DSS, and RFS. The Kaplan-Meier and the log-rank test methods were used to evaluate survival outcomes. RESULTS: After a median follow-up of 51 months, 262 deaths were recorded (42 from EC [16%], and 220 [84%] from other causes). Median AACCI score for the study cohort was 3 (range, 0 to 15). On the basis of AACCI, patients were grouped as follows: 0 to 2 (group 1, n=379), 3 to 4 (group 2, n=532), and >/=5 (group 3, n=221). By AACCI grouping, the 5-year RFS, DSS, and OS were 95%, 98%, and 97% for group 1, 89%, 95%, and 87% for group 2, and 86%, 95% and 72% for group 3 (P<0.0001). The cause of death in the first 10 years after hysterectomy in our study was mainly non-uterine cancer-related (78% vs. 22% for uterine cancer-related) causes. On multivariate analyses, higher AACCI, lymphovascular space invasion (LVSI), higher tumor grade, age, and involvement of the lower uterine segment were significant predictors of shorter OS. On multivariate analysis for DSS and RFS, only high tumor grade and LVSI were significant predictors. CONCLUSIONS: The cause of death for women with early stage EC is mainly nonuterine cancer-related. Comorbidity score is a significant predictor of OS in our study cohort. Comorbidity scores may be useful as a stratification factor in any prospective clinical trial for women with early-stage EC.

Public Health Sciences
Epstein MM, **Divine G**, Chao CR, **Wells KE**, Feigelson HS, Scholes D, Roblin D, Yood MU, Engel LS, **Taylor A**, Fortuny J, Habel LA, and **Johnson CC**. Statin use and risk of multiple myeloma: An analysis from the Cancer Research Network *Int J Cancer* 2017;PMID: 28425616. Full Text

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Animal and human data suggest statins may be protective against developing multiple myeloma; however, findings may be biased by the interrelationship with lipid levels. We investigated the association between statin use and risk of multiple myeloma in a large US population, with an emphasis on accounting for this potential bias. We conducted a case-control study nested within 6 US integrated healthcare systems participating in the National Cancer Institute-funded Cancer Research Network. Adults aged >/=40 years who were diagnosed with multiple myeloma from 1998-2008 were identified through cancer registries (N=2532). For each case, 5 controls were matched on age, sex, health plan, and membership duration prior to diagnosis/index date. Statin prescriptions were ascertained from electronic pharmacy records. To address potential biases related to lipid levels and medication prescribing practices, multivariable marginal structural models were used to model statin use (>/=6 cumulative months) and risk of multiple, with examination of multiple latency periods. Statin use 48-72 months prior to diagnosis/index date was associated with a suggestive 20-28% reduced risk of developing multiple myeloma, compared to non-users. Recent initiation of statins was not associated with myeloma risk (risk ratio range 0.90-0.99 with 0-36 months latency). Older patients had more consistent protective associations across all latency periods (risk ratio range 0.67-0.87). Our results suggest that the association between statin use and multiple myeloma risk may vary by exposure window and age. Future research is warranted to investigate the timing of statin use in relation to myeloma diagnosis.

Public Health Sciences
Evans KL, Wirtz H, Li J, **She RC**, Maya J, Depre C, Hamer A, and **Lanfear D**. Genetics of heart rate observational study (genhrate) *J Am Coll Cardiol* 2017; 69(11):685-685. PMID: Not assigned. Abstract

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Public Health Sciences
Mann ET, **Havstad SL**, **Sitarik A**, **Bellemore SM**, **Levin AM**, Lynch SV, Ownby DR, **Johnson CC**, Lukacs NW, **Zoratti EM**, **Woodcroft KJ**, and **Bobbitt KR**. Characterization of basophils in infants in the microbes, allergy, asthma and Pets (MAAP) birth cohort *J Allergy Clin Immunol* 2017; 139(2):AB168. PMID: Not assigned. Abstract

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RATIONALE: Basophils are mature circulating granulocytic cells that play an important role in IgE-dependent immune responses. The objective of this study was to prospectively examine, in very early life, basophils for FcεRIa and activation markers, which are involved in a Th2 response. METHODS: Cord blood and venous blood at 6 months of age were obtained from 65 infants enrolled in the MAAP (Microbes, Allergy, Asthma and Pets) birth cohort. Basophil percentages were determined by manual differential count of 200 cells in whole blood smears. The enriched granulocyte fraction collected after Ficoll separation of peripheral blood mononuclear cells was examined by flow cytometry. Basophils were defined as low side scatter/Class II 2/CD123+ cells. Cells expressing FcεRIa or the activation markers CD203c or CD63 were examined and were reported as % of basophils expressing these markers. Paired t-tests were used to assess change over time. RESULTS: Basophils represented a mean 0.78% (range 0 to 2.5%) and 0.88% (range 0 to 4.0%) of the differential among cord and 6 month blood samples, respectively. There was a statistically significant increase from birth to 6 months of age in the proportion of basophils expressing FcεRIa (mean increase 12.7%, p=0.007), CD203c (mean increase 16.7%, p<0.001) or CD63 (mean increase 20.3%,

p<0.001). CONCLUSIONS: The longitudinal investigation of basophils in samples from the first months of life makes this study distinctive. The increase in the proportion of basophils that were either CD203c+, CD63+, or FcεRIa+ suggests the rapid development of this aspect of innate immunity during the earliest prenatal period.

Public Health Sciences

Monu SR, **Ren Y**, **Masjoan Juncos JX**, **Kutskill K**, **Wang H**, **Kumar N**, **Peterson EL**, and **Carretero OA**. Connecting tubule glomerular feedback mediates tubuloglomerular feedback resetting post-unilateral nephrectomy *Am J Physiol Renal Physiol* 2017:ajprenal.00619.02016. PMID: 28424211. Full Text

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Unilaterally nephrectomized rats (UNx) have higher glomerular capillary pressure (PGC) that can cause significant glomerular injury in the remnant kidney. PGC is controlled by the ratio of afferent (Af-Art) and efferent arteriole resistance. Af-Art resistance in turn is regulated by two intrinsic feedback mechanisms: 1) Tubuloglomerular feedback (TGF) that causes Af-Art constriction in response to increased NaCl in the macula densa and 2) connecting tubule glomerular feedback (CTGF) that causes Af-Art dilatation in response to an increase in NaCl transport in the connecting tubule via the epithelial sodium channel (ENaC). Resetting of TGF post-UNx can allow systemic pressure to be transmitted to the glomerulus and cause renal damage, but the mechanism behind this resetting is unclear. Since CTGF is an Af-Art dilatory mechanism, we hypothesized that CTGF is increased after UNx, and contributes to TGF resetting. To test this hypothesis, we performed UNx in Sprague Dawley (SD) rats. Twenty-four hours after surgery, we performed micropuncture of individual nephrons and measured stop-flow pressure (PSF). PSF is an indirect measurement of PGC. Maximal TGF response at 40nl/min was 8.9 +/- 1.24 mmHg in sham-UNx rats and 1.39 +/- 1.02 mmHg in UNx rats indicating TGF resetting after UNx. When CTGF was inhibited with the ENaC blocker Benzamil (1muM/L), the TGF response was 12.29 +/- 2.01 mmHg in UNx rats and 13.03 +/- 1.25 mmHg in sham-UNx rats, indicating restoration of the TGF responses in UNx. We conclude that enhanced CTGF contributes to TGF resetting after UNx.

Public Health Sciences

Ng MCY, Graff M, Lu Y, Justice AE, Mudgal P, Liu CT, Young K, Yanek LR, Feitosa MF, Wojczynski MK, Rand K, Brody JA, Cade BE, Dimitrov L, Duan Q, Guo X, Lange LA, Nalls MA, Okut H, Tajuddin SM, Tayo BO, Vedantam S, Bradfield JP, Chen G, Chen WM, Chesi A, Irvin MR, **Padhukasahasram B**, Smith JA, Zheng W, Allison MA, Ambrosone CB, Bandera EV, Bartz TM, Berndt SI, Bernstein L, Blot WJ, Bottinger EP, Carpten J, Chanock SJ, Chen YI, Conti DV, Cooper RS, Fornage M, Freedman BI, Garcia M, Goodman PJ, Hsu YH, Hu J, Huff CD, Ingles SA, John EM, Kittles R, Klein E, Li J, McKnight B, Nayak U, Nemesure B, Ogunniyi A, Olshan A, Press MF, Rohde R, **Rybicki BA**, Salako B, Sanderson M, Shao Y, Siscovick DS, Stanford JL, Stevens VL, Stram A, Strom SS, Vaidya D, Witte JS, Yao J, Zhu X, Ziegler RG, Zonderman AB, Adeyemo A, Ambs S, Cushman M, Faul JD, Hakonarson H, **Levin AM**, Nathanson KL, Ware EB, Weir DR, Zhao W, Zhi D, Arnett DK, Grant SFA, Kardia SLR, Oloapde OI, Rao DC, Rotimi CN, Sale MM, **Williams LK**, Zemel BS, Becker DM, Borecki IB, Evans MK, Harris TB, Hirschhorn JN, Li Y, Patel SR, Psaty BM, Rotter JI, Wilson JG, Bowden DW, Cupples LA, Haiman CA, Loos RJF, and North KE. Discovery and fine-mapping of adiposity loci using high density imputation of genome-wide association studies in individuals of African ancestry: African ancestry anthropometry genetics consortium *PLoS Genet* 2017; 13(4):e1006719. PMID: 28430825. http://journals.plos.org/plosgenetics/article?id=10.1371/journal.pgen.1006719

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Genome-wide association studies (GWAS) have identified >300 loci associated with measures of adiposity including body mass index (BMI) and waist-to-hip ratio (adjusted for BMI, WHRadjBMI), but few have been identified through screening of the African ancestry genomes. We performed large scale meta-analyses and replications in up to 52,895 individuals for BMI and up to 23,095 individuals for WHRadjBMI from the African Ancestry Anthropometry Genetics Consortium (AAAGC) using 1000 Genomes phase 1 imputed GWAS to improve coverage of both common and low frequency variants in the low linkage disequilibrium African ancestry genomes. In the sex-combined analyses, we identified one novel locus (TCF7L2/HABP2) for WHRadjBMI and eight previously established loci at P < 5x10-8:

seven for BMI, and one for WHRadjBMI in African ancestry individuals. An additional novel locus (SPRYD7/DLEU2) was identified for WHRadjBMI when combined with European GWAS. In the sex-stratified analyses, we identified three novel loci for BMI (INTS10/LPL and MLC1 in men, IRX4/IRX2 in women) and four for WHRadjBMI (SSX2IP, CASC8, PDE3B and ZDHHC1/HSD11B2 in women) in individuals of African ancestry or both African and European ancestry. For four of the novel variants, the minor allele frequency was low (<5%). In the trans-ethnic fine mapping of 47 BMI loci and 27 WHRadjBMI loci that were locus-wide significant (P < 0.05 adjusted for effective number of variants per locus) from the African ancestry sex-combined and sex-stratified analyses, 26 BMI loci and 17 WHRadjBMI loci contained </= 20 variants in the credible sets that jointly account for 99% posterior probability of driving the associations. The lead variants in 13 of these loci had a high probability of being causal. As compared to our previous HapMap imputed GWAS for BMI and WHRadjBMI including up to 71,412 and 27,350 African ancestry individuals, respectively, our results suggest that 1000 Genomes imputation showed modest improvement in identifying GWAS loci including low frequency variants. Trans-ethnic meta-analyses further improved fine mapping of putative causal variants in loci shared between the African and European ancestry populations.

Public Health Sciences

Orandi D, **Havstad S**, **Sitarik A**, **Bobbitt K**, **Jones K**, **Levin A**, Lukacs N, Lynch SV, **Wegienka G**, **Woodcroft K**, Ownby D, Johnson C, and **Zoratti E**. An analysis of potential associations between delivery mode and dog-keeping to basophil FCER1 and activation marker expression during infancy *J Allergy Clin Immunol* 2017; 139(2):AB167. PMID: Not assigned. Abstract

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RATIONALE: Early-life exposures, including dog-keeping and vaginal delivery, are associated with lower rates of childhood allergy. The underlying immune mechanism(s) are unknown. Basophils are innate immune cells capable of promoting Th2 polarization and allergy development. We explored associations of these exposures with basophil FcεR1 and activation marker expression during the first 6 months of life. METHODS: Basophil-lineage cells (low side scatter/Class II-/CD123+ from the enriched granulocyte fraction) FcεR1, CD63 and CD203c were identified by flow cytometry in cord blood and at age 6 months in the Microbes, Allergy, Asthma and Pets birth cohort. Concomitant total IgE levels were determined. Dog-keeping during pregnancy and delivery mode data was collected prospectively. Analysis included non-parametric testing using Kruskal-Wallis and Wilcoxon rank sum comparisons. RESULTS: No associations between dog-keeping (any vs. none) and basophil marker expression were apparent. However, children from homes with >1 dog had lower proportions of basophils expressing CD63 at 6 months (median=11.9%, n=18) than those with 0 or 1 dog (median=21.3%, n=33; median=30.7%, n=26, respectively; p=0.045). A trend for lower percentage FcεR1 expression with >1 dog was noted (p=0.096). Vaginal delivery was associated with proportionally fewer basophils expressing FcεR1 versus c-section in cord blood only (median=13.7%, n=80; median=50%, n=16, respectively; p=0.031). Cord and 6 month IgE levels did not correlate with basophil marker expression. CONCLUSIONS: Early-life exposure to multiple dogs is associated with lower proportions of basophils expressing CD63 at 6 months. Natural parturition is associated with lower proportions of basophils expressing FcεR1 in cord blood. These associations may relate to lowered allergy risk.

Public Health Sciences

Sherenian MG, Cho SH, **Levin AM**, Min JY, Sen S, Oh S, Huntsman S, Eng C, Farber HJ, Rodriguez-Cintron W, Rodriguez-Santana JR, Serebrisky D, Borrell L, **Williams LK**, Thyne S, Seibold MA, Burchard E, and Kumar R. PAI-1 gain of function genotype and airway obstruction in asthma *J Allergy Clin Immunol* 2017; 139(2):AB171. PMID: Not assigned. Abstract

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RATIONALE: A gain of function promoter polymorphism in Plasminogen Activator Inhibitor -1 (PAI-1) modulates airway remodeling. We sought to determine if this polymorphism is associated with greater airway obstruction in children with asthma. METHODS: We studied 2070 Latino children (8-21y) from the GALA II cohort with genotypic and pulmonary function data. The rs2227631 snp was categorized as wild-type (AA) or any risk allele (AG, GG). We examined the association of the polymorphism with asthma and airway obstruction within asthmatics (FEV1/FVC <80%) via multivariate logistic regression. We estimated the relationship of the PAI-1 risk allele with FEV1/FVC by multivariate linear regression, stratified by asthma status. We replicated associations in the SAPPHIRE cohort of African American adults (n=1056). RESULTS: There was an interaction between asthma and the PAI-1 polymorphism on FEV1/FVC (p=0.03). The genotype was associated with lower FEV1/FVC in subjects with asthma (β=-1.25, SE50.45, p=0.006), but not in normal controls (β=-0.38, SE50.69, p=0.58). Compared to nonasthmatic subjects without the polymorphism, subjects with asthma and the genotype had an approximately 5% decrease in

FEV1/FVC (β= -5.18, SE50.79, p=0.000). The presence of the polymorphism in asthmatics was associated with a 75% increase in risk of clinical obstruction defined as FEV1/FVC < 80%-predicted (OR=1.76, SE50.45, p=0.03). All findings were replicated in the SAPPHIRE cohort. CONCLUSIONS: The PAI-1 gain of function mutation is only associated with decreased FEV1/FVC ratio in asthmatics, with a 75% increased odds of airway obstruction. Further research is needed to determine if PAI-1 modifies the progression of airway obstruction in asthmatic subjects.

Public Health Sciences

Snyder J, **Schultz L**, and **Walbert T**. The role of tumor board conferences in neuro-oncology: a nationwide provider survey *J Neurooncol* 2017;PMID: 28421461. Full Text

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The tumor board or multidisciplinary cancer meeting (MCM) is the foundation of high value multidisciplinary oncology care, coordinating teams of specialists. Little is known on how these meetings are implemented in Neuro-oncology. Benefits of MCMs include coordination, direction for complicated cases, education, and a forum for communication, emerging technology, and clinical trials. This study identifies participation and utilization of neuro-oncology MCMs. A cross-sectional descriptive survey was dispersed through an internet questionnaire. The Society of Neuro-Oncology and the American Brain Tumor Association provided a list of dedicated neuro-oncology centers. All National Cancer Institute designated centers, and participants in the Adult Brain Tumor Consortium or the Brain Tumor Trials Collaborative were included, identifying 85 centers. Discussion included primary brain tumors (100%), challenging cases (98%), recurrent disease (96%), neoplastic spine disease (93%), metastatic brain lesions (89%), pre-surgical cases (82%), pathology (76%), and paraneoplastic disease (40%). MCMs were composed of neuro-oncologists, neurosurgeons, and radiation oncologists (100%), radiologists (98%), pathologists (96%), and clinical trial participants (64%). Individual preparation ranged from 15 to 300 min. MCMs were valued for clinical decision making (94%), education (89%), and access to clinical trials (69%). 13% documented MCMs in the medical record. 38% of centers used a molecular tumor board; however, many commented with uncertainty as to how this is defined. Neuro-oncology MCMs at leading U.S. institutions demonstrate congruity of core disciplines, cases discussed, and perceived value. We identified variability in preparation time and implementation of MCM recommendations. There is high uncertainty as to the definition and application of a molecular tumor board.

Public Health Sciences

Thaxton S, Rouen P, Groh C, **Li J**, and **Peterson E**. Practice standards and health-related quality of life in kidney disease *Am J Kidney Dis* 2017; 69(4):A97-A97. PMID: Not assigned. Abstract

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Public Health Sciences

Tsafrir Z, **Aoun J**, Papalekas E, **Taylor A**, Schiff L, **Theoharis E**, and **Eisenstein D**. Risk factors for trachelectomy following supracervical hysterectomy *Acta Obstet Gynecol Scand* 2017; 96(4):421-425. PMID: 28107774. Full Text

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INTRODUCTION: We identified risk factors for trachelectomy after supracervical hysterectomy (SCH) due to persistence of symptoms. MATERIAL AND METHODS: A retrospective case-control study in a university-affiliated hospital. Seventeen women who underwent a trachelectomy following SCH for nonmalignant indications between June 2002 and October 2014 were compared with 68 randomly selected women (controls) who underwent a SCH within the same time period. Demographics and clinical characteristics were compared between the study and control

groups. Univariate analysis identified potential risk factors for trachelectomy following SCH. Univariate logistic regression models predicted which patients would have a trachelectomy following SCH. RESULTS: The occurrence of trachelectomy following SCH during the study period was 0.9% (17/1892). The study group was younger than the control group (mean age 38 +/- 6 years vs. 44 +/- 5 years; p < 0.001). Patients who had a history of endometriosis [odds ratio (OR) 6.23, 95% CI 1.11-40.5, p = 0.038] had increased risk for trachelectomy. Pathology diagnosed endometriosis only among women in the study group. Preoperative diagnosis of abnormal uterine bleeding (OR 0.22, 95% CI 0.06-0.075, p = 0.016), anemia (OR 0.12, 95% CI 0.01-0.53; p = 0.003), and fibroid uterus (OR 0.24, 95% CI 0.07-0.82, p = 0.024) reduced the risk for future trachelectomy. CONCLUSION: Young age and endometriosis are significant risk factors for trachelectomy following SCH.

Public Health Sciences

Worsham MJ, **Chen KM**, **Datta I**, **Stephen JK**, **Chitale D**, and **Divine G**. Network integration of epigenomic data: Leveraging the concept of master regulators in ER negative breast cancer *Cancer Research* 2017; 77:1. PMID: Not assigned. Abstract

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Public Health Sciences

Zhang L, **Chopp M**, **Lu M**, **Zhang T**, **Li C**, Winter S, Brandstaetter H, Doppler E, Meier D, **Pabla P**, and **Zhang ZG**. Demonstration of therapeutic window of Cerebrolysin in embolic stroke: A prospective, randomized, blinded, and placebo-controlled study *Int J Stroke* 2017:1747493017702665. PMID: 28382851. Article Request Form

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Background and aims In an effort to characterize the effects of Cerebrolysin for treatment of stroke that are essential for successful clinical translation, we have demonstrated that Cerebrolysin dose dependently enhanced neurological functional recovery in experimental stroke. Here, we conduct a prospective, randomized, placebo-controlled, blinded study to examine the therapeutic window of Cerebrolysin treatment of rats subjected to embolic stroke. Methods Male Wistar rats age 3-4 months (n = 100) were subjected to embolic middle cerebral artery occlusion. Animals were randomized to receive saline or Cerebrolysin daily for 10 consecutive days starting 4, 24, 48, and 72 h after middle cerebral artery occlusion. Neurological outcome was measured weekly with a battery of behavioral tests (adhesive removal test, modified neurological severity score (mNSS), and foot-fault test). Global test was employed to assess Cerebrolysin effect on neurological recovery with estimation of mean difference between Cerebrolysin and control-treated groups and its 95% confidence interval in the intent-to-treat population, where a negative value of the mean difference and 95% confidence interval < 0 indicated a significant treatment effect. All rats were sacrificed 28 days after middle cerebral artery occlusion and infarct volume was measured. Results Cerebrolysin treatment initiated within 48 h after middle cerebral artery occlusion onset significantly improved functional outcome; mean differences and 95% confidence interval were -11.6 (-17.7, -5.4) at 4 h, -7.1 (-13.5, -0.8) at 24 h, -8.4 (-14.2, -8.6) at 48 h, and -4.9 (-11.4, 1.5) at 72 h. There were no differences on infarct volume and mortality rate among groups. Conclusions With a clinically relevant rigorous experimental design, our data demonstrate that Cerebrolysin treatment effectively improves stroke recovery when administered up to 48 h after middle cerebral artery occlusion.

Pulmonary

Schmidt GA, Girard TD, Kress JP, Morris PE, **Ouellette DR**, Alhazzani W, Burns SM, Epstein SK, Esteban A, Fan E, Ferrer M, Fraser GL, Gong MN, Hough CL, Mehta S, Nanchal R, Patel S, Pawlik AJ, Schweickert WD, Sessler CN, Strom T, Wilson KC, and Truwit JD. Liberation from mechanical ventilation in critically ill adults: Executive summary of an official american college of chest physicians/american thoracic society clinical practice guideline *Chest* 2017; 151(1):160-165. PMID: 27818329. Full Text

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BACKGROUND: This clinical practice guideline addresses six questions related to liberation from mechanical ventilation in critically ill adults. It is the result of a collaborative effort between the American Thoracic Society (ATS) and the American College of Chest Physicians (CHEST). METHODS: A multidisciplinary panel posed six clinical questions in a population, intervention, comparator, outcomes (PICO) format. A comprehensive literature search and evidence synthesis was performed for each question, which included appraising the quality of evidence using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach. The Evidence-to-Decision framework was applied to each question, requiring the panel to evaluate and weigh the importance of the problem, confidence in the evidence, certainty about how much the public values the main outcomes, magnitude and balance of desirable and undesirable outcomes, resources and costs associated with the intervention, impact on health disparities, and acceptability and feasibility of the intervention. RESULTS: Evidence-based recommendations were formulated and graded initially by subcommittees and then modified following full panel discussions. The recommendations were confirmed by confidential electronic voting; approval required that at least 80% of the panel members agree with the recommendation. CONCLUSIONS: The panel provides recommendations regarding liberation from mechanical ventilation. The details regarding the evidence and rationale for each recommendation are presented in the American Journal of Respiratory and Critical Care Medicine and CHEST.

Pulmonary

Selim R, **Gorgis SA**, **Al-Darzi W**, **Abdelrahim E**, and **Digiovine B**. A case of isolated acquired factor VIII inhibitor *J Gen Intern Med* 2017; 32(2):S394-S395. PMID: Not assigned. Abstract

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LEARNING OBJECTIVE #1: Diagnose and manage the presence of factor VIII inhibitor. CASE: We present the case of a 76-year-old lady with a history of breast cancer post mastectomy who was transferred to our Intensive Care Unit (ICU) for acute blood loss anemia. The patient had initially presented 3 weeks prior to an outside hospital (OSH) after a fall with a hemoglobin of 4.7 g/dL (from 11.7 g/dL), PTT at 73, creatinine at 3.8 mg/dL, and BUN at 55 mg/dL. CT demonstrated a large intramuscular hematoma anterior to the right femur and a retroperitoneal hematoma. She was given several units of blood, and hemoglobin remained stable. Femoral dialysis catheter placement was then attempted due to worsening renal function with resultant profuse bleeding. Given her persistent bleeding of unknown etiology, she was transferred for escalation of care. On arrival to the ICU, the patient required suturing of the femoral site. Workup of her elevated PPT was initiated. Monoclonal protein evaluation, cardiolipin antibodies, beta 2 glycoprotein were all within normal limits. ANA was mildly positive. Her Factor VIII levels were <1% with elevated inhibitor level. Mixing study was consistent with presence of an inhibitor. She was believed to have acquired factor VIII inhibitor. CT was done to rule out an associated malignancy and was negative. She was given 4 days of high dose decadron, followed by daily cyclophosphamide and prednisone, as well as intermittent doses of Novoseven (factor VII), Obizur (factor VIII), and later Feiba (longer acting factor VII). She did not require further doses as her hemoglobin remained stable with resolution of bleeding. She was discharged on low dose oral prednisone

maintenance therapy. IMPACT: Our case highlights the importance of consideration of other etiologies for coagulopathy, especially in patients with no known coagulopathic disorders. Though factor VIII inhibitor is uncommon, it could be an aqcuired disorder in adults with otherwise unexplained elevation in PTT. DISCUSSION: Acquired Factor VIII inhibitor is a rare disorder that may present with severe bleeding episodes that may be life-threatening, with mortality rates up to 22%. The most commonly associated illnesses reported in the literature include autoimmune disorders and malignancy/pre-malignant states. Diagnosis is made both clinically and based on laboratory evaluation; an isolated prolonged PTT (normal PT and platelets), and a mixing study consistent with the presence of an inhibitor, in the absence of heparin contamination and lupus anticoagulant. Factor VIII activity should be measured, and the strength of inhibitor quantified. Acute bleeding episodes with low-titer inhibitors can be treated using human factor VIII concentrates, whereas factor VIII bypassing agents (prothrombin complex concentrates or recombinant activated factor VII) are effective in the presence of high-titer inhibitors. The first-line treatment for the eradication of factor VIII autoantibodies is a combination of steroids and cyclophosphamide.

Radiation Oncology

Elshaikh MA, **Vance S**, **Kamal M**, **Burmeister C**, **Hanna RK**, **Rasool N**, and **Siddiqui F**. Influence of comorbidity on the risk of death: A single institution study of 1132 women with early-stage uterine cancer *Am J Clin Oncol* 2017; 40(2):183-188. PMID: 25222075. Full Text

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PURPOSE/OBJECTIVE(S): The impact of competing medical comorbidity on survival endpoints in women with early stage endometrial carcinoma (EC) is not well studied. The study goal was to utilize a validated comorbidity scoring system to determine its impact on all-cause mortality as well as on recurrence-free survival (RFS), disease-specific survival (DSS), and overall survival (OS) in patients with early-stage EC. MATERIALS AND METHODS: For this IRB-approved study, we reviewed our prospectively maintained uterine cancer database of 1720 patients. We identified 1132 patients with EC FIGO stages I-II who underwent hysterectomy from 1984 to 2011. Age-adjusted Charlson Comorbidity Index (AACCI) at time of hysterectomy was retrospectively calculated by physician chart review. The cause of death (uterine cancer-related and unrelated) was correlated with AACCI. Univariate and multivariate modeling with Cox regression analysis was used to determine significant predictors of OS, DSS, and RFS. The Kaplan-Meier and the log-rank test methods were used to evaluate survival outcomes. RESULTS: After a median follow-up of 51 months, 262 deaths were recorded (42 from EC [16%], and 220 [84%] from other causes). Median AACCI score for the study cohort was 3 (range, 0 to 15). On the basis of AACCI, patients were grouped as follows: 0 to 2 (group 1, n=379), 3 to 4 (group 2, n=532), and >/=5 (group 3, n=221). By AACCI grouping, the 5-year RFS, DSS, and OS were 95%, 98%, and 97% for group 1, 89%, 95%, and 87% for group 2, and 86%, 95% and 72% for group 3 (P<0.0001). The cause of death in the first 10 years after hysterectomy in our study was mainly non-uterine cancer-related (78% vs. 22% for uterine cancer-related) causes. On multivariate analyses, higher AACCI, lymphovascular space invasion (LVSI), higher tumor grade, age, and involvement of the lower uterine segment were significant predictors of shorter OS. On multivariate analysis for DSS and RFS, only high tumor grade and LVSI were significant predictors. CONCLUSIONS: The cause of death for women with early stage EC is mainly nonuterine cancer-related. Comorbidity score is a significant predictor of OS in our study cohort. Comorbidity scores may be useful as a stratification factor in any prospective clinical trial for women with early-stage EC.

Radiation Oncology

Muir B, Culberson W, Davis S, Kim GY, **Huang Y**, Lee SW, Lowenstein J, Sarfehnia A, Siebers J, and Tolani N. Insight gained from responses to surveys on reference dosimetry practices *J Appl Clin Med Phys* 2017;PMID: 28397396. Full Text

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PURPOSE: To present the results and discuss potential insights gained through surveys on reference dosimetry practices. METHODS: Two surveys were sent to medical physicists to learn about the current state of reference dosimetry practices at radiation oncology clinics worldwide. A short survey designed to maximize response rate was made publicly available and distributed via the AAPM website and a medical physics list server. Another, much more involved survey, was sent to a smaller group of physicists to gain insight on detailed dosimetry practices. The questions were diverse, covering reference dosimetry practices on topics like measurements required for beam quality specification, the actual measurement of absorbed dose and ancillary equipment required like electrometers and environment monitoring measurements. RESULTS: There were 190 respondents to the short survey and seven respondents to the detailed survey. The diversity of responses indicates nonuniformity in reference dosimetry practices and differences in interpretation of reference dosimetry protocols. CONCLUSIONS: The results of these surveys offer insight on clinical reference dosimetry practices and will be useful in identifying current and future needs for reference dosimetry.

Radiation Oncology
Ritter TA, Matuszak M, **Chetty IJ**, Mayo CS, Wu J, Iyengar P, Weldon M, Robinson C, Xiao Y, and Timmerman RD. Application of critical volume-dose constraints for stereotactic body radiation therapy in nrg radiation therapy trials *Int J Radiat Oncol Biol Phys* 2017; 98(1):34-36. PMID: Not assigned. Full Text

T.A. Ritter, Department of Radiation Oncology, Hunter Holmes McGuire VA Medical Center, Richmond, United States

Radiation Oncology
Stinchcombe T, Zhang Y, Vokes E, Schiller J, Bradley J, Kelly K, Curran W, Schild S, **Movsas B**, Clamon G, Govindan R, Blumenschein G, Socinski M, Ready N, Akerley W, Cohen H, Pang H, and Wang X. A pooled analysis comparing the outcomes of elderly to younger patients on nctn trials of concurrent ccrt for stage 3 NSCLC *J Thorac Oncol* 2017; 12(1):S374-S375. PMID: Not assigned. Abstract

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Background: Concurrent chemoradiotherapy (CCRT) is the standard treatment (TRT) for stage 3 NSCLC. Elderly patients (pts) are common, may have increased toxicity,& poorer results from CCRT. Methods: Individual patient data (IPD) from NCTN phase 2/3 trials of CCRT for stage 3 NSCLC from 1990- 2012 was collected. We compared the overall survival (OS), progression-free survival (PFS), & adverse events (AE's) for pts age ≥70 years (yrs) (elderly) vs. <70 yrs (younger). Unadjusted & adjusted Hazard Ratios (HRs) for survival time & their confidence intervals (CIs) were estimated by single-predictor & multivariable Cox models. Unadjusted & adjusted Odds Ratio (OR) for AE's & their CIs were obtained from single-predictor & multivariable logistic regression models. Results: IPD from 16 trials were analyzed; 2,768 pts were younger & 832 were elderly. Median OS & PFS for elderly & younger pts are in the table. In the unadjusted & multivariable models elderly pts had worse OS (HR=1.23; 95%CI =1.13-1.35, and 1.20; 95%CI=1.10-1.32, respectively). In the unadjusted & multivariable models, elderly & younger pts had a similar PFS (HR=1.02; 95% CI=0.94-1.11 and 1.01, 95% CI=0.92-1.10, respectively). Elderly pts had a higher rate of grade ≥3 AE's in the unadjusted & multivariable models (OR=1.25; 95% CI=1.00-1.57 and 1.30; 95%CI=1.03-1.62, respectively). A lower percentage of elderly pts compared to younger completed TRT (47% and 57%, respectively; P<0.0001) & higher percentage stopped due to AE's (20% and 13%; P<0.0001). Grade ≥ 3 AE's (occurring at a rate ≥ 2.5%) with a higher rate in the elderly: neutropenia, dyspnea, fatigue, anorexia, vomiting, dehydration, hypoxia, hypotension, & pneumonitis (P<0.05). (Table presented) Conclusion: Elderly pts in CCRT trials had worse OS, similar PFS, & a higher rate of severe AE's.

Radiation Oncology
Williams A, **Ghanem T**, **Siddiqui F**, and **Chang S**. Clinical assessment of cognitive function in head and neck cancer *Psycho-Oncology* 2017; 26:74-74. PMID: Not assigned. Abstract

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Radiology
Stone M, **Eyler W**, Rhodenizer J, and **van Holsbeeck M**. Accuracy of sonography in plantar plate tears in cadavers *J Ultrasound Med* 2017;PMID: 28398696. Full Text

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OBJECTIVES: Sonography is often used in the evaluation of forefoot disorders, and its use has been suggested in the diagnosis of plantar plate tears. This study aimed to assess the accuracy of sonography in the diagnosis of plantar plate tears of the lesser digits using gross dissection as the reference standard. METHODS: The second through fifth digits of 6 cadavers were examined with sonography to evaluate for plantar plate tears. The examination was performed by a single musculoskeletal radiologist in longitudinal and short axes, and plates were graded as torn or intact. The digits were then dissected by a single podiatrist blinded to the prior sonographic results to assess the integrity of the plates. RESULTS: Ten plantar plates were graded as torn by sonography, all occurring in the distal plate near the phalangeal insertion. Seven of these plates were identified as torn on direct inspection. Fourteen plantar plates were found to be intact on sonography, 12 of which were intact on gross inspection. Overall, the accuracy, sensitivity, and specificity of sonography were 79.2%, 77.8%, and 80.0%, respectively. No correlation was seen between the accuracy of sonography and plate size, using plate number as a surrogate marker for plate size (P = .822). CONCLUSIONS: Sonography is an appropriate modality in the setting of suspected plantar plate tears, with acceptable accuracy, sensitivity, and specificity. No decline in accuracy was seen with smaller plates. Thus, sonography may be especially useful when small anatomy or technical factors make magnetic resonance imaging challenging to perform and interpret.

Rheumatology

Sreih AG, Ezzedine R, Leng L, Fan J, Yao J, Reid D, Carette S, Cuthbertson D, Dellaripa P, Hoffman GS, Khalidi NA, Koening CL, Langford CA, McAlear CA, **Maksimowicz-Mckinnon K**, Monach PA, Seo P, Specks U, St Clair W, Stone J, Ytterberg SR, Edberg J, Merkel PA, and Bucala R. The role of macrophage migration inhibitory factor in the pathogenesis of granulomatosis with polyangiitis *Rheumatology* 2017; 56:118-119. PMID: Not assigned. Abstract

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Sleep Medicine

Herring WJ, Connor KM, Snyder E, Snavely DB, Zhang Y, Hutzelmann J, Matzura-Wolfe D, Benca RM, Krystal AD, Walsh JK, Lines C, **Roth T**, and Michelson D. Suvorexant in elderly patients with insomnia: Pooled analyses of data from phase III randomized controlled clinical trials *Am J Geriatr Psychiatry* 2017;PMID: 28427826. Full Text

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OBJECTIVE: Suvorexant is an orexin receptor antagonist approved for treating insomnia at doses of 10-20 mg. Previously reported phase III results showed that suvorexant was effective and well-tolerated in a combined-age population (elderly and nonelderly adults). The present analysis evaluated the clinical profile of suvorexant specifically in the elderly. METHODS: Prespecified subgroup analyses of pooled 3-month data from two (efficacy) and three (safety) randomized, double-blind, placebo-controlled, parallel-group trials. In each trial, elderly (>/=65 years) patients with insomnia were randomized to suvorexant 30 mg, suvorexant 15 mg, and placebo. By design, fewer patients were randomized to 15 mg. Patient-reported and polysomnographic (subset of patients) sleep maintenance and onset endpoints were measured. RESULTS: Suvorexant 30 mg (N = 319) was effective compared with placebo (N = 318) on patient-reported and polysomnographic sleep maintenance, and onset endpoints at Night 1 (polysomnographic endpoints)/Week 1 (patient-reported endpoints), Month 1, and Month 3. Suvorexant 15 mg (N = 202 treated) was also effective across these measures, although the onset effect was less evident at later time points. The percentages of patients discontinuing because of adverse events over 3 months were 6.4% for 30 mg (N

= 627 treated), 3.5% for 15 mg (N = 202 treated), and 5.5% for placebo (N = 469 treated). Somnolence was the most common adverse event (8.8% for 30 mg, 5.4% for 15 mg, 3.2% for placebo). CONCLUSION: Suvorexant generally improved sleep maintenance and onset over 3 months of nightly treatment and was well-tolerated in elderly patients with insomnia (clinicaltrials.gov; NCT01097616, NCT01097629, NCT01021813).

Sleep Medicine
Roehrs TA, and **Roth T**. Increasing presurgery sleep reduces postsurgery pain and analgesic use following joint replacement: a feasibility study *Sleep Med* 2017; 33:109-113. PMID: 28449888. Full Text

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STUDY OBJECTIVES: To determine whether presurgery sleep extension in short-sleeping volunteers scheduled for total knee/hip replacement surgery would reduce postsurgery pain and analgesic use. METHODS: Eighteen short sleepers, defined by sleep times below the national mean (ie, </=7 h) nightly, were randomized to one week of a 2-h nightly extension of their time in bed (EXT) or maintenance of their habitual time in bed (HAB) prior to knee or hip replacement surgery. Compliance was monitored by wrist actigraphy. Outcomes were the postsurgery daily dose of opiates (converted to morphine milligram equivalents) and the daily pain ratings (acquired 3-4 times across the day) on a 0-10 rating scale (0 = no pain to 10 = worst pain experienced) over the three to four day inpatient recovery. RESULTS: On a diary before the presurgery time in bed (TIB) manipulation, there were no significant differences in reported nightly sleep times between those randomized to the EXT group [6.0 (+/-0.78) h] and the HAB group [6.5 (+/-0.50) h]. During the one-week presurgery TIB manipulation, three participants failed to extend their TIB. Among those extending TIB (n = 7), compared to the HAB group, the EXT group spent significantly more nightly TIB (8.0 vs. 6.9 h, $p < 0.05$), which resulted in 1 h of more sleep (6.8 vs. 5.8 h, $p < 0.04$). On the three- to four-day postsurgery inpatient recovery, the EXT group reported significantly less average daily pain (4.4 vs. 5.6, $p < 0.04$) and less daily morphine milligram equivalent intake (20.3 vs. 38.6 mg, $p < 0.02$) than those by the HAB group. CONCLUSIONS: In this feasibility study, we found that a presurgery extended TIB and associated increase in sleep time in short-sleeping patients scheduled for undergoing joint replacement results in reduced postsurgery pain ratings and opiate use.

Sleep Medicine
Roth T, Black J, Cluydts R, Charef P, Cavallaro M, Kramer F, Zammit G, and Walsh J. Dual orexin receptor antagonist, almorexant, in elderly patients with primary insomnia: A randomized, controlled study *Sleep* 2017; 40(2):8. PMID: 28364509. Full Text

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Objective: Sleep laboratory study to determine the dose-related efficacy and safety of almorexant in elderly patients with primary chronic insomnia. Methods: Patients aged >= 65 years with primary insomnia were enrolled into a prospective, randomized, double-blind, placebo-controlled, multicenter dose-finding study with a five-period, five-way Latin square cross-over design. Patients were randomized to one of 10 unique sequences of two-night treatment with oral almorexant 25, 50, 100, or 200 mg capsules, or matching placebo. The primary efficacy endpoint was polysomnography (PSG)-determined mean wake time after sleep onset (WASO). Secondary and exploratory efficacy endpoints were also assessed. Results: 112 patients were randomized (mean [SD] age 72.1 [5.0] years; 69.9% female). Significant, dose-related improvements (reductions) in mean WASO were observed with almorexant. Least-squares mean (95% CI) treatment effects in the almorexant 200, 100, 50, and 25 mg dose groups versus placebo were -46.5 minutes (-53.0, -39.9; p<.0001), -31.4 minutes (-38.0, -24.9; p<.0001), -19.2 minutes (-25.7, -12.6; p<.0001), and -10.4 minutes (-17.0, -3.9; p =.0018), respectively. Mean total sleep time was significantly increased with each almorexant dose (mean increases versus placebo ranged 55.1-14.3 minutes; p <.0001 for each dose). Latency to persistent sleep was statistically significantly reduced only with almorexant 200 mg versus placebo (mean [95% CI] treatment effect -10.2 minutes, [-15.4, -5.0]; p=.0001). No unexpected safety concerns were identified.

Adverse events were similar between all almorexant dose groups and placebo. Conclusions: Two-night oral administration of almorexant was effective and well tolerated in treating primary insomnia in elderly patients.

Surgery

DeMeireles A, Cassidy R, Ross R, Stricklen A, **Carlin AM**, Finks JF, and Ghaferi AA. Variation in psychological well-being and body image in patients before and after bariatric surgery *Surgical Endoscopy and Other Interventional Techniques* 2017; 31:S7. PMID: Not assigned. Abstract

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Introduction: Massive weight loss with bariatric surgery has the potential to improve body image and psychological well-being. However, traditional instruments used to measure health related quality of life (HRQL) have not been tailored to bariatric patients. Therefore, we sought to utilize a new patient-reported outcome (PRO) instrument to assess psychological well-being and satisfaction with body image before and after bariatric surgery. Methods: We administered the Body-Q survey to two cohorts of patients in the Michigan Bariatric Surgery Collaborative (MBSC)\-pre-bariatric surgery (n=287) and one-year post-bariatric surgery (n=1669). The Body-Q is a patient-reported outcome instrument designed to measure patient perceptions of weight loss. It has been validated in large populations of patients who have undergone bariatric surgery or body contouring procedures to assess PROs in this subset of patients. We linked the survey data to prospectively collected data from the MBSC to assess associations between body image/psychological well-being and clinical characteristics and outcomes such as age, gender, race, income, marital status, BMI, percent excess body weight loss (% EBWL), and comorbidity burden. Results: Higher preoperative body image scores were associated with black race only ($p<0.01$). Higher preoperative psychological well-being scores were associated with male gender ($p<0.001$) and black race ($p<0.010$. There was no association with BMI or other demographic factors in the preoperative setting. Postoperative body image was positively (ie, higher scores) associated with male gender ($p<0.001$), lower BMI ($p<0.0001$), and higher mean %EBWL ($p<0.0001$). Postoperative psychological well-being was positively associated with male gender ($p<0.001$), black race ($p<0.01$), lower BMI ($p<0.01$), and higher mean %EBWL ($p<0.0001$). When patients were divided into terciles by their body image and psychological well-being scores, the mean %EBWL in the highest scoring terciles were 65.7% and 63.4%, respectively, as compared to 51.9% and 56.2% in the lowest terciles, repectively. Conclusions: There are large variations in psychological and body image outcomes in patients both before and after bariatric surgery. Recognition of these differences and factors contributing to lower reported levels of psychological well-being and body image may help providers provide appropriate counseling in the perioperative period.

Surgery

Gaye MM, Ding T, Shion H, Hussein A, Hu Y, Zhou S, **Hammoud ZT**, Lavine BK, Mechref Y, Gebler JC, and Clemmer DE. Delineation of disease phenotypes associated with esophageal adenocarcinoma by MALDI-IMS-MS analysis of serum N-linked glycans *Analyst* 2017;PMID: 28367546. Article Request Form

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N-Linked glycans, extracted from patient sera and healthy control individuals, are analyzed by Matrix-assisted laser desorption ionization (MALDI) in combination with ion mobility spectrometry (IMS), mass spectrometry (MS) and pattern recognition methods. MALDI-IMS-MS data were collected in duplicate for 58 serum samples obtained from individuals diagnosed with Barrett's esophagus (BE, 14 patients), high-grade dysplasia (HGD, 7 patients), esophageal adenocarcinoma (EAC, 20 patients) and disease-free control (NC, 17 individuals). A combined mobility distribution of 9 N-linked glycans is established for 90 MALDI-IMS-MS spectra (training set) and analyzed using a genetic algorithm for feature selection and classification. Two models for phenotype delineation are subsequently developed and as a result, the four phenotypes (BE, HGD, EAC and NC) are unequivocally differentiated. Next, the two models are tested against 26 blind measurements. Interestingly, these models allowed for the correct phenotype prediction of as many as 20 blinds. Although applied to a limited number of blind samples, this methodology appears promising as a means of discovering molecules from serum that may have capabilities as markers of disease.

Surgery
Grossman PM, Ali SS, Aronow HD, Boros M, **Nypaver TJ**, Schreiber TL, Park YJ, Henke PK, and Gurm HS. Contrast-induced nephropathy in patients undergoing endovascular peripheral vascular intervention: Incidence, risk factors, and outcomes as observed in the Blue Cross Blue Shield of Michigan Cardiovascular Consortium *J Interv Cardiol* 2017;PMID: 28370487. Full Text

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BACKGROUND: The incidence, risk factors, and outcomes associated with Contrast-induced nephropathy (CIN) after Percutaneous Vascular Intervention (PVI) in contemporary medical practice are largely unknown. METHODS: A total of 13 126 patients undergoing PVI were included in the analysis. CIN was defined as an increase in serum creatinine from pre-PVI baseline to post-PVI peak Cr of >/=0.5 mg/dL. RESULTS: CIN occurred in 3% (400 patients) of the cohort, and 26 patients (6.5%) required dialysis. Independent predictors of CIN were high and low body weight, diabetes, heart failure, anemia, baseline renal dysfunction, critical limb ischemia, and a higher acuity of the PVI procedure and a contrast dose that was greater than three times the calculated creatinine clearance (CCC) (adjusted OR 1.4, 95% CI: 1.1-1.8, P = 0.003). CIN was strongly associated with adverse outcome including in-hospital death (adjusted OR 18.1, CI 10.7-30.6, P < 0.001), myocardial infarction (adjusted OR 16.2, CI 8.9-29.5, P < 0.001), transient ischemic attack/stroke (adjusted OR 5.5, CI 3.2-14.9, P = 0.001), vascular access complications (adjusted OR 3.4, CI 2.3-5, P < 0.001), and transfusion (adjusted OR 7, CI 5.4-9, P < 0.001). Hospital stay was longer in patients who developed CIN versus those who did not. CONCLUSIONS: CIN is not an uncommon complication associated with PVI, can be reliably predicted from pre-procedural variables, including a contrast dose of greater than three times the CCC and is strongly associated with the risk of in-hospital death, MI, stroke, transfusion, and increased hospital length of stay.

Surgery
Patel P. Emergency surgery in patients with prior mesh *Hernia* 2017; 21(1):S63. PMID: Not assigned. Abstract

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The use of prosthetics in hernia repair is increasingly common. As this population ages, so does the incidence of emergency abdominal surgery. The fate of the mesh at the time of reoperation can be difficult to determine. The decision of mesh removal, wound closure, and use of antibiotics is determined by a multitude of factors such as: the type of mesh used, mesh location, degree of contamination, adhesiolysis and the reason for reoperation. We will discuss these factors and their impact on intra-operative decision making.

Surgery
Takahashi K, **Go P**, **Stone CH**, **Safwan M**, **Putchakayala KG**, **Kane WJ**, **Malinzak LE**, **Kim DY**, and **Denny JE**. Mycophenolate mofetil and pulmonary fibrosis after kidney transplantation: A case report *Am J Case Rep* 2017; 18:399-404. PMID: 28408734. Full Text

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BACKGROUND Mycophenolate mofetil (MMF) induced lung disease has been described in only a few isolated reports. We report a case of fatal respiratory failure associated with MMF after kidney transplantation. CASE REPORT A 50-year-old Hispanic male with a history of end-stage renal disease secondary to hypertension underwent deceased donor kidney transplantation. His preoperative evaluations were normal except for a chest x-ray which showed bilateral interstitial opacities. Tacrolimus and MMF were started on the day of surgery. His postoperative course was uneventful and he was discharged on postoperative day 5. One month later, he presented with shortness of breath and a cough with blood-tinged sputum. His respiratory condition deteriorated rapidly, requiring intubation. Chest computer tomography (CT) demonstrated patchy ground-glass opacities with interlobular septal thickening. Comprehensive pulmonary, cardiac, infectious, and immunological evaluations were all negative. Open lung biopsy revealed extensive pulmonary fibrosis with no evidence of infection. He temporarily improved after discontinuation of tacrolimus and MMF, however, on resuming MMF his respiratory status deteriorated again and he

subsequently died from hypoxic respiratory failure. CONCLUSIONS An awareness of pulmonary lung disease due to MMF is important to prevent adverse outcomes after organ transplantation. MMF must be used with utmost care in recipients with underlying lung disease as their pulmonary condition might make them more susceptible to any harmful effects of MMF.

Surgery

Vuyyuru S, and **Kharbutli B**. Epidermoid cyst of the spleen, a case report *Int J Surg Case Rep* 2017; 35:57-59. PMID: 28441587. Full Text

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INTRODUCTION: Splenic tumors are rare and are either primary or secondary, benign or malignant. Most have none to minimal symptomatology and are found incidentally. Splenic cysts can be infectious, congenital, or traumatic. Epidermoid cysts and parasitic cysts are examples of primary cysts and usually have a classic presentation on imaging. Despite advanced imaging modalities and patient's clinical presentation, it can be difficult to diagnose an epidermoid cyst without histological examination. The purpose of this paper is to discuss typical findings of primary splenic cysts on imaging, but how they may differ in appearance. PRESENTATION OF CASE: 51 year old female who presented with vague abdominal discomfort and was found to have a large splenic mass with cystic components on imaging which did not demonstrate a typical primary splenic cyst appearance. Patient underwent an uneventful hand-assisted laparoscopic total splenectomy and had an uneventful recovery with histopathology revealing an epidermoid splenic cyst. CONCLUSION: Primary splenic cysts are difficult to diagnose and differentiate with imaging alone. They have a variable presentation and can present like as a cystic mass. It is important to include them in the differential diagnosis of splenic masses since histopathology is the final determinant of the diagnosis.

Urology

Alanee SR, Shah S, Zabor EC, Vijai J, Ostrovnaya I, Garcia-Grossman IR, Pendse DV, Littman J, Regazzi AM, Offit K, and Bajorin DF. Evaluating the association of multiple single nucleotide polymorphisms with response to gemcitabine and platinum combination chemotherapy in urothelial carcinoma of the bladder *Int J Clin Pharmacol Ther* 2017; 55(3):203-209. PMID: 28177276. Article Request Form

OBJECTIVE: To examine germline single nucleotide polymorphisms (SNPs) as markers of response to gemcitabine platinum (GP) combination chemotherapy in urothelial carcinoma (UC). METHODS: Saliva or blood was prospectively collected from 216 patients treated with GP for UC of the bladder between 1991 and 2011. Based on reported associations with gemcitabine and cisplatin response or putative mechanisms of gemcitabine or cisplatin/carboplatin activity, we selected SNPs of interest and were able to genotype 59 SNPs (using the SequenomMass ARRAYiPLEX platform) in 261 patients randomly split 2/3 into a training set (n = 174) and 1/3 into a test set (n = 87). Logistic regression was used to test the association between response to GP and SNPs. RESULTS: The median age at diagnosis was 64 years (range: 28 - 85) for the discovery set and 67 years (range: 30 - 84) for the validation set. Males composed 76% and 69%, and white non-Hispanics composed 88% and 91% of the training and test validation sets, respectively. Three SNPs on GALNTL4 (rs7937567, rs12278731, and rs9988868) and one intergenic SNP (rs1321391) were significantly associated with response to GP in the training set and were used to build a SNP score. However, when assessed in the test set, the SNP score was not significantly associated with response. CONCLUSION: Multiple SNPs selected from previous studies failed to predict response to GP in this cohort. Larger studies capable of accounting for population-based allele frequency heterogeneity may be required for replication of genetic alterations important to pharmacogenomics..

Urology

Leow JJ, Leong EK, Serrell EC, Chang SL, Gruen RL, Siang Png K, Beaule LT, Trinh QD, **Menon MM**, and Sammon JD. Systematic review of the volume-outcome relationship for radical prostatectomy: A 2017 update *Eur Urol Focus* 2017;PMID: Not assigned. Full Text

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Context: Radical prostatectomy (RP) is one of the most complex urological procedures performed. Higher surgical volume has been found previously to be associated with better patient outcomes and reduced costs to the health care

system. This has resulted in some regionalization of care toward high-volume facilities and providers; however, the preponderance of RPs is still performed at low-volume institutions. Objective: To provide an updated systematic review of the association of hospital and surgeon volume on patient and system outcomes after RP, including robot-assisted RP. Evidence acquisition: A systematic review of literature was undertaken, searching PubMed (1959-2016) for original articles. Selection criteria included RP, hospital and/or surgeon volumes as predictor variables, categorization of hospital and/or surgeon volumes, and measurable end points. Evidence synthesis: Overall 49 publications fulfilled the inclusion criteria. Most of the studies demonstrated that higher-volume surgeries are associated with better outcomes including reduced mortality, morbidity, postoperative complications, length of stay, readmission, and cost-associated factors. The volume-outcome relationship is maintained in robotic surgery. Eleven studies assessed hospital and surgeon volume simultaneously, and findings reflect that neither is an independent predictor variable affecting outcomes. The studies varied in how volume cutoffs were categorized as well as how the volume-outcome relationship was methodologically evaluated. Conclusions: Contemporary evidence continues to support the relationship between high-volume surgeries with improved RP outcomes. Recent studies demonstrate that the volume-outcome relationship applies to robot-assisted RP and may be applied for potential cost savings in health care. An increase in the number of international studies suggests reproducibility of the association. Although regionalization of surgical care remains a contentious issue, there is an increasing body of evidence that short-term outcomes are improved at high-volume centers for RP. Patient summary: This systematic review of the latest literature found that higher surgical volume was associated with improved outcomes for radical prostatectomy. Contemporary evidence continues to support the relationship between high-volume surgeries with improved radical prostatectomy outcomes. Recent studies demonstrate that the volume-outcome relationship applies to robot-assisted radical prostatectomy and may be applied for potential cost savings in health care.

Urology

Leyh-Bannurah SR, Gazdovich S, Budaus L, Zaffuto E, Briganti A, **Abdollah F**, Montorsi F, Schiffmann J, **Menon M**, Shariat SF, Fisch M, Chun F, Steuber T, Huland H, Graefen M, and Karakiewicz PI. Local therapy improves survival in metastatic prostate cancer *Eur Urol* 2017;PMID: 28385454. Full Text

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BACKGROUND: Treatment of the primary, termed local therapy (LT), may improve survival in metastatic prostate cancer (mPCa) versus no local therapy (NLT). OBJECTIVE: To assess cancer-specific mortality (CSM) after LT versus NLT in mPCa. DESIGN, SETTING, AND PARTICIPANTS: Within the Surveillance, Epidemiology and End Results database (2004-2013), 13 692 mPCa patients were treated with LT (radical prostatectomy [RP] or radiation therapy [RT]) or NLT. OUTCOME MEASUREMENTS AND STATISTICAL ANALYSIS: Multivariable competing risk regression analyses (MVA CRR) tested CSM after propensity score matching (PSM) in two analyses, (1) NLT versus LT and (2) RP versus RT, and were complemented with interaction, sensitivity, unmeasured confounder, and landmark analyses. RESULTS AND LIMITATIONS: Of 13 692 mPCa patients, 474 received LT: 313 underwent RP and 161 RT. In MVA CRR, after PSM, LT (n=474) results in lower CSM (subhazard ratio [SHR] 0.40, 95% confidence interval [CI] 0.32-0.50) versus NLT (n=1896). In MVA CRR after PSM, RP (n=161) results in lower CSM (SHR 0.59, 95% CI 0.35-0.99) versus RT (n=161). Invariably, lowest CSM rates were recorded for Gleason </=7, </=cT3, and M1a substage. Interaction and sensitivity analyses confirmed the robustness of results, and landmark analyses rejected the bias favouring LT. A strong unmeasured confounder (HR=5), affecting 30% of NLT patients, could obliterate LT benefit. Data were retrospective. CONCLUSIONS: In mPCa, LT results in lower mortality relative to

NLT. Within LT, lower mortality is recorded after RP than RT. Patients with most favourable grade, local stage, and metastatic substage derive most benefit from LT. They also derive most benefit from RP, when LT types are compared (RP vs RT). It is important to consider study limitations until ongoing clinical trials confirm the proposed benefits. PATIENT SUMMARY: Individuals with prostate cancer that spreads outside of the prostate might still benefit from prostate-directed treatments, such as radiation or surgery, in addition to receiving androgen deprivation therapy.

Urology
Seisen T, Sun M, Lipsitz SR, **Abdollah F**, Leow JJ, **Menon M**, Preston MA, Harshman LC, Kibel AS, Nguyen PL, Bellmunt J, Choueiri TK, and Trinh QD. Comparative effectiveness of trimodal therapy versus radical cystectomy for localized muscle-invasive urothelial carcinoma of the bladder *Eur Urol* 2017;PMID: 28412065. Full Text

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Given the lack of randomized evidence comparing trimodal therapy (TMT) to radical cystectomy (RC) for muscle-invasive urothelial carcinoma of the bladder (UCB), we performed an observational cohort study to examine the comparative effectiveness of these two definitive treatments. Within the National Cancer Data Base (2004-2011),we identified 1257 (9.8%) and 11 586 (90.2%) patients who received TMT and RC, respectively. Inverse probability of treatment weighting (IPTW)-adjusted Kaplan-Meier analysis showed that median overall survival (OS) was similar between the TMT (40 mo, 95% confidence interval [CI] 34-46) and RC groups (43 mo 95% CI 41-45; p=0.3). In IPTW-adjusted Cox regression analysis with a time-varying covariate, TMT was associated with a significant adverse impact on long-term OS (hazard ratio 1.37, 95% CI 1.16-1.59; p<0.001). Interaction terms indicated that the adverse treatment effect of TMT versus RC decreased with age (p=0.004), while there was no significant interaction with gender (p=0.6), Charlson comorbidity index (p=0.09) or cT stage (p=0.8). In conclusion, we found that TMT was generally associated with worse long-term OS compared to RC for muscle-invasive UCB. However, the survival benefit of RC should be weighed against the risks of surgery, especially in older patients. These results are preliminary and emphasize the need for a randomized controlled trial to compare TMT versus RC. PATIENT SUMMARY: We examined the comparative effectiveness of trimodal therapy versus radical cystectomy for muscle-invasive urothelial carcinoma of the bladder. We found that trimodal therapy was generally associated with worse long-term overall survival, although there may be no difference with radical cystectomy in older individuals.

Urology
Sood A, and **Abdollah F**. Re: Diagnostic accuracy of multi-parametric magnetic resonance imaging and transrectal ultrasound biopsy in prostate cancer (promis): A paired validating confirmatory study *Eur Urol* 2017;PMID: 28412064. Full Text

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Urology
Thamilselvan V, **Menon M**, Stein GS, **Valeriote F**, and **Thamilselvan S**. Combination of carmustine and selenite Inhibits EGFR mediated growth signaling in androgen-independent prostate cancer cells *J Cell Biochem* 2017;PMID: 28430389. Full Text

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Although aberrant androgen receptor (AR) signaling is a central mechanism for castration resistant prostate cancer (CRPC) progression, AR-independent survival and growth signaling is also present in CRPC. The current therapeutic options for patients with CRPC are limited and new drugs are desperately needed to eliminate these crucial growth signaling pathways. Overexpression of EGFR in CRPC primarily mediates the proliferation of androgen-independent

prostate cancer (AIPC) cells. We have previously shown that combination of carmustine and selenite effectively induces apoptosis and growth inhibition by targeting AR and AR-variants in castration resistant prostate cancer cells. In this study, we investigated whether the combination of carmustine and selenite could inhibit EGFR mediated growth signaling and induce apoptosis in AIPC cells. EGF exposure dose and time dependently increased phospho-EGFR (Tyr845, Tyr1068, and Tyr1045), pAkt (Ser473), and pERK1/2 (Thr204/Tyr202) protein expression levels in AIPC cells. Combination of carmustine and selenite treatment markedly suppressed EGF-stimulated proliferation and survival of AIPC cells and effectively induced apoptosis. The ROS generated by the combination of carmustine and selenite exhibited a strong inhibitory on EGF stimulated EGFR and its downstream signaling molecules such as Akt/NF-kB and ERK1/2/Cyclin D1. Individual agent treatment showed only partial effect. Overall, our findings demonstrated that the combination of carmustine and selenite treatment substantially inhibits EGFR signaling, proliferation and induces apoptosis in AIPC cells. The results of the study further indicate that combination of carmustine and selenite can overcome the obstacles of EGFR mediated AR-independent growth response in castration resistant prostate cancer.