



## Henry Ford Health System Publication List – December 2020

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, and Web of Science during the month, and then imported into EndNote for formatting. There are **99 unique citations** listed this month, with **8 articles on COVID-19**. Articles are listed first, followed by conference abstracts, books and book chapters, and a bibliography of publications on COVID-19. 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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#### **Articles**

#### Allergy and Immunology

Choi T, Devries M, Bacharier L, Busse W, Camargo CA, Jr., Cohen R, Demuri GP, Evans MD, Fitzpatrick AM, Gergen PJ, Grindle K, Gruchalla R, Hartert T, Hasegawa K, Khurana Hershey GK, Holt P, Homil K, Jartti T, Kattan M, Kercsmar C, **Kim H**, Laing IA, LeBeau P, Lee KE, Le Souëf PN, Liu A, Mauger DT, Ober C, Pappas T, Patel SJ, Phipatanakul W, Pongracic J, Seroogy C, Sly PD, Tisler C, Wald ER, Wood R, Gangnon R, Jackson DJ, Lemanske RF, Jr., Gern JE, and Bochkov YA. Enhanced Neutralizing Antibody Responses to Rhinovirus C and Age-Dependent Patterns of Infection. *Am J Respir Crit Care Med* 2020. PMID: 33357024. Full Text

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RATIONALE: Rhinovirus C (RV-C) can cause asymptomatic infection and respiratory illnesses ranging from the common cold to severe wheezing. OBJECTIVES: To identify how age and other individual-level factors are associated with susceptibility to RV-C illnesses. METHODS: Longitudinal data from the Childhood Origins of ASThma (COAST) birth cohort study were analyzed to determine relationships between age and RV-C infections. Neutralizing antibodies specific for rhinovirus A (RV-A) and RV-C (3 types each) were determined using a novel polymerase chain reaction-based assay. We pooled data from 14 study cohorts in the United States, Finland, and Australia and used mixed-effects logistic regression to identify factors related to the proportion of RV-C versus RV-A detection. MEASUREMENTS AND MAIN RESULTS: In COAST, RV-A and RV-C infections were similarly common in infancy, while RV-C was detected much less often than RV-A during both respiratory illnesses and scheduled surveillance visits (p<0.001, chi-square) in older children. The prevalence of neutralizing antibodies to RV-A or RV-C types was low (5%-27%) at age 2 years, but by age 16, RV-C seropositivity was more prevalent (78% vs. 18% for RV-A, p<0.0001). In the pooled analysis, the RV-C to RV-A detection ratio during illnesses was significantly related to age (p<0.0001), CDHR3 genotype (p<0.05), and wheezing illnesses (p<0.05). Furthermore, certain RV types (e.g., C2, C11, A78, A12) were consistently more virulent and prevalent over time. DISCUSSION: Knowledge of prevalent RV types, antibody responses, and populations at risk based on age and genetics may guide the development of vaccines or other novel therapies against this important respiratory pathogen.

## Behavioral Health Services/Psychiatry

**Chawa MS**, **Yeh HH**, **Gautam M**, **Thakrar A**, **Akinyemi EO**, and **Ahmedani BK**. The Impact of Socioeconomic Status, Race/Ethnicity, and Patient Perceptions on Medication Adherence in Depression Treatment. *Prim Care Companion CNS Disord* 2020; 22(6). PMID: 33306887. Request Article

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OBJECTIVE: Nonadherence to pharmacotherapy for psychiatric conditions is associated with poor outcomes, including increased risk of relapse, increased health care costs, and reduced quality of life. The objective of this study was to investigate the strength of association between socioeconomic factors, race/ethnicity, and patient perceptions with medication adherence in individuals with depression. METHODS: Baseline surveys were sent out in 2012 to 4,216 adult patients within a large health system who presented with a clinical diagnosis of major depressive disorder (ICD-9), recorded at least twice in the electronic medical record in the year 2011. A total of 1,573 patients responded to the baseline survey. Of those, 1,209 patients who completed the survey and had used antidepressants in the last 12 months

were recruited for the study. Perception of medication risk was assessed using the Beliefs About Medicines Questionnaire, and adherence to medications was assessed using the Morisky Medication Adherence Scale, Logistic regression was used to investigate the relationship between perception of medicine risk and treatment adherence. RESULTS: For non-Hispanic white individuals, medication adherence was higher among those who were least concerned about the risk of medications (64%: 95% CI, 58-70) compared to those who were most concerned (34%; 95% CI, 26-43). In the logistic regression model, less concern about medications and their side effects was associated with higher medication adherence (odds ratio = 2.6; 95% CI, 1.77-3.84; P < .0001). This association remained significant after adjustment for age, race, education level, and extramedical use of other medications or substances. Moreover, patients with older age and lower education level as well as those who were non-Hispanic white and had no extramedical use of other medications/substances were more likely to be adherent to medications. CONCLUSIONS: This study contributes quantitative data on factors that impact treatment adherence. Identifying patients at increased risk of nonadherence, having discussions with patients early in the treatment process to understand their concerns regarding treatment options, being sensitive to cultural beliefs, and patiently proceeding with the decision-making process could help ensure better outcomes.

# Behavioral Health Services/Psychiatry

Gritti ES, Meyer GJ, Bornstein RF, Marino DP, and **Marco JD**. Narcissism and Reactions to a Self-Esteem Insult: An Experiment Using Predictions from Self-Report and the Rorschach Task. *J Pers Assess* 2020:1-40. PMID: 33270469. Request Article

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We used self-reported narcissistic grandiosity and vulnerability and a component derived from 11 potential grandiosity and narcissism variables (GNVs) coded from Rorschach behavior to predict fluctuations in self-esteem and their links to anger and defensive reactions. We assessed state mood, state self-esteem, and performance attributions in 105 college students who underwent a self-esteem manipulation involving success followed by failure on cognitive testing. Self-reported grandiosity predicted the disavowal of effortful ability as a factor in failure, but we did not replicate other previously reported findings for this variable. Self-reported vulnerability predicted oscillations in self-reported mood and self-esteem. The GNV scale predicted spontaneously expressed hostility and externalization following self-esteem insult, and attributions mediated its relationship with anger expressed after failure. We discuss implications of these results and recommend additional replication research.

### Cardiology/Cardiovascular Research

Abedini NC, Guo G, Hummel SL, Bozaan D, Beasley M, **Cowger J**, and Chopra V. Factors influencing palliative care referral for hospitalised patients with heart failure: an exploratory, randomised, multi-institutional survey of hospitalists and cardiologists. *BMJ Open* 2020; 10(12):e040857. PMID: 33323440. Full Text

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OBJECTIVE: To identify factors influencing cardiologists' and hospitalists' decisions regarding palliative care referral among hospitalised patients with advanced heart failure. DESIGN: An exploratory. randomised vignette-based survey. SETTING: Cardiology and hospitalist divisions at three Michigan State institutions and the Society of Hospital Medicine's Michigan Chapter. PARTICIPANTS: 145 hospitalists and 64 cardiologists, OUTCOME MEASURES: Primary outcomes included participants' reports of their likelihood of referring a standardised patient with an acute heart failure exacerbation with multiple prior hospital admissions and acute renal failure to palliative care (scale of 0%-100%) after the initial stem and after being cued with three randomised vignette modifiers, including the presence versus the absence of continuity with an outpatient cardiologist; the presence versus the absence of documented advance care planning; and the patient voicing that he is accepting of his severe illness versus wanting everything done. Adjusted generalised linear models and predictive margins were used to evaluate the impact of each randomised modifier on referral decisions. An interaction term evaluated the effect of provider specialty on outcomes. Secondary outcomes included participants' reports of their general practices around palliative care delivery to hospitalised patients with heart failure. RESULTS: Response rate was 31.3%. Predictive margins from generalised linear models demonstrated a statistically significantly higher likelihood of referral to inpatient palliative care if the patient lacked an outpatient cardiologist (mean difference: 6.3% (95% CI 1.8% to 10.8%)); had prior advance care planning documentation (mean difference: 9.7% (95% CI 4.4% to 15.0%)); and was accepting of illness severity (mean difference: 29.6% (95% CI 24.8% to 34.4%)). No interaction effect was noted based on provider specialty. Most hospitalists and cardiologists were unaware of palliative care guidelines for patients with heart failure (74.3% vs 70.3%, p=0.71). CONCLUSIONS: A number of patient and provider factors influence palliative care referral decisions in hospitalised patients with advanced heart failure.

### Cardiology/Cardiovascular Research

Blumer V, Greene SJ, Ortiz M, Kittipibul V, Hernandez GA, Fudim M, **Lemor A**, Mentz RJ, and Vest AR. In-hospital outcomes after bariatric surgery in patients with heart failure. *Am Heart J* 2020; 230:59-62. PMID: 32991845. Full Text

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Based on the largest publicly available all-payer inpatient database in the United States, this study sought to evaluate real-world outcomes after bariatric surgery among patients with heart failure.

# Cardiology/Cardiovascular Research

Goldsweig AM, Tak HJ, Alraies MC, Park J, Smith C, Baker J, Lin L, Patel N, **O'Neill WW**, and **Basir MB**. Mechanical circulatory support following out-of-hospital cardiac arrest: Insights from the National Cardiogenic Shock Initiative. *Cardiovasc Revasc Med* 2020. PMID: 33358390. Full Text

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BACKGROUND: Evidence is limited regarding the role of mechanical circulatory support (MCS) in patients with acute coronary syndromes (ACS) complicated by cardiogenic shock (CGS). In particular, the role of MCS in patients with out-of-hospital cardiac arrest (OHCA) is unknown. METHODS: The National Cardiogenic Shock Initiative (NCSI) is a multicenter United States registry of patients with ACS complicated by CGS treated with MCS. We compared the rate of survival to hospital discharge among patients with OHCA, in-hospital cardiac arrest (IHCA), or no cardiac arrest. We subsequently used multivariable analyses to determine independent predictors of OHCA survival. RESULTS: Survival to hospital discharge occurred in 85.7% (42/49) of OHCA, 72.4% (50/69) of IHCA, and 74.5% (111/149) of non-cardiac arrest patients. By multivariable analysis, pre-procedural predictors of survival included vounger age, female sex, fewer diseased vessels, left anterior descending coronary artery culprit, lower troponin, higher lactate, and delayed initiation of MCS. Procedural and post-procedural predictors of survival included fewer vessels treated, complete revascularization, higher post-MCS cardiac power output, and fewer inotropic medications required. CONCLUSIONS: This study demonstrates that excellent outcomes may be achieved following OHCA when MCS is employed for patients appropriately selected by prognostic demographic, anatomic, and health status characteristics. A larger study population, currently being enrolled, is needed to validate the observation further.

## Cardiology/Cardiovascular Research

Jain V, **Gupta K**, Bhatia K, Bansal A, Arora S, **Khandelwal AK**, Rosenberg JR, Levisay JP, Tommaso CL, Ricciardi MJ, and Qamar A. Management of STEMI during the COVID-19 pandemic: Lessons learned in 2020 to prepare for 2021. *Trends Cardiovasc Med* 2020. PMID: 33338636. Full Text

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As the prevalence of asymptomatic COVID-19 continues to increase, there is an increasing possibility that patients with COVID-19 may presen with ST-segment elevation myocardial infarction (STEMI). With social distancing and restricted access to preventive healthcare and emergency services, the management of acute cardiac emergencies such as myocardial infarction has suffered collateral damage. Thus far, global trends suggest a decrease in STEMI activations with possible worse outcomes due to delayed presentation and management. In this review, we discuss the challenges to STEMI management in the COVID-19 era and provide potential solutions for adherence to evidence-based therapies as the pandemic progresses into the year 2021.

### Cardiology/Cardiovascular Research

**McCord J**, Hana A, Cook B, Hudson MP, Miller J, Akoegbe G, Mueller C, Moyer M, Jacobsen G, and **Nowak R**. The Role of Cardiac Testing with the 0/1-Hour High-Sensitivity Cardiac Troponin Algorithm Evaluating for Acute Myocardial Infarction. *Am Heart J* 2020. PMID: 33373603. Full Text

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BACKGROUND: The role of cardiac testing in the 3 zones (rule-out, observation, and rule-in) of the 0/1-hour algorithm to evaluate for acute myocardial infarction (AMI) has not been well-studied. This study evaluated the 0/1-hour algorithm with a high-sensitivity cardiac troponin (hs-cTnI) assay and investigated cardiac testing in the 3 zones. METHODS: Patients (n = 552) at a single urban center were enrolled if they were evaluated for AMI. Blood samples were obtained at presentation, 1 hour, and 3 hours for hs-cTnI. Follow-up at 30-45 days for death/AMI was done. The results of echocardiograms, stress testing, and coronary angiography were recorded. RESULTS: In total, 45 (8.2%) had AMI (27 Type 1 and 18 Type 2) during the index hospitalization while at follow-up death/AMI occurred in 11 (2.0%) of patients. The rule-out algorithm had a negative predictive value for AMI of 99.6% while the rule-in zone had a positive predictive value of 56.6%. The MACE rate at follow-up was 0.4% for those in the rule-out group. There were 6/95 (6.3%) abnormal stress tests in the rule-out zone and 4 of these were false positives. CONCLUSIONS: The 0/1-hour algorithm had high diagnostic sensitivity and negative predictive value for AMI, and adverse events were very low in patients in the rule-out zone. Noninvasive testing in rule-out zone patients had low diagnostic yield.

## Cardiology/Cardiovascular Research

Sabbah HN, Zhang K, Gupta RC, Xu J, Singh-Gupta V, Ma M, Stauber K, Nguyen N, and Adams J. Intravenous Infusion of the  $\beta(3)$ -Adrenergic Receptor Antagonist APD418 Improves Left Ventricular Systolic Function in Dogs with Systolic Heart Failure:  $\beta(3)$ -Adrenergic Receptor Antagonist in Heart Failure. *J Card Fail* 2020. PMID: 33352205. Full Text

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BACKGROUND: Unlike β(1)- and β(2)-adrenergic receptors (ARs), β(3)-AR stimulation inhibits cardiac contractility and relaxation. In the failing left ventricular (LV) myocardium, β(3)-ARs are upregulated, and can be maladaptive in the setting of decompensation by contributing to LV dysfunction. This study examined the effects of intravenous (i.v.) infusions of the β(3)-AR antagonist APD418 on cardiovascular function and safety in dogs with systolic heart failure (HF). METHODS: Three separate studies were performed in 21 dogs with coronary microembolization-induced HF (LV ejection fraction, LVEF~35%). Studies 1 and 2 (n=7 dogs each) were APD418 dose-escalation studies (dosing range 0.35 to 15.0 mg/kg/hr) designed to identify an effective dose of APD418 to be used in study 3. Study 3, the sustained efficacy study, (n=7 dogs) was a 6-hour constant i.v. infusion of APD418 at a dose of 4.224 mg/kg (0.70 mg/kg/hr) measuring key hemodynamic endpoints (e.g. EF, CO, Ei/Ai). RESULTS: Study 1 and 2 showed a dose-dependent increase of LVEF and Ei/Ai, the latter being an index of LV diastolic function. In study 3, infusion of APD418 over 6 hours increased LVEF from 31±1% to 38±1% (p<0.05) and increased Ei/Ai from 3.4±0.4 to 4.9±0.5, (p<0.05). Vehicle had no effect on LVEF or Ei/Ai. In study 3, APD418 had no significant effects on HR or systemic blood pressure. CONCLUSIONS: Intravenous infusions of APD418 in dogs with systolic HF elicit significant positive inotropic and lusitropic effects. The findings support the development of APD418 for the in-hospital treatment of patients with acute exacerbation of chronic HF.

## Cardiology/Cardiovascular Research

Sandau KE, Lee CS, Faulkner KM, Pozehl B, Eckman P, Garberich R, Weaver CE, Joseph SM, Hall S, Carey SA, Chaudhry SP, Schroeder SE, Hoffman RO, 3rd, Feldman D, Birati EY, Soni M, Marble JF, Jurgens CY, Hoglund B, and **Cowger JA**. Health-Related Quality of Life in Patients With a Left Ventricular Assist Device (QOLVAD) Questionnaire: Initial Psychometrics of a New Instrument. *J Cardiovasc Nurs* 2020. PMID: 33306621. Full Text

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BACKGROUND: Patients with a left ventricular assist device are a unique and growing population who deserve their own valid, reliable instrument for health-related quality of life. OBJECTIVE: We developed and tested the Health-Related Quality of Life with a Left Ventricular Assist Device (QOLVAD) questionnaire. METHODS: In a prospective, descriptive study, patients from 7 sites completed the QOLVAD and comparator questionnaires. Construct validity was tested using confirmatory factor analysis. Convergent validity was tested using correlations of QOLVAD scores to well-established measures of subjective health status, depression, anxiety, and meaning/faith. Reliability and test-retest reliability were quantified. RESULTS: Patients (n = 213) were 58.7 ± 13.9 years old; 81.0% were male, 73.7% were White, and 48.0% had bridge to transplant. Questionnaires were completed at a median time of 44 weeks post ventricular assist device. The 5 QOLVAD domains had acceptable construct validity (root mean square error of approximation = 0.064, comparative and Tucker-Lewis fit indices > 0.90, weighted root mean square residual = 0.95). The total score and domain-specific scores were significantly correlated with the instruments to which they were compared. Internal consistency reliability was acceptable for all subscales ( $\alpha$  = .79-.83) except the cognitive domain ( $\alpha$  = .66). Unidimensional reliability for the total score was acceptable ( $\alpha$  = .93), as was factor determinacy for multidimensional reliability (0.95). Total test-retest reliability was 0.875 (P < .001). CONCLUSION: Our analysis provided initial support for validity and reliability of the QOLVAD for total score, physical, emotional, social, and meaning/spiritual domains. The QOLVAD has potential in research and clinical settings to guide decision making and referrals; further studies are needed.

# Cardiology/Cardiovascular Research

Tajti P, Xenogiannis I, Gargoulas F, Karmpaliotis D, **Alaswad K**, Jaffer FA, Patel MP, Burke MN, Garcia S, Krestyaninov O, Koutouzis M, Jaber W, and Brilakis ES. Technical and procedural outcomes of the retrograde approach to chronic total occlusion interventions. *EuroIntervention* 2020; 16(11):e891-e899. PMID: 31638578. Request Article

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AIMS: The retrograde approach is critical for achieving high success rates in chronic total occlusion (CTO) percutaneous coronary intervention (PCI), but has been associated with higher risk of complications. We examined the contemporary outcomes of the retrograde approach to CTO PCI aiming to identify areas in need of improvement. METHODS AND RESULTS: We compared the technical and procedural outcomes of retrograde (n=1,515) and antegrade-only CTO PCIs (n=2,686) in a contemporary multicentre CTO registry. The mean age of patients undergoing retrograde PCI was 65±10 years and 86% were men, with high prevalence of prior myocardial infarction (51%), prior PCI (71%), and coronary artery bypass graft surgery (45%). The mean J-CTO score (3±1 vs 2±1, p<0.001) was higher in retrograde PCIs. The most commonly used collateral channels were septals (65%), epicardials (32%). saphenous venous grafts (14%) and left internal mammary artery grafts (2%). Overall technical (79% vs 91%, p<0.001) and procedural (75% vs 90%, p<0.001) success rates were lower with the retrograde approach, and these patients had a higher rate of in-hospital major complications than antegrade-only PCI patients (5.1% vs 0.8%, p<0.001), due to higher mortality (1.1% vs 0.1%, p<0.001), acute myocardial infarction (1.9% vs 0.2%, p<0.001), repeat PCI (0.7% vs 0.1%, p=0.001), and pericardiocentesis (1.7% vs 0.3%, p<0.001). CONCLUSIONS: In summary, the retrograde approach to CTO PCI is performed in higher complexity lesions and is associated with lower success rates and a higher rate of major complications. CLINICAL TRIAL REGISTRATION: NCT02061436, Prospective Global Registry for the Study of Chronic Total Occlusion Intervention (PROGRESS-CTO).

### Center for Health Policy and Health Services Research

Chawa MS, Yeh HH, Gautam M, Thakrar A, Akinyemi EO, and Ahmedani BK. The Impact of Socioeconomic Status, Race/Ethnicity, and Patient Perceptions on Medication Adherence in Depression Treatment. *Prim Care Companion CNS Disord* 2020; 22(6). PMID: 33306887. Request Article

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OBJECTIVE: Nonadherence to pharmacotherapy for psychiatric conditions is associated with poor outcomes, including increased risk of relapse, increased health care costs, and reduced quality of life. The objective of this study was to investigate the strength of association between socioeconomic factors. race/ethnicity, and patient perceptions with medication adherence in individuals with depression. METHODS: Baseline surveys were sent out in 2012 to 4,216 adult patients within a large health system who presented with a clinical diagnosis of major depressive disorder (ICD-9), recorded at least twice in the electronic medical record in the year 2011. A total of 1,573 patients responded to the baseline survey. Of those, 1,209 patients who completed the survey and had used antidepressants in the last 12 months were recruited for the study. Perception of medication risk was assessed using the Beliefs About Medicines Questionnaire, and adherence to medications was assessed using the Morisky Medication Adherence Scale. Logistic regression was used to investigate the relationship between perception of medicine risk and treatment adherence. RESULTS: For non-Hispanic white individuals, medication adherence was higher among those who were least concerned about the risk of medications (64%: 95% CI, 58-70) compared to those who were most concerned (34%; 95% CI, 26-43). In the logistic regression model, less concern about medications and their side effects was associated with higher medication adherence (odds ratio = 2.6; 95% CI, 1.77-3.84; P < .0001). This association remained significant after adjustment for age, race, education level, and extramedical use of other medications or substances. Moreover, patients with older age and lower education level as well as those who were non-Hispanic white and had no extramedical use of other medications/substances were more likely to be adherent to medications. CONCLUSIONS: This study contributes quantitative data on factors that impact treatment adherence. Identifying patients at increased risk of nonadherence, having discussions with patients early in the treatment process to understand their concerns regarding treatment options, being sensitive to

cultural beliefs, and patiently proceeding with the decision-making process could help ensure better outcomes.

## Center for Health Policy and Health Services Research

Shashikumar SA, Waken RJ, Luke AA, **Nerenz DR**, and Joynt Maddox KE. Association of Stratification by Proportion of Patients Dually Enrolled in Medicare and Medicaid With Financial Penalties in the Hospital-Acquired Condition Reduction Program. *JAMA Intern Med* 2020. PMID: 33346779. <u>Full Text</u>

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IMPORTANCE: The Hospital-Acquired Condition Reduction Program (HACRP) is a value-based payment program focused on safety events. Prior studies have found that the program disproportionately penalizes safety-net hospitals, which may perform more poorly because of unmeasured severity of illness rather than lower quality. A similar program, the Hospital Readmissions Reduction Program, stratifies hospitals into 5 peer groups for evaluation based on the proportion of their patients dually enrolled in Medicare and Medicaid, but the effect of stratification on the HACRP is unknown. OBJECTIVE: To characterize the hospitals penalized by the HACRP and the distribution of financial penalties before and after stratification. DESIGN, SETTING, AND PARTICIPANTS: This economic evaluation used publicly available data on HACRP performance and penalties merged with hospital characteristics and cost reports. A total of 3102 hospitals participating in the HACRP in fiscal year 2020 (covering data from July 1, 2016, to December 31, 2018) were studied. EXPOSURES: Hospitals were divided into 5 groups based on the proportion of patients dually enrolled, and penalties were assigned to the lowest-performing quartile of hospitals in each group rather than the lowest-performing quartile overall. MAIN OUTCOMES AND MEASURES: Penalties in the prestratification vs poststratification schemes. RESULTS: The study identified 3102 hospitals evaluated by the HACRP. Safety-net hospitals received \$111 333 384 in penalties before stratification compared with an estimated \$79 087 744 after stratification-a savings of \$32 245 640. Hospitals less likely to receive penalties after stratification included safety-net hospitals (33.6% penaltized before stratification vs 24.8% after stratification,  $\Delta = -8.8$  percentage points [pp], P < .001), public hospitals  $(34.1\% \text{ vs } 30.5\%, \Delta = -3.6 \text{ pp. P} = .003)$ , hospitals in the West  $(26.8\% \text{ vs } 23.2\%, \Delta = -3.6 \text{ pp. P} < .001)$ . hospitals in Medicaid expansion states (27.3% vs 25.6%,  $\Delta = -1.7$  pp, P = .003), and hospitals caring for the most patients with disabilities (32.2% vs 28.3%,  $\Delta$  = -3.9 pp, P < .001) and from racial/ethnic minority backgrounds (35.1% vs 31.5%,  $\Delta$  = -3.6 pp, P < .001). In multivariate analyses, safety-net status and treating patients with highly medically complex conditions were associated with higher odds of moving from penalized to nonpenalized status. CONCLUSIONS AND RELEVANCE: This economic evaluation suggests that stratification of hospitals would be associated with a narrowing of disparities in penalties and a marked reduction in penalties for safety-net hospitals. Policy makers should consider adopting stratification for the HACRP.

## **Dermatology**

Buechler CR, **Veenstra J**, and **Gold LS**. Topical Therapies for Psoriasis in Phase 3 Trials. *Current Dermatology Reports* 2020; 9(4):331-338. Request Article

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Purpose of Review: This review will discuss new topical therapeutics for psoriasis that have undergone or published phase III trials in the last 5 years, as well as promising therapeutics in development. Recent Findings: New corticosteroid-only additions to the marketplace include formulations that improve absorption and ease-of-use, including betamethasone dipropionate (BD) 0.05% spray, halobetasol propionate (HP) 0.05% foam and 0.01% lotion, and clobetasol propionate 0.025% cream. Combination

therapies include BD 0.064% plus calcipotriene 0.005% (Cal/BD) foam, Cal/BD cream, and HP 0.01% plus tazarotene 0.045% lotion. New treatments are on the horizon, with trials nearing completion for topical phosphodiesterase-4 inhibitors and tapinarof, and trials being planned for turmeric, rose bengal disodium, JAK-inhibitors, and pegcantratinib. Summary: New therapeutic modalities can improve patient satisfaction and adherence, provide better control of disease, and improve quality of life. Thoughtful selection of the appropriate therapy from this growing arsenal will help improve patient care.

## Dermatology

**Friedman BJ**, **Robinson G**, and **Kohen L**. Dermoscopic Features of Spitz Tumor With LMNA-NTRK1 Fusion. *Dermatol Pract Concept* 2021; 11(1):e2020101. PMID: 33354405. Request Article

Department of Dermatology, Henry Ford Health System, Detroit, MI, USA. Department of Pathology and Laboratory Medicine, Henry Ford Health System, Detroit, MI, USA.

### Dermatology

**Fu C, Zhou L, Mi QS**, and **Jiang A**. Dc-based vaccines for cancer immunotherapy. *Vaccines* 2020; 8(4):1-16. Full Text

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As the sentinels of the immune system, dendritic cells (DCs) play a critical role in initiating and regulating antigen-specific immune responses. Cross-priming, a process that DCs activate CD8 T cells by crosspresenting exogenous antigens onto their MHCI (Major Histocompatibility Complex class I), plays a critical role in mediating CD8 T cell immunity as well as tolerance. Current DC vaccines have remained largely unsuccessful despite their ability to potentiate both effector and memory CD8 T cell responses. There are two major hurdles for the success of DC-based vaccines: tumor-mediated immunosuppression and the functional limitation of the commonly used monocyte-derived dendritic cells (MoDCs). Due to their resistance to tumor-mediated suppression as inert vesicles, DC-derived exosomes (DCexos) have garnered much interest as cell-free therapeutic agents. However, current DCexo clinical trials have shown limited clinical benefits and failed to generate antigen-specific T cell responses. Another exciting development is the use of naturally circulating DCs instead of in vitro cultured DCs, as clinical trials with both human blood cDC2s (type 2 conventional DCs) and plasmacytoid DCs (pDCs) have shown promising results, pDC vaccines were particularly encouraging, especially in light of promising data from a recent clinical trial using a human pDC cell line, despite pDCs being considered tolerogenic and playing a suppressive role in tumors. However, how pDCs generate anti-tumor CD8 T cell immunity remains poorly understood, thus hindering their clinical advance. Using a pDC-targeted vaccine model, we have recently reported that while pDC-targeted vaccines led to strong cross-priming and durable CD8 T cell immunity, cross-presenting pDCs required cDCs to achieve cross-priming in vivo by transferring antigens to cDCs. Antigen transfer from pDCs to bystander cDCs was mediated by pDC-derived exosomes (pDCexos), which similarly required cDCs for cross-priming of antigen-specific CD8 T cells. pDCexos thus represent a new addition in our arsenal of DC-based cancer vaccines that would potentially combine the advantage of pDCs and DCexos.

# <u>Dermatology</u>

**Lyons AB**, **Narla S**, **Torres AE**, **Parks-Miller A**, **Kohli I**, **Ozog DM**, **Lim HW**, and **Hamzavi IH**. Skin and eye protection against ultraviolet C from ultraviolet germicidal irradiation devices during the COVID-19 pandemic. *Int J Dermatol* 2020. PMID: 33259055. <u>Full Text</u>

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With the COVID-19 pandemic depleting personal protective equipment worldwide, various methods including ultraviolet C (UVC) germicidal irradiation (UVGI) have been implemented to decontaminate N95

filtering facepiece respirators. These devices pose a risk for UVC exposure to the operator with reported adverse effects generally limited to the eyes and skin. Our hospitals are currently using UVC devices for N95 decontamination with a few reported cases of face and neck erythema from exposure. Because sunscreens are designed and tested for UVA and UVB protection only, their effects on blocking UVC are largely unknown. Therefore, our objective was to determine if various sunscreens, UV goggles, and surgical mask face shields minimize UVC exposure from UVGI devices. Our study clearly demonstrated that healthcare workers responsible for the disinfection of PPE using UVGI devices should always at least utilize clear face shields or UV goggles and sunscreen to protect against side effects of UVC exposure.

#### Dermatology

Price KN, **Lyons AB**, **Hamzavi IH**, Hsiao JL, and Shi VY. Facilitating Clinical Trials Participation of Low Socioeconomic Status Patients. *Dermatology* 2020:1-4. PMID: 33321504. Full Text

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# **Dermatology**

Smith J, **Ezekwe N**, **Pourang A**, and **Hamzavi I**. Multifocal Myositis and Elevated CPK associated with the use of Ustekinumab for Hidradenitis Suppurativa. *Br J Dermatol* 2020. PMID: 33370450. <u>Full Text</u>

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ustekinumab (UST) is a human interleukin (IL)-12/IL-23 monoclonal antibody that has been approved by the Food and Drug Administration (FDA) to treat moderate to severe plaque psoriasis, psoriatic arthritis, and Crohn's disease. Off-label use of UST has shown promising results for hidradenitis suppurativa (HS) in patients that have failed therapy with adalimumab, the only FDA approved treatment for HS.

#### Dermatology

**Torres AE**, and **Lim HW**. Photobiomodulation for the management of hair loss. *Photodermatol Photoimmunol Photomed* 2020. PMID: 33377535. <u>Full Text</u>

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Photobiomodulation, otherwise known as low-level laser (or light) therapy, is an emerging modality for the management of hair loss. Several randomized trials have demonstrated that it is safe and potentially effective on its own or in combination with standard therapies. These devices come in many forms including wearable caps or helmets that afford hands-free and discreet use. Models with light-emitting diodes (LEDs) are less expensive compared to laser-based devices and do not require laser safety considerations, thus facilitating ease of home use. Limitations include cost of the unit, risk of information bias, and lack of standardized protocols. Finally, as with any hair loss treatment, patients' expectations with regards to therapeutic outcomes must be managed.

## <u>Dermatology</u>

van Geel N, **Hamzavi I**, **Kohli I**, Wolkerstorfer A, **Lim HW**, Bae JM, Lui H, Harris JE, Pandya AG, Thng Tien Guan S, Abdallah M, Esmat S, Seneschal J, Speeckaert R, Grine L, Kang HY, Raboobee N, Xiang LF, Bekkenk M, Picardo M, and Taieb A. Standardizing serial photography for assessing and monitoring vitiligo: A core set of international recommendations for essential clinical and technical specifications. *J Am Acad Dermatol* 2020; 83(6):1639-1646. PMID: 31678332. Full Text

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BACKGROUND: Clinical photography is an important component of the initial assessment and follow-up of patients with vitiligo in clinical practice and research settings. Standardization of this photographic process is essential to achieve useful, high-quality, and comparable photographs over time. OBJECTIVE: The aim is to develop an international consensus for a core set of recommendations for standardized vitiligo clinical photography. METHODS: Based an international meeting of vitiligo experts, a standard operating procedure was developed for vitiligo photography in daily practice and research settings. This protocol was subsequently reviewed by 20 vitiligo experts until agreement was reached. RESULTS: The resulting protocol includes a set of 10 and 15 photographs for clinical practice and research purposes, respectively. The photographic series are based on anatomic units included in the Vitiligo Extent Score. Furthermore, graphic representations of standardized positioning and suggestions for guidelines to standardize the process (background color, lighting, position marking, scales, materials, instruments) for both color and ultraviolet photographs are described. CONCLUSIONS: This consensus-based protocol for vitiligo photography will harmonize imaging for both clinical practice, translational research, and clinical trials. It can improve outcome assessment, foster multicenter collaboration, and promote better communication with patients regarding outcomes of treatment.

#### Dermatology

**Vellaichamy G**, Townsend SM, **Lyons AB**, and **Hamzavi IH**. T-cell/histiocyte-rich large B-cell lymphoma in a 27-year-old with hidradenitis suppurativa, psoriasis, and vitiligo: Implications for screening. *JAAD Case Reports* 2020; 6(12):1252-1253. Full Text

# **Dermatology**

Yu Q, Parajuli N, Yi Q, Mishina Y, Elder JT, Zhou L, and Mi QS. ALK3 is not required for the embryonic development, homeostasis and repopulation of epidermal Langerhans cells in steady and inflammatory states. *J Invest Dermatol* 2020. PMID: 33359325. Full Text

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## **Diagnostic Radiology**

Khalil LS, Meta FS, Tramer JS, Klochko CL, Scher C, Van Holsbeeck M, Kolowich PA, Makhni EC, Moutzouros V, and Okoroha KR. Elbow Torque is Reduced in Asymptomatic College Pitchers with Elbow Laxity: A Dynamic Ultrasound Study. *Arthroscopy* 2020. PMID: 33359823. Full Text

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PURPOSE: To determine the relationship between medial elbow torque, as measured by wearable sensor technology, and adaptations of the medial elbow structures on dynamic ultrasound imaging in asymptomatic collegiate pitchers. METHODS: Thirty-four pitchers from NCAA DII universities were eligible for preseason testing. Exclusion criteria included age <18, history of surgery, non-pitcher, or current restrictions. Pitchers were fitted with a wearable sensor sleeve which recorded elbow torque, arm slot, arm speed, and arm rotation. Pitchers threw 5 fastballs in a standardized manner off the mound at game-speed effort. Pitchers also underwent dynamic ultrasound imaging of their elbow by a musculoskeletal sonographer, with standardized valgus loading. Images were deidentified and measurements of the ulnar collateral ligament (UCL) and ulnohumeral joint space (UHJS), to assess elbow laxity, were performed by a musculoskeletal radiologist. RESULTS: Final analysis included 28 pitchers with average (standard deviation) age of 20.1(1.3) years [range 18-23] and playing experience of 15.3(1.8) years [range 11-19]. Dominant UCL thickness (p<.001), loaded UHJS (p=0.039), and delta UHJS (p<.001) were significantly greater than non-dominant. There was an inverse correlation between loaded UHJS and medial elbow torque (r =-0.4, p<.001). Additionally, every 1mm increase in UHJS significantly reduced medial elbow torque by 2.27Nm (p=0.032) and arm slot by 8.8° (p=0.019), and increased arm rotation by 5.3° (p=0.043). Pitchers with loaded UHJS ≥4.4mm and delta UHJS ≥1.25mm had significantly reduced medial elbow torque (p<.001). Pitchers with UCL thickness ≥1.65mm had significantly increased medial elbow torque (47.4 vs 44.8Nm, p=0.006). CONCLUSIONS: Pitchers with increased dynamic elbow laxity were found to experience reduced medial elbow torque while pitching. Additionally, pitchers with greater UCL thickness on ultrasound were found to experience increased medial elbow torque while pitching. This study's findings suggest a relationship between anatomical adaptations found on ultrasound of the pitching elbow and medial elbow torque.

### Diagnostic Radiology

**Poyiadji N**, **Klochko C**, **Palazzolo J**, **Brown ML**, and **Griffith B**. Impact of the COVID-19 pandemic on radiology physician work RVUs at a large subspecialized radiology practice. *Clin Imaging* 2020; 73:38-42. PMID: 33302235. Full Text

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PURPOSE: As the COVID-19 pandemic continues, efforts by radiology departments to protect patients and healthcare workers and mitigate disease spread have reduced imaging volumes. This study aims to quantify the pandemic's impact on physician productivity across radiology practice areas as measured by physician work Relative Value Units (wRVUs). MATERIALS AND METHODS: All signed diagnostic and procedural radiology reports were curated from January 1st to July 1st of 2019 and 2020. Physician work RVUs were assigned to each study type based on the Medicare Physician Fee Schedule. Utilizing divisional assignments, radiologist schedules were mapped to each report to generate a sum of wRVUs credited to that division for each week. Differential impact on divisions were calculated relative to a matched timeframe in 2019 and a same length pre-pandemic time period in 2020. RESULTS: All practice areas saw a substantial decrease in wRVUs from the 2020 pre- to intra-pandemic time period with a mean decrease of 51.5% (range 15.4%-76.9%). The largest declines were in Breast imaging. Musculoskeletal, and Neuroradiology, which had decreases of 76.9%, 75.3%, and 67.5%, respectively. The modalities with the greatest percentage decrease were mammography, MRI, and non-PET nuclear medicine. CONCLUSION: All radiology practice areas and modalities experienced a substantial decrease in wRVUs. The greatest decline was in Breast imaging, Neuroradiology, and Musculoskeletal radiology. Understanding the differential impact of the pandemic on practice areas will help radiology departments prepare for the potential depth and duration of the pandemic by better understanding staffing needs and the financial effects.

## **Diagnostic Radiology**

Wallis J, Klein R, Bradshaw T, Catana C, Hatt M, Laforest R, Liu C, Mawlawi O, **McCall K**, Osborne D, Tang J, Wells RG, and Ghesani M. PIDSC Remote Viewing Guidelines Document. *J Nucl Med Technol* 2020. PMID: 33380520. Request Article

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# Diagnostic Radiology

Yeni YN, Oravec D, Drost J, Bevins N, Morrison C, and Flynn MJ. Bone health assessment via digital wrist tomosynthesis in the mammography setting. *Bone* 2020; 144:115804. PMID: 33321264. Full Text

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Bone fractures attributable to osteoporosis are a significant problem. Though preventative treatment options are available for individuals who are at risk of a fracture, a substantial number of these individuals are not identified due to lack of adherence to bone screening recommendations. The issue is further complicated as standard diagnosis of osteoporosis is based on bone mineral density (BMD) derived from dual energy x-ray absorptiometry (DXA), which, while helpful in identifying many at risk, is limited in fully predicting risk of fracture. It is reasonable to expect that bone screening would become more prevalent

and efficacious if offered in coordination with digital breast tomosynthesis (DBT) exams, provided that osteoporosis can be assessed using a DBT modality. Therefore, the objective of the current study was to explore the feasibility of using digital tomosynthesis imaging in a mammography setting. To this end, we measured density, cortical thickness and microstructural properties of the wrist bone, correlated these to reference measurements from microcomputed tomography and DXA, demonstrated the application in vivo in a small group of participants, and determined the repeatability of the measurements. We found that measurements from digital wrist tomosynthesis (DWT) imaging with a DBT scanner were highly repeatable ex vivo (error = 0.05%-9.62%) and in vivo (error = 0.06%-10.2%). In ex vivo trials, DWT derived BMDs were strongly correlated with reference measurements (R = 0.841-0.980), as were cortical thickness measured at lateral and medial cortices (R = 0.991 and R = 0.959, respectively) and the majority of microstructural measures (R = 0.736-0.991). The measurements were quick and tolerated by human patients with no discomfort, and appeared to be different between young and old participants in a preliminary comparison. In conclusion, DWT is feasible in a mammography setting, and informative on bone mass, cortical thickness, and microstructural qualities that are known to deteriorate in osteoporosis. To our knowledge, this study represents the first application of DBT for imaging bone. Future clinical studies are needed to further establish the efficacy for diagnosing osteoporosis and predicting risk of fragility fracture using DWT.

#### **Emergency Medicine**

Horiuchi YU, Wettersten N, Veldhuisen DJV, Mueller C, Filippatos G, **Nowak R**, Hogan C, Kontos MC, Cannon CM, MÜeller GA, Birkhahn R, Taub P, Vilke GM, Barnett O, Mc DK, Mahon N, NuÑez J, Briguori C, Passino C, Maisel A, and Murray PT. Potential Utility of Cardiorenal Biomarkers for Prediction and Prognostication of Worsening Renal Function in Acute Heart Failure. *J Card Fail* 2020. PMID: 33296713. Full Text

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BACKGROUND: Multiple different pathophysiologic processes can contribute to worsening renal function (WRF) in acute heart failure. METHODS AND RESULTS: We retrospectively analyzed 787 patients with

acute heart failure for the relationship between changes in serum creatinine and biomarkers including brain natriuretic peptide, high sensitivity cardiac troponin I, galectin 3, serum neutrophil gelatinase-associated lipocalin, and urine neutrophil gelatinase-associated lipocalin. WRF was defined as an increase of greater than or equal to 0.3 mg/dL or 50% in creatinine within first 5 days of hospitalization. WRF was observed in 25% of patients. Changes in biomarkers and creatinine were poorly correlated (r ≤ 0.21) and no biomarker predicted WRF better than creatinine. In the multivariable Cox analysis, brain natriuretic peptide and high sensitivity cardiac troponin I, but not WRF, were significantly associated with the 1-year composite of death or heart failure hospitalization. WRF with an increasing urine neutrophil gelatinase-associated lipocalin predicted an increased risk of heart failure hospitalization. CONCLUSIONS: Biomarkers were not able to predict WRF better than creatinine. The 1-year outcomes were associated with biomarkers of cardiac stress and injury but not with WRF, whereas a kidney injury biomarker may prognosticate WRF for heart failure hospitalization.

## **Emergency Medicine**

**Lazar MH**, **Fadel R**, **Gardner-Gray J**, **Tatem G**, **Caldwell MT**, **Swiderek J**, and **Jennings JH**. Racial Differences in a Detroit, MI, ICU Population of Coronavirus Disease 2019 Patients. *Crit Care Med* 2020. PMID: 33372746. Full Text

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OBJECTIVES: To investigate the potential influence of racial differences in outcomes of patients infected by coronavirus disease 2019-positive patients who require intensive care in an urban hospital. DESIGN: Retrospective cohort study. SETTING: Henry Ford Health System Multidisciplinary ICU, a total of 156 beds spread throughout the hospital in Detroit, MI. PATIENTS: We obtained data from the electronic medical record of all adult severe acute respiratory syndrome coronavirus-2-positive patients managed in the ICU of Henry Ford Hospital in Detroit, MI, between March 13, 2020, and July 31, 2020. Included patients were divided into two groups: people of color (including Black, Asian, Hispanic/Latino, and Arab) and White. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: A total of 365 patients were evaluated: 219 were Black (60.0%), 129 were White (35.3%), two were Asian (0.6%), eight were Hispanic/Latino (2.2%), and seven were Arab (1.9%). People of color were younger (62.8 vs 67.1; p = 0.007), with equal distribution of sex. People of color had less coronary artery disease (34 [14.4%] vs 35 [27.1%]; p =0.003) and less self-reported use of regular alcohol consumption (50 [21.2%] vs 12 [9.3%]; p = 0.004) than Whites, with no differences in diabetes (125 [53.0%] vs 66 [51.2%]; p = 0.742), hypertension (188 [79.7%] vs 99 [76.8%]; p = 0.516), congestive heart failure (41 [17.4%] vs 32 [24.8%]; p = 0.090), or chronic kidney disease (123 [54.1%] vs 55 [42.6%]; p = 0.083). There was no difference in ICU length of stay between people of color (18 d [CI, 7-47 d]) and Whites (18 d [CI, 6-48 d]; p = 0. 0.979). Neither frequency (72.5% vs 71.3%; p = ns) nor median time to mechanical ventilation between people of color (9 d [CI, 6-15 d]) and Whites (10 d [CI, 5-16 d]; p = 0.733) was different. Overall, 188 patients (51.5 %) died in the hospital. The 28-day mortality was lower in people of color (107/236; 45.3%) versus Whites (73/129; 56.6%) (adjusted odds ratio 0.60; p = 0.034), and there was an increased median survival time in people of color (20 d) versus Whites (13.5 d; hazard ratio 0.62; p = 0.002). The inhospital mortality was lower in people of color versus White, but the difference was not statistically significant (113 [47.9%] vs 75 [58.1%], respectively; p = 0.061). Finally, there was no significant difference in days of symptoms prior to admission, frequency of presenting symptoms, or frequency or severity of acute respiratory distress syndrome between the two groups, CONCLUSIONS: In critically ill patients infected with coronavirus disease 2019, people of color had a lower 28-day mortality than Whites with no difference in hospital mortality, ICU length of stay, or rates of intubation. These findings are contrary to previously held beliefs surrounding the pandemic.

# **Emergency Medicine**

**McCord J**, **Hana A**, **Cook B**, **Hudson MP**, **Miller J**, Akoegbe G, Mueller C, **Moyer M**, Jacobsen G, and **Nowak R**. The Role of Cardiac Testing with the 0/1-Hour High-Sensitivity Cardiac Troponin Algorithm Evaluating for Acute Myocardial Infarction. *Am Heart J* 2020. PMID: 33373603. Full Text

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BACKGROUND: The role of cardiac testing in the 3 zones (rule-out, observation, and rule-in) of the 0/1-hour algorithm to evaluate for acute myocardial infarction (AMI) has not been well-studied. This study evaluated the 0/1-hour algorithm with a high-sensitivity cardiac troponin (hs-cTnI) assay and investigated cardiac testing in the 3 zones. METHODS: Patients (n = 552) at a single urban center were enrolled if they were evaluated for AMI. Blood samples were obtained at presentation, 1 hour, and 3 hours for hs-cTnI. Follow-up at 30-45 days for death/AMI was done. The results of echocardiograms, stress testing, and coronary angiography were recorded. RESULTS: In total, 45 (8.2%) had AMI (27 Type 1 and 18 Type 2) during the index hospitalization while at follow-up death/AMI occurred in 11 (2.0%) of patients. The rule-out algorithm had a negative predictive value for AMI of 99.6% while the rule-in zone had a positive predictive value of 56.6%. The MACE rate at follow-up was 0.4% for those in the rule-out group. There were 6/95 (6.3%) abnormal stress tests in the rule-out zone and 4 of these were false positives. CONCLUSIONS: The 0/1-hour algorithm had high diagnostic sensitivity and negative predictive value for AMI, and adverse events were very low in patients in the rule-out zone. Noninvasive testing in rule-out zone patients had low diagnostic yield.

### **Emergency Medicine**

Viarasilpa T, Panyavachiraporn N, Osman G, Kowalski RG, Miller J, Barkley GL, and Mayer SA. Differentiation of psychogenic nonepileptic attacks from status epilepticus among patients intubated for convulsive activity. *Epilepsy Behav* 2020; 115:107679. PMID: 33360401. Full Text

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BACKGROUND AND OBJECTIVE: Patients with psychogenic nonepileptic attacks (PNEA) sometimes receive aggressive treatment leading to intubation. This study aimed to identify patient characteristics that can help differentiate PNEA from status epilepticus (SE). METHODS: We retrospectively identified patients with a final diagnosis of PNEA or SE, who were intubated for emergent convulsive symptoms and underwent continuous electroencephalography (cEEG) between 2012 and 2017. Patients who had acute brain injury or progressive brain disease as the cause of SE were excluded. We compared clinical features and laboratory values between the two groups, and identified risk factors for PNEA-related convulsive activity. RESULTS: Over a six-year period, 24 of 148 consecutive patients (16%) intubated for convulsive activity had a final diagnosis of PNEA rather than SE. Compared to patients intubated for SE, intubated PNEA patients more likely were <50 years of age, female, white, had a history of a psychiatric disorder, had no history of an intracranial abnormality, and had a maximum systolic blood pressure <140 mm Hg (all P < 0.001). Patients with 0-2 of these six risk factors had a 0% (0/88) likelihood of having PNEA, those with 3-4 had a 15% (6/39) chance of having PNEA, and those with 5-6 had an 86% (18/21) chance of having PNEA. Sensitivity for PNEA among those with 5-6 risk factors was 75% (95% CI: 53-

89%) and specificity was 98% (95% CI: 93-99%). CONCLUSIONS: In the absence of a clear precipitating brain injury, approximately one in six patients intubated for emergent convulsive symptoms had PNEA rather than SE. Although PNEA cannot be diagnosed only by the presence of these risk factors, these simple characteristics could raise clinical suspicion for PNEA in the appropriate setting. Urgent neurological consultation may prevent unnecessary intubation of this at-risk patient population.

# **Endocrinology and Metabolism**

D'Souza SC, and **Kruger DF**. Considerations for Insulin-Treated Type 2 Diabetes Patients During Hospitalization: A Narrative Review of What We Need to Know in the Age of Second-Generation Basal Insulin Analogs. *Diabetes Ther* 2020; 11(12):2775-2790. PMID: 33000382. <u>Full Text</u>

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With the availability of second-generation basal insulin analogs, insulin degludec (100 and 200 units/ml [degludec]) and insulin glargine 300 units/ml (glargine U300), clinicians now have long-acting, efficacious treatment options with stable pharmacokinetic profiles and associated low risks of hypoglycemia that may be desirable for many patients with type 2 diabetes. In this narrative review, we summarize the current evidence on glycemic control in hospitalized patients and review the pharmacokinetic properties of degludec and glargine U300 in relation to the challenges these may pose during the hospitalization of patients with type 2 diabetes who are receiving outpatient regimens involving these newer insulins. Their increased use in clinical practice requires that hospital healthcare professionals (HCPs) have appropriate protocols to transfer patients from these second-generation insulins to formulary insulin on admission, and ensure the safe discharge of patients and transition back to degludec or glargine U300. However, there is no guidance available on this. Based on the authors' clinical experience, we identify key issues to consider when arranging hospital care of such patients. We also summarize the limited available evidence on the potential utility of these second-generation basal insulin analogs in the non-critical inpatient setting and identify avenues for future research. To address current knowledge gaps, it is important that HCPs are educated about the differences between standard formulary insulins and second-generation insulins, and the importance of clear communication during patient transitions.

## Family Medicine

Coritsidis GN, **Yaphe S**, Rahkman I, Lubowski T, Munro C, Kuang Lee T, Stern A, and Bhat P. Outpatient Antibiotic Prescribing Patterns for Adult End-Stage Renal Disease Patients in New York State. *Clin Infect Dis* 2020. PMID: 33277995. <u>Full Text</u>

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IMPORTANCE: Infections are important complications of end-stage renal disease (ESRD) with few studies having investigated oral antibiotic use. Inappropriate antibiotic prescribing can contribute to multidrug resistant organisms (MDRO) and Clostridioides difficile (CDI) infections seen in ESRD. This study investigates antibiotic prescribing practices in ESRD across New York State (NYS). METHODS: Retrospective case-control study from 2016 to 2017 of NYS ESRD and non-ESRD patients analyzing Medicare part B billing codes, 7 days before and 3 days after part D claims. Frequencies of each infection, each antibiotic, dosages, and the antibiotics associated with infections were assessed using chisquare analysis. A NYS small dialysis organization comprising approximately 2200 patients was also analyzed. Outcomes measured were the frequencies of infections and of each antibiotic prescribed. Incidence measures included antibiotics/1000 and individuals receiving antibiotics/1000. RESULTS: 48,100 infections were treated in 35,369 ESRD patients and 2,544,443 infections treated in 3,777,314 non-ESRD patients. ESRD patients were younger, male, and African American. ESRD and non-ESRD patients receiving antibiotics was 520.29/1000 and 296.48/1000, respectively (p<0.05). The prescription incidence was 1359.95/1000 ESRD vs 673.61/1000 non-ESRD patients. In 36%, trimethoprim-

sulfamethoxazole dosage was elevated by current ESRD guidelines. Top infectious categories included non-specific symptoms, skin, and respiratory for ESRD; and respiratory, nonspecific symptoms, and genitourinary in non-ESRD. CONCLUSIONS: This study Identifies issues with appropriate antibiotic usage stressing the importance of antibiotic education to nephrologist and non-nephrologist providers. It provides support for outpatient antibiotic stewardship programs.

## Gastroenterology

**Piraka C**. Cool it now: a new addition for resecting 10- to 14-mm polyps. *Gastrointest Endosc* 2020; 92(6):1247-1249. PMID: 33236996. Full Text

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#### Global Health Initiative

**Nauriyal V**, Rai SM, Joshi RD, Thapa BB, **Kaljee L**, **Prentiss T**, **Maki G**, Shrestha B, Bajracharya DC, Karki K, Joshi N, Acharya A, Banstola L, Poudel SR, Joshi A, Dahal A, Palikhe N, Khadka S, Giri P, Lamichhane A, and **Zervos M**. Evaluation of an Antimicrobial Stewardship Program for Wound and Burn Care in Three Hospitals in Nepal. *Antibiotics (Basel)* 2020; 9(12). PMID: 33339283. Full Text

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Antimicrobial stewardship (AMS) programs can decrease non-optimal use of antibiotics in hospital settings. There are limited data on AMS programs in burn and chronic wound centers in low- and middleincome countries (LMIC). A post-prescription review and feedback (PPRF) program was implemented in three hospitals in Nepal with a focus on wound and burn care. A total of 241 baseline and 236 postintervention patient chart data were collected from three hospitals. There was a significant decrease in utilizing days of therapy per 1000 patient days (DOT/1000 PD) of penicillin (p = 0.02), aminoglycoside (p < 0.001), and cephalosporin (p = 0.04). Increases in DOT/1000 PD at post-intervention were significant for metronidazole (p < 0.001), quinolone (p = 0.01), and other antibiotics (p < 0.001). Changes in use of antibiotics varied across hospitals, e.g., cephalosporin use decreased significantly at Kirtipur Hospital (p < 0.001) and Pokhara Academy of Health Sciences (p = 0.02), but not at Kathmandu Model Hospital (p = 0.59). An independent review conducted by infectious disease specialists at the Henry Ford Health System revealed significant changes in antibiotic prescribing practices both overall and by hospital. There was a decrease in mean number of intravenous antibiotic days between baseline (10.1 (SD 8.8)) and post-intervention (8.8 (SD 6.5)) (t = 3.56; p < 0.001), but no difference for oral antibiotics. Compared to baseline, over the 6-month post-intervention period, we found an increase in justified use of antibiotics (p < 0.001), de-escalation (p < 0.001), accurate documentation (p < 0.001), and adherence to the study antibiotic prescribing guidelines at 72 h (p < 0.001) and after diagnoses (p < 0.001). The evaluation data presented provide evidence that PPRF training and program implementation can contribute to hospitalbased antibiotic stewardship for wound and burn care in Nepal.

# Hematology-Oncology

**Maahs L**, **Tang A**, **Saheli ZA**, Jacob B, Polasani R, and **Hwang C**. Real-world effectiveness of the pegfilgrastim on-body injector in preventing severe neutropenia. *J Oncol Pharm Pract* 2020:1078155220980517. PMID: 33323023. <u>Full Text</u>

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INTRODUCTION: Granulocyte colony-stimulating factors are used in medical oncology for the prevention of neutropenia. On-body injectors (OBI) have an advantage over the traditional injection (TI) method of not requiring a second visit to the clinic, but these devices are subject to failure. The objective of this study was to assess the efficacy of OBIs in the real-world. METHODS: Women with breast cancer diagnosed between June 2015 and June 2016 treated with cytotoxic chemotherapy and a granulocyte colony-stimulating factor were retrospectively identified from the medical records of Henry Ford Hospital. The primary outcome was the incidence of severe neutropenia (SN), defined as an absolute neutrophil count (ANC) ≤500. Secondary outcomes included incidence of neutropenia (ANC ≤ 1500), neutropenia fever, and mortality. A secondary analysis of the data was performed to identify predictors of SN. RESULTS: A total of 837 cycles of chemotherapy were analyzed. The OBI was used in 395 cycles and the TI in 442. The OBI group had patients that were older, had higher baseline ANC, and were more often white. The incidences of SN, neutropenic fever and neutropenia were not different between groups. Patients with a lower baseline ANC and white ethnicity were at a higher risk for SN. AC (doxorubicin and cyclophosphamide) was the most commonly used chemotherapy regimen (38% of total cycles). CONCLUSIONS: There was no difference in the efficacy of the OBI and TI methods for preventing SN, neutropenic fever and neutropenia.

## Hematology-Oncology

Shapiro AD, Ragni MV, Borhany M, Abajas YL, Tarantino MD, Holstein K, Croteau SE, Liesner R, Tarango C, Carvalho M, McGuinn C, Funding E, Kempton CL, Bidlingmaier C, Cohen A, Oldenburg J, Kearney S, Knoll C, **Kuriakose P**, Acharya S, Reiss UM, Kulkarni R, Witkop M, Lethagen S, Donfield S, LeBeau P, Berntorp E, and Astermark J. Natural history study of factor IX deficiency with focus on treatment and complications (B-Natural). *Haemophilia* 2020. PMID: 33278853. Full Text

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INTRODUCTION: Haemophilia B (HB) is less well studied than haemophilia A (HA): despite similarities between the two inherited bleeding disorders, important differences remain that require further research. AIM: B-Natural is a multi-centre, prospective, observational study of HB, designed to increase understanding of clinical manifestations, treatment, quality-of-life (QoL), inhibitor development, immune tolerance induction (ITI) outcome, renal function and create a biorepository for future investigations. METHODS: Participants include sibling pairs/groups without a current/history of inhibitors and singletons or siblings with a current/history of inhibitors followed for six months. Demographics, medical, social history and treatment were recorded. A physical examination including joint range of motion (ROM) was performed; QoL was assessed. Samples were collected for F9 gene mutation, HLA typing, non-inhibitory antibodies and renal function testing. RESULTS: Twenty-four centres enrolled 224 individuals from 107 families including 29 with current/history of inhibitors. Of these, 68, 30.4%, had severe (<1% FIX level of normal); 114, 50.9%, moderate (1%-5%); and 42, 18.8%, mild (>5-<40%) disease. At enrolment, 53.1% had 50 + exposure days to exogenous FIX. Comparison of joint scores showed significant (P < .05) differences between those with severe (with/without inhibitors), and those with moderate/mild disease. The majority with severe disease, 80.0% with current/history of inhibitors and 64.3% of those without, were treated with prophylaxis. CONCLUSION: B-Natural provides data supporting an increased understanding of HB and its impact throughout life. The need for optimal disease control to normalize physical and psychosocial outcomes is underscored, and further analyses will contribute to an increased understanding of critical issues in HB.

## Hypertension and Vascular Research

**Dham D**, **Roy B**, **Gowda A**, **Pan G**, Sridhar A, Zeng X, Thandavarayan RA, and **Selvaraj Palaniyandi S**. 4-hydroxy-2-nonenal, a lipid peroxidation product, as a biomarker in diabetes and its complications: challenges and opportunities. *Free Radic Res* 2020:1-50. PMID: 33336611. Request Article

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Over 30 million Americans are diagnosed with diabetes and this number is only expected to increase. There are various causes that induce complications with diabetes, including oxidative stress. In oxidative stress, lipid peroxidation-derived reactive carbonyl species (RCS) such as 4-hydroxy-2-nonenal (4-HNE) is shown to cause damage in organs that leads to diabetic complications. We provided evidence to show that 4-HNE or/and 4-HNE-protein adducts are elevated in various organ systems of diabetic patients and animal models. We then discussed the advantages and disadvantages of different methodologies used for the detection of 4-HNE in diabetic tissues. We also discussed how novel approaches such as electrochemistry and nanotechnology can be used for monitoring 4-HNE levels in the biological systems in real-time. Thus, this review enlightens the involvement of 4-HNE in the pathogenesis of diabetes and its complications and efficient methods to identify it. Furthermore, the article presents that 4-HNE can be developed as a biomarker for end-organ damage in diabetes such as diabetic cardiac complications.

#### Infectious Diseases

Heldman MR, Kates OS, Haydel BM, Florman SS, Rana MM, **Chaudhry ZS**, **Ramesh MS**, Safa K, Kotton CN, Blumberg EA, Besharatian BD, Tanna SD, Ison MG, Malinis M, Azar MM, Rakita RM, Morillas JA, Majeed A, Sait AS, Spaggiari M, Hemmige V, Mehta SA, Neumann H, Badami A, Jeng A, Goldman JD, Lala A, Hemmersbach-Miller M, McCort ME, Bajrovic V, Ortiz-Bautista C, Friedman-Moraco R, Sehgal S, Lease ED, Limaye AP, and Fisher CE. Healthcare resource use among solid organ transplant recipients hospitalized with COVID-19. *Clin Transplant* 2020:e14174. PMID: 33349940. <u>Full Text</u>

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# Infectious Diseases

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BACKGROUND: LY-CoV555, a neutralizing monoclonal antibody, has been associated with a decrease in viral load and the frequency of hospitalizations or emergency department visits among outpatients with coronavirus disease 2019 (Covid-19). Data are needed on the effect of this antibody in patients who are hospitalized with Covid-19. METHODS: In this platform trial of therapeutic agents, we randomly assigned hospitalized patients who had Covid-19 without end-organ failure in a 1:1 ratio to receive either LY-CoV555 or matching placebo. In addition, all the patients received high-quality supportive care as background therapy, including the antiviral drug remdesivir and, when indicated, supplemental oxygen and glucocorticoids. LY-CoV555 (at a dose of 7000 mg) or placebo was administered as a single intravenous infusion over a 1-hour period. The primary outcome was a sustained recovery during a 90day period, as assessed in a time-to-event analysis. An interim futility assessment was performed on the basis of a seven-category ordinal scale for pulmonary function on day 5. RESULTS: On October 26, 2020, the data and safety monitoring board recommended stopping enrollment for futility after 314 patients (163 in the LY-CoV555 group and 151 in the placebo group) had undergone randomization and infusion. The median interval since the onset of symptoms was 7 days (interguartile range, 5 to 9). At day 5, a total of 81 patients (50%) in the LY-CoV555 group and 81 (54%) in the placebo group were in one of the two most favorable categories of the pulmonary outcome. Across the seven categories, the odds ratio of being in a more favorable category in the LY-CoV555 group than in the placebo group was 0.85 (95% confidence interval [CI], 0.56 to 1.29; P = 0.45). The percentage of patients with the primary safety outcome (a composite of death, serious adverse events, or clinical grade 3 or 4 adverse events through day 5) was similar in the LY-CoV555 group and the placebo group (19% and 14%, respectively; odds ratio, 1.56; 95% CI, 0.78 to 3.10; P = 0.20). The rate ratio for a sustained recovery was 1.06 (95% CI, 0.77 to 1.47). CONCLUSIONS: Monoclonal antibody LY-CoV555, when coadministered with remdesivir, did not demonstrate efficacy among hospitalized patients who had Covid-19 without end-organ failure. (Funded by Operation Warp Speed and others; TICO ClinicalTrials.gov number, NCT04501978.).

# Infectious Diseases

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The SARS-CoV-2 virus spreading across the world has led to surges of COVID-19 illness, hospitalizations, and death. The complex and multifaceted pathophysiology of life-threatening COVID-19 illness including viral mediated organ damage, cytokine storm, and thrombosis warrants early interventions to address all components of the devastating illness. In countries where therapeutic nihilism is prevalent, patients endure escalating symptoms and without early treatment can succumb to delayed in-hospital care and death. Prompt early initiation of sequenced multidrug therapy (SMDT) is a widely and currently available solution to stem the tide of hospitalizations and death. A multipronged therapeutic approach includes 1) adjuvant nutraceuticals, 2) combination intracellular anti-infective therapy, 3) inhaled/oral corticosteroids, 4) antiplatelet agents/anticoagulants, 5) supportive care including supplemental oxygen, monitoring, and telemedicine. Randomized trials of individual, novel oral therapies have not delivered tools for physicians to combat the pandemic in practice. No single therapeutic option thus far has been entirely effective and therefore a combination is required at this time. An urgent immediate pivot from single drug to SMDT regimens should be employed as a critical strategy to deal with the large numbers of acute COVID-19 patients with the aim of reducing the intensity and duration of symptoms and avoiding hospitalization and death.

### Infectious Diseases

**Nauriyal V**, Rai SM, Joshi RD, Thapa BB, **Kaljee L**, **Prentiss T**, **Maki G**, Shrestha B, Bajracharya DC, Karki K, Joshi N, Acharya A, Banstola L, Poudel SR, Joshi A, Dahal A, Palikhe N, Khadka S, Giri P, Lamichhane A, and **Zervos M**. Evaluation of an Antimicrobial Stewardship Program for Wound and Burn Care in Three Hospitals in Nepal. *Antibiotics (Basel)* 2020; 9(12). PMID: 33339283. Full Text

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Antimicrobial stewardship (AMS) programs can decrease non-optimal use of antibiotics in hospital settings. There are limited data on AMS programs in burn and chronic wound centers in low- and middleincome countries (LMIC). A post-prescription review and feedback (PPRF) program was implemented in three hospitals in Nepal with a focus on wound and burn care. A total of 241 baseline and 236 postintervention patient chart data were collected from three hospitals. There was a significant decrease in utilizing days of therapy per 1000 patient days (DOT/1000 PD) of penicillin (p = 0.02), aminoglycoside (p < 0.001), and cephalosporin (p = 0.04). Increases in DOT/1000 PD at post-intervention were significant for metronidazole (p < 0.001), quinolone (p = 0.01), and other antibiotics (p < 0.001). Changes in use of antibiotics varied across hospitals, e.g., cephalosporin use decreased significantly at Kirtipur Hospital (p < 0.001) and Pokhara Academy of Health Sciences (p = 0.02), but not at Kathmandu Model Hospital (p = 0.59). An independent review conducted by infectious disease specialists at the Henry Ford Health System revealed significant changes in antibiotic prescribing practices both overall and by hospital. There was a decrease in mean number of intravenous antibiotic days between baseline (10.1 (SD 8.8)) and post-intervention (8.8 (SD 6.5)) (t = 3.56; p < 0.001), but no difference for oral antibiotics. Compared to baseline, over the 6-month post-intervention period, we found an increase in justified use of antibiotics (p < 0.001), de-escalation (p < 0.001), accurate documentation (p < 0.001), and adherence to the study antibiotic prescribing guidelines at 72 h (p < 0.001) and after diagnoses (p < 0.001). The evaluation data

presented provide evidence that PPRF training and program implementation can contribute to hospital-based antibiotic stewardship for wound and burn care in Nepal.

## Internal Medicine

Gupta K, Ramakrishnan S, Zachariah G, Rao JS, Mohanan PP, Venugopal K, Sateesh S, Sethi R, Jain D, Bardolei N, Mani K, Kakar TS, Jain V, Gupta P, Gupta R, Bansal S, Nath RK, Tyagi S, Wander GS, Gupta S, Mandal S, Senguttuvan NB, Subramanyam G, Roy D, Datta S, Ganguly K, Routray SN, Mishra SS, Singh BP, Bharti BB, Das MK, Deb PK, Deedwania P, Seth A, Shivkumar Rao J, Sinha AK, Bhushan S, Verma SK, Bhargava B, Roy A, Sood S, Isser HS, Pandit N, Trehan V, Gupta MD, Girish MP, Ahuja R, Manchanda SC, Mohanty A, Jain P, Shrivastava S, Kalra IPS, Sarang BS, Ratti HS, Sahib GB, Gupta R, Amit SKA, Goswami KC, Bahl VK, Chopra HK, Koshy G, Nair T, Shyam N, Roby A, George R, Kumar S, Kader A, Abraham M, Viswanathan S, Jabir A, Menon J, Unni G, Mathew C, Jayagopal PB, Sajeev, Ashokan PK, Asharaf, Pancholia AK, Gupta AK, Das R, Aggarwal D, Malviya A, Ali SM, Barward P, Singh N, Tomar YS, Chaddha D, Dani S, Vyas C, Bhatt K, Doshi S, Meena CB, Subramanyam, Muruganandam AM, Narain V, Saran RK, Jain P, Kumar S, Goel PK, Das MK, Kumar S, Chandra S, Banerjee A, and Guha S. Impact of the 2017 ACC/AHA guidelines on the prevalence of hypertension among Indian adults: Results from a cross-sectional survey. *International Journal of Cardiology: Hypertension* 2020; 7. Full Text

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Background: The impact of the 2017 American College of Cardiology (ACC)/American Heart Association (AHA) guidelines for diagnosis and management of hypertension on the prevalence of hypertension in India is unknown. Methods: We analyzed data from the Cardiac Prevent 2015 survey to estimate the change in the prevalence of hypertension. The JNC8 guidelines defined hypertension as a systolic blood pressure of ≥140 mmHg or diastolic blood pressure of ≥90 mmHg. The 2017 ACC/AHA guidelines define hypertension as a systolic blood pressure of ≥130 mmHg or diastolic blood pressure of ≥80 mmHg. We standardized the prevalence as per the 2011 census population of India. We also calculated the prevalence as per the World Health Organization (WHO) World Standard Population (2000–2025). Results: Among 180,335 participants (33.2% women), the mean age was  $40.6 \pm 14.9$  years ( $41.1 \pm 15.0$ and 39.7 ± 14.7 years in men and women, respectively). Among them, 8,898 (4.9%), 99,791 (55.3%), 35,694 (11.9%), 23,084 (12.8%), 9,989 (5.5%) and 2,878 (1.6%) participants belonged to age group 18-19, 20–44, 45–54, 55–64, 65–74 and ≥ 75 years respectively. The prevalence of hypertension according to the JNC8 and 2017 ACC/AHA guidelines was 29.7% and 63.8%, respectively- an increase of 115%. With the 2011 census population of India, this suggests that currently, 486 million Indian adults have hypertension according to the 2017 ACC/AHA guidelines, an addition of 260 million as compared to the JNC8 guidelines. Conclusion: According to the 2017 ACC/AHA guidelines, 3 in every 5 Indian adults have hypertension.

## Internal Medicine

Jain V, **Gupta K**, Bhatia K, Bansal A, Arora S, **Khandelwal AK**, Rosenberg JR, Levisay JP, Tommaso CL, Ricciardi MJ, and Qamar A. Management of STEMI during the COVID-19 pandemic: Lessons learned in 2020 to prepare for 2021. *Trends Cardiovasc Med* 2020. PMID: 33338636. Full Text

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As the prevalence of asymptomatic COVID-19 continues to increase, there is an increasing possibility that patients with COVID-19 may presen with ST-segment elevation myocardial infarction (STEMI). With social distancing and restricted access to preventive healthcare and emergency services, the management of acute cardiac emergencies such as myocardial infarction has suffered collateral damage. Thus far, global trends suggest a decrease in STEMI activations with possible worse outcomes due to delayed presentation and management. In this review, we discuss the challenges to STEMI management in the COVID-19 era and provide potential solutions for adherence to evidence-based therapies as the pandemic progresses into the year 2021.

### Internal Medicine

**Lazar MH**, **Fadel R**, **Gardner-Gray J**, **Tatem G**, **Caldwell MT**, **Swiderek J**, and **Jennings JH**. Racial Differences in a Detroit, MI, ICU Population of Coronavirus Disease 2019 Patients. *Crit Care Med* 2020. PMID: 33372746. Full Text

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OBJECTIVES: To investigate the potential influence of racial differences in outcomes of patients infected by coronavirus disease 2019-positive patients who require intensive care in an urban hospital. DESIGN: Retrospective cohort study. SETTING: Henry Ford Health System Multidisciplinary ICU, a total of 156 beds spread throughout the hospital in Detroit, MI. PATIENTS: We obtained data from the electronic medical record of all adult severe acute respiratory syndrome coronavirus-2-positive patients managed in the ICU of Henry Ford Hospital in Detroit, MI, between March 13, 2020, and July 31, 2020. Included patients were divided into two groups: people of color (including Black, Asian, Hispanic/Latino, and Arab) and White. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: A total of 365 patients were evaluated: 219 were Black (60.0%), 129 were White (35.3%), two were Asian (0.6%), eight were Hispanic/Latino (2.2%), and seven were Arab (1.9%). People of color were younger (62.8 vs 67.1; p = 0.007), with equal distribution of sex. People of color had less coronary artery disease (34 [14.4%] vs 35 [27.1%]; p =0.003) and less self-reported use of regular alcohol consumption (50 [21.2%] vs 12 [9.3%]; p = 0.004) than Whites, with no differences in diabetes (125 [53.0%] vs 66 [51.2%]; p = 0.742), hypertension (188 [79.7%] vs 99 [76.8%]; p = 0.516), congestive heart failure (41 [17.4%] vs 32 [24.8%]; p = 0.090), or chronic kidney disease (123 [54.1%] vs 55 [42.6%]; p = 0.083). There was no difference in ICU length of stay between people of color (18 d [CI, 7-47 d]) and Whites (18 d [CI, 6-48 d]; p = 0. 0.979). Neither frequency (72.5% vs 71.3%; p = ns) nor median time to mechanical ventilation between people of color (9 d [CI, 6-15 d]) and Whites (10 d [CI, 5-16 d]; p = 0.733) was different. Overall, 188 patients (51.5 %) died in the hospital. The 28-day mortality was lower in people of color (107/236; 45.3%) versus Whites (73/129; 56.6%) (adjusted odds ratio 0.60; p = 0.034), and there was an increased median survival time in people of color (20 d) versus Whites (13.5 d; hazard ratio 0.62; p = 0.002). The inhospital mortality was lower in people of color versus White, but the difference was not statistically significant (113 [47.9%] vs 75 [58.1%], respectively; p = 0.061). Finally, there was no significant difference in days of symptoms prior to admission, frequency of presenting symptoms, or frequency or severity of acute respiratory distress syndrome between the two groups. CONCLUSIONS: In critically ill patients infected with coronavirus disease 2019, people of color had a lower 28-day mortality than Whites with no difference in hospital mortality, ICU length of stay, or rates of intubation. These findings are contrary to previously held beliefs surrounding the pandemic.

#### Internal Medicine

**Maahs L**, **Tang A**, **Saheli ZA**, Jacob B, Polasani R, and **Hwang C**. Real-world effectiveness of the pegfilgrastim on-body injector in preventing severe neutropenia. *J Oncol Pharm Pract* 2020:1078155220980517. PMID: 33323023. Full Text

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INTRODUCTION: Granulocyte colony-stimulating factors are used in medical oncology for the prevention of neutropenia. On-body injectors (OBI) have an advantage over the traditional injection (TI) method of not requiring a second visit to the clinic, but these devices are subject to failure. The objective of this study was to assess the efficacy of OBIs in the real-world. METHODS: Women with breast cancer diagnosed between June 2015 and June 2016 treated with cytotoxic chemotherapy and a granulocyte colony-stimulating factor were retrospectively identified from the medical records of Henry Ford Hospital. The primary outcome was the incidence of severe neutropenia (SN), defined as an absolute neutrophil count (ANC) ≤500. Secondary outcomes included incidence of neutropenia (ANC ≤ 1500), neutropenia fever, and mortality. A secondary analysis of the data was performed to identify predictors of SN. RESULTS: A total of 837 cycles of chemotherapy were analyzed. The OBI was used in 395 cycles and the TI in 442. The OBI group had patients that were older, had higher baseline ANC, and were more often white. The incidences of SN, neutropenic fever and neutropenia were not different between groups. Patients with a lower baseline ANC and white ethnicity were at a higher risk for SN. AC (doxorubicin and cyclophosphamide) was the most commonly used chemotherapy regimen (38% of total cycles). CONCLUSIONS: There was no difference in the efficacy of the OBI and TI methods for preventing SN. neutropenic fever and neutropenia.

#### Internal Medicine

**McCord J, Hana A, Cook B, Hudson MP, Miller J,** Akoegbe G, Mueller C, **Moyer M**, Jacobsen G, and **Nowak R**. The Role of Cardiac Testing with the 0/1-Hour High-Sensitivity Cardiac Troponin Algorithm Evaluating for Acute Myocardial Infarction. *Am Heart J* 2020. PMID: 33373603. Full Text

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BACKGROUND: The role of cardiac testing in the 3 zones (rule-out, observation, and rule-in) of the 0/1-hour algorithm to evaluate for acute myocardial infarction (AMI) has not been well-studied. This study evaluated the 0/1-hour algorithm with a high-sensitivity cardiac troponin (hs-cTnI) assay and investigated cardiac testing in the 3 zones. METHODS: Patients (n = 552) at a single urban center were enrolled if they were evaluated for AMI. Blood samples were obtained at presentation, 1 hour, and 3 hours for hs-cTnI. Follow-up at 30-45 days for death/AMI was done. The results of echocardiograms, stress testing, and coronary angiography were recorded. RESULTS: In total, 45 (8.2%) had AMI (27 Type 1 and 18 Type 2) during the index hospitalization while at follow-up death/AMI occurred in 11 (2.0%) of patients. The rule-out algorithm had a negative predictive value for AMI of 99.6% while the rule-in zone had a positive predictive value of 56.6%. The MACE rate at follow-up was 0.4% for those in the rule-out group. There were 6/95 (6.3%) abnormal stress tests in the rule-out zone and 4 of these were false positives. CONCLUSIONS: The 0/1-hour algorithm had high diagnostic sensitivity and negative predictive value for AMI, and adverse events were very low in patients in the rule-out zone. Noninvasive testing in rule-out zone patients had low diagnostic yield.

### **Internal Medicine**

Piscoya A, **Ng-Sueng LF**, Parra Del Riego A, Cerna-Viacava R, Pasupuleti V, Roman YM, Thota P, White CM, and Hernandez AV. Efficacy and harms of remdesivir for the treatment of COVID-19: A systematic review and meta-analysis. *PLoS One* 2020; 15(12):e0243705. PMID: 33301514. Full Text

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BACKGROUND: Efficacy and safety of treatments for hospitalized COVID-19 are uncertain. We systematically reviewed efficacy and safety of remdesivir for the treatment of COVID-19. METHODS: Studies evaluating remdesivir in adults with hospitalized COVID-19 were searched in several engines until August 21, 2020. Primary outcomes included all-cause mortality, clinical improvement or recovery, need for invasive ventilation, and serious adverse events (SAEs). Inverse variance random effects metaanalyses were performed. RESULTS: We included four randomized controlled trials (RCTs) (n = 2296) [two vs. placebo (n = 1299) and two comparing 5-day vs. 10-day regimens (n = 997)], and two case series (n = 88). Studies used intravenous remdesivir 200mg the first day and 100mg for four or nine more days. One RCT (n = 236) was stopped early due to AEs; the other three RCTs reported outcomes between 11 and 15 days. Time to recovery was decreased by 4 days with remdesivir vs. placebo in one RCT (n = 1063), and by 0.8 days with 5-days vs. 10-days of therapy in another RCT (n = 397). Clinical improvement was better for 5-days regimen vs. standard of care in one RCT (n = 600). Remdesivir did not decrease all-cause mortality (RR 0.71, 95%CI 0.39 to 1.28, I2 = 43%) and need for invasive ventilation (RR 0.57, 95%CI 0.23 to 1.42, I2 = 60%) vs. placebo at 14 days but had fewer SAEs; 5-day decreased need for invasive ventilation and SAEs vs. 10-day in one RCT (n = 397). No differences in allcause mortality or SAEs were seen among 5-day, 10-day and standard of care. There were some concerns of bias to high risk of bias in RCTs. Heterogeneity between studies could be due to different severities of disease, days of therapy before outcome determination, and how ordinal data was analyzed. CONCLUSIONS: There is paucity of adequately powered and fully reported RCTs evaluating effects of remdesivir in hospitalized COVID-19 patients. Until stronger evidence emerges, we cannot conclude that remdesivir is efficacious for treating COVID-19.

## Neurology

Farbman ES, Waters CH, **LeWitt PA**, Rudzińska M, Klingler M, Lee A, Qian J, Oh C, and Hauser RA. A 12-month, dose-level blinded safety and efficacy study of levodopa inhalation powder (CVT-301, Inbrija) in patients with Parkinson's disease. *Parkinsonism Relat Disord* 2020; 81:144-150. PMID: 33130477. <u>Full Text</u>

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INTRODUCTION: CVT-301 (Inbrija®) is a levodopa inhalation powder for on-demand treatment of OFF episodes in Parkinson's disease patients treated with carbidopa/levodopa. Safety and efficacy results of a 12-month, dose-level blinded extension study of a phase 3 trial (SPAN<sup>SM</sup>-PD) of CVT-301 are presented. METHODS: Patients were receiving oral carbidopa/levodopa and adjunctive CVT-301 treatment, blinded to dose (60 mg or 84 mg, N = 325). Study visits occurred every 3 months. Pulmonary function was assessed by spirometry. Other safety assessments included dyskinesia and adverse events (AEs). Secondary objectives of the study included maintenance of improvement assessments for occurrence of an ON state during the 60-min post-dose period, change in total daily OFF time, and Patient Global Impression of Change (PGIC). RESULTS: Most frequent AEs (≥5%) were cough (15.4%), fall (13.1%), upper respiratory tract infection (7.1%), and dyskinesia (5.1%). Severe AEs (>1 event) were cough (1.9%)

and dyskinesia (0.6%). Twelve-month mean changes from baseline for FEV(1), FVC, and DL(CO) were -0.092 L, -0.097 L, and -0.922 mL/min/mmHg, respectively. At 12 months, 73.0% of patients on 84 mg achieved an ON state within 60 min. Total daily OFF time was reduced by 0.55 h (month 1) and 0.88 h (month 12) for the 84 mg dose. Percentage of patients self-reported as improved by PGIC was 65.5-91.9% over 12 months. CONCLUSION: CVT-301 was generally well-tolerated. Twelve-month decline in pulmonary function was consistent with a prior PD control group. Exploratory efficacy results showed CVT-301 maintained improvement at achieving ON states in patients experiencing OFF episodes, decreasing daily OFF time, and maintaining improvement in PGIC.

# Neurology

**Lashkari A**, **Davoodi-Bojd E**, Fahmy L, **Li L**, Nejad-Davarani SP, **Chopp M**, **Jiang Q**, and **Cerghet M**. Impairments of white matter tracts and connectivity alterations in five cognitive networks of patients with multiple sclerosis. *Clin Neurol Neurosurg* 2020; 201:106424. PMID: 33348120. Full Text

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INTRODUCTION: MS is associated with structural and functional brain alterations leading to cognitive impairments across multiple domains including attention, memory, and speed of information processing. Here, we analyzed the white matter damage and topological organization of white matter tracts in specific brain regions responsible for cognition in MS. METHODS: Brain DTI, rs-fMRI, T1, T2, and T2-FLAIR were acquired for 22 MS subjects and 22 healthy controls. Automatic brain parcellation was performed on T1weighted images. Skull-stripped T1-weighted intensity inverted images were co-registered to the b0 image. Diffusion-weighted images were processed to perform whole brain tractography. The rs-fMRI data were processed, and the connectivity matrixes were analyzed to identify significant differences in the network of nodes between the two groups using NBS analysis. In addition, diffusion entropy maps were produced from DTI data sets using in-house software, RESULTS; MS subjects exhibited significantly reduced mean FA and entropy in 38 and 34 regions, respectively, out of a total of 54 regions. The connectivity values in both structural and functional analyses were decreased in most regions of the default mode network and in four other cognitive networks in MS subjects compared to healthy controls. MS also induced significant reduction in the normalized hippocampus and corpus callosum volumes: the normalized hippocampus volume was significantly correlated with EDSS scores. CONCLUSION: MS subjects have significant white matter damage and reduction of FA and entropy in various brain regions involved in cognitive networks. Structural and functional connectivity within the default mode network and an additional four cognitive networks exhibited significant changes compared with healthy controls.

#### <u>Neurology</u>

Venkat P, Ning R, Zacharek A, Culmone L, Liang L, Landschoot-Ward J, and Chopp M. Treatment with an Angiopoietin-1 mimetic peptide promotes neurological recovery after stroke in diabetic rats. *CNS Neurosci Ther* 2020. PMID: 33346402. Full Text

Department of Neurology, Henry Ford Hospital, Detroit, Michigan, USA. Department of Physics, Oakland University, Rochester, Michigan, USA.

AIM: Vasculotide (VT), an angiopoietin-1 mimetic peptide, exerts neuroprotective effects in type one diabetic (T1DM) rats subjected to ischemic stroke. In this study, we investigated whether delayed VT treatment improves long-term neurological outcome after stroke in T1DM rats. METHODS: Male Wistar rats were induced with T1DM, subjected to middle cerebral artery occlusion (MCAo) model of stroke, and

treated with PBS (control), 2 µg/kg VT, 3 µg/kg VT, or 5.5 µg/kg VT. VT treatment was initiated at 24 h after stroke and administered daily (i.p.) for 14 days. We evaluated neurological function, lesion volume. vascular and white matter remodeling, and inflammation in the ischemic brain. In vitro, we evaluated the effects of VT on endothelial cell capillary tube formation and inflammatory responses of primary cortical neurons (PCN) and macrophages. RESULTS: Treatment of T1DM-stroke with 3 µg/kg VT but not 2 µg/kg or 5.5 µg/kg significantly improves neurological function and decreases infarct volume and cell death compared to control T1DM-stroke rats. Thus, 3 µg/kg VT dose was employed in all subsequent in vivo analysis. VT treatment significantly increases axon and myelin density, decreases demyelination. decreases white matter injury, increases number of oligodendrocytes, and increases vascular density in the ischemic border zone of T1DM stroke rats. VT treatment significantly decreases MMP9 expression and decreases the number of M1 macrophages in the ischemic brain of T1DM-stroke rats. In vitro, VT treatment significantly decreases endothelial cell death and decreases MCP-1, endothelin-1, and VEGF expression under high glucose (HG) and ischemic conditions and significantly increases capillary tube formation under HG conditions when compared to non-treated control group. VT treatment significantly decreases inflammatory factor expression such as MMP9 and MCP-1 in macrophages subjected to LPS activation and significantly decreases IL-1β and MMP9 expression in PCN subjected to ischemia under HG conditions. CONCLUSION: Delayed VT treatment (24 h after stroke) significantly improves neurological function, promotes vascular and white matter remodeling, and decreases inflammation in the ischemic brain after stroke in T1DM rats.

## Neurology

Viarasilpa T, Panyavachiraporn N, Osman G, Kowalski RG, Miller J, Barkley GL, and Mayer SA. Differentiation of psychogenic nonepileptic attacks from status epilepticus among patients intubated for convulsive activity. *Epilepsy Behav* 2020; 115:107679. PMID: 33360401. Full Text

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BACKGROUND AND OBJECTIVE: Patients with psychogenic nonepileptic attacks (PNEA) sometimes receive aggressive treatment leading to intubation. This study aimed to identify patient characteristics that can help differentiate PNEA from status epilepticus (SE). METHODS: We retrospectively identified patients with a final diagnosis of PNEA or SE, who were intubated for emergent convulsive symptoms and underwent continuous electroencephalography (cEEG) between 2012 and 2017. Patients who had acute brain injury or progressive brain disease as the cause of SE were excluded. We compared clinical features and laboratory values between the two groups, and identified risk factors for PNEA-related convulsive activity. RESULTS: Over a six-year period, 24 of 148 consecutive patients (16%) intubated for convulsive activity had a final diagnosis of PNEA rather than SE. Compared to patients intubated for SE. intubated PNEA patients more likely were <50 years of age, female, white, had a history of a psychiatric disorder, had no history of an intracranial abnormality, and had a maximum systolic blood pressure <140 mm Hg (all P < 0.001). Patients with 0-2 of these six risk factors had a 0% (0/88) likelihood of having PNEA, those with 3-4 had a 15% (6/39) chance of having PNEA, and those with 5-6 had an 86% (18/21) chance of having PNEA. Sensitivity for PNEA among those with 5-6 risk factors was 75% (95% CI: 53-89%) and specificity was 98% (95% CI: 93-99%). CONCLUSIONS: In the absence of a clear precipitating brain injury, approximately one in six patients intubated for emergent convulsive symptoms had PNEA rather than SE. Although PNEA cannot be diagnosed only by the presence of these risk factors, these

simple characteristics could raise clinical suspicion for PNEA in the appropriate setting. Urgent neurological consultation may prevent unnecessary intubation of this at-risk patient population.

## Neurology

Zaganas I, Mastorodemos V, Spilioti M, Mathioudakis L, Latsoudis H, Michaelidou K, Kotzamani D, Notas K, Dimitrakopoulos K, Skoula I, Ioannidis S, Klothaki E, Erimaki S, Stavropoulos G, Vassilikos V, Amoiridis G, Efthimiadis G, Evangeliou A, and **Mitsias P**. Genetic cause of heterogeneous inherited myopathies in a cohort of Greek patients. *Molecular Genetics and Metabolism Reports* 2020; 25. <u>Full Text</u>

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Inherited muscle disorders are caused by pathogenic changes in numerous genes. Herein, we aimed to investigate the etiology of muscle disease in 24 consecutive Greek patients with myopathy suspected to be genetic in origin, based on clinical presentation and laboratory and electrophysiological findings and absence of known acquired causes of myopathy. Of these, 16 patients (8 females, median 24 years-old, range 7 to 67 years-old) were diagnosed by Whole Exome Sequencing as suffering from a specific type of inherited muscle disorder. Specifically, we have identified causative variants in 6 limb-girdle muscular dystrophy genes (6 patients; ANO5, CAPN3, DYSF, ISPD, LAMA2, SGCA), 3 metabolic myopathy genes (4 patients; CPT2, ETFDH, GAA), 1 congenital myotonia gene (1 patient; CLCN1), 1 mitochondrial myopathy gene (1 patient; MT-TE) and 3 other myopathy-associated genes (4 patients; CAV3, LMNA, MYOT). In 6 additional family members affected by myopathy, we reached genetic diagnosis following identification of a causative variant in an index patient. In our patients, genetic diagnosis ended a lengthy diagnostic process and, in the case of Multiple acyl-CoA dehydrogenase deficiency and Pompe's disease, it enabled specific treatment to be initiated. These results further expand the genotypic and phenotypic spectrum of inherited myopathies.

## Neurosurgery

De Bonis P, Musio A, Mongardi L, Lofrese G, **La Marca F**, Visani J, Cavallo MA, and Scerrati A. Transpars approach for L5-S1 foraminal and extra-foraminal lumbar disc herniations: technical note. *J Neurosurg Sci* 2020. PMID: 33297610. Request Article

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BACKGROUND: The short pars and the narrowed surgical corridor for far lateral L5S1 herniation make the transpars approach challenging. The aim of this study is to determine the feasibility, efficacy and safety of the transpars microscopic approach for the treatment of L5-S1 foraminal and extraforaminal lumbar disc herniation. METHODS: From 2015 to 2019, patients with L5-S1 far lateral lumbar disc herniation were prospectively recruited. Drug intake, working days lost, NRS-leg, NRS-back, nerve-root palsy, Oswestry disability-index, Macnab criteria were recorded before surgery and at follow-up. Patients were seen at 1-6-12 months after surgery. Lumbar dynamic x-rays were performed at 6-12 months after surgery and again at 2-4 years after surgery. Key-steps of surgery are described. RESULTS: Fourteen patients were enrolled. NRS-leg and NRS-back scores significantly improved (from 7.93 to 1.43 and from 3.2 to 0.6, respectively-p<0.0001). Oswestry score significantly decreased (from 63.14 to 19.36 at 12 months; p<0.0001). L5 Root palsy improved in all cases (from 3.72/5 to 5/5; p<0.0001). At 12-months, excellent or good outcome (Macnab criteria) was achieved in 12 (85.7%) and 2 (14.3%) patients, respectively. All patients who were not retired returned to work within 30 days after surgery. No recurrence, instability or re-operations occurred. CONCLUSIONS: The trans pars microscopic approach is feasible, safe and effective for L5-S1 foraminal and extraforaminal disc herniation. During surgery, the

key-point is the oblique working angle, directed caudally, parallel to L5 pedicle. The iliac crest does not seem to constitute an obstacle.

#### Neurosurgery

Noll KR, **Walbert T**, and Wefel JS. Impaired neurocognitive function in glioma patients: from pathophysiology to novel intervention strategies. *Curr Opin Neurol* 2020; 33(6):716-722. PMID: 33009006. Full Text

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PURPOSE OF REVIEW: This review succinctly summarizes the recent literature regarding etiological contributors to impaired neurocognitive function (NCF) in adult patients with glioma. A brief overview of intervention and prevention strategies is also provided. RECENT FINDINGS: A majority of patients with glioma exhibit NCF deficits, most frequently in memory and executive functioning. Impairments are often disabling and associated with reduced quality of life and survival. Cause is multifactorial and includes the tumour itself, treatments received and associated comorbidities. Although modern techniques such as brain mapping, dosing modifications and prophylactic medication aim to improve the NCF outcomes following neurosurgical resection and radiation therapy, a sizeable proportion of patients continue to evidence treatment-related NCF declines related to adverse effects to both local and distributed cerebral networks. Numerous patient and tumour characteristics, including genetic markers and sociodemographic factors, influence the pattern and severity of NCF impairment. Some rehabilitative and pharmacologic approaches show promise in mitigating NCF impairment in this population, though benefits are somewhat modest and larger scale intervention studies are needed. SUMMARY: Research regarding NCF in patients with glioma has dramatically proliferated, providing insights into the mechanisms underlying impaired NCF and pointing to potential interventions, though further work is needed.

## Neurosurgery

Park P, Chang V, Yeh HH, Schwalb JM, Nerenz DR, Schultz LR, Abdulhak MM, Easton R, Perez-Cruet M, Kashlan ON, Oppenlander ME, Szerlip NJ, Swong KN, and Aleem IS. Impact of Michigan's new opioid prescribing laws on spine surgery patients: analysis of the Michigan Spine Surgery Improvement Collaborative. *J Neurosurg Spine* 2020:1-6. PMID: 33307531. Full Text

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OBJECTIVE: In 2017, Michigan passed new legislation designed to reduce opioid abuse. This study evaluated the impact of these new restrictive laws on preoperative narcotic use, short-term outcomes, and readmission rates after spinal surgery. METHODS: Patient data from 1 year before and 1 year after initiation of the new opioid laws (beginning July 1, 2018) were queried from the Michigan Spine Surgery Improvement Collaborative database. Before and after implementation of the major elements of the new laws, 12,325 and 11,988 patients, respectively, were treated. RESULTS: Patients before and after passage of the opioid laws had generally similar demographic and surgical characteristics. Notably, after passage of the opioid laws, the number of patients taking daily narcotics preoperatively decreased from 3783 (48.7%) to 2698 (39.7%; p < 0.0001). Three months postoperatively, there were no differences in minimum clinically important difference (56.0% vs 58.0%, p = 0.1068), numeric rating scale (NRS) score of back pain (3.5 vs 3.4, p = 0.1156), NRS score of leg pain (2.7 vs 2.7, p = 0.3595), satisfaction (84.4% vs 84.7%, p = 0.6852), or 90-day readmission rate (5.8% vs 6.2%, p = 0.3202) between groups. Although there was no difference in readmission rates, pain as a reason for readmission was marginally more

common (0.86% vs 1.22%, p = 0.0323). CONCLUSIONS: There was a meaningful decrease in preoperative narcotic use, but notably there was no apparent negative impact on postoperative recovery, patient satisfaction, or short-term outcomes after spinal surgery despite more restrictive opioid prescribing. Although the readmission rate did not significantly increase, pain as a reason for readmission was marginally more frequently observed.

### Neurosurgery

Raslan AM, Ben-Haim S, Falowski SM, Machado AG, Miller J, Pilitsis JG, Rosenberg WS, Rosenow JM, Sweet J, Viswanathan A, Winfree CJ, and **Schwalb JM**. Congress of Neurological Surgeons Systematic Review and Evidence-Based Guideline on Neuroablative Procedures for Patients With Cancer Pain. *Neurosurgery* 2020. PMID: 33355345. Full Text

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BACKGROUND: Managing cancer pain once it is refractory to conventional treatment continues to challenge caregivers committed to serving those who are suffering from a malignancy. Although neuromodulation has a role in the treatment of cancer pain for some patients, these therapies may not be suitable for all patients. Therefore, neuroablative procedures, which were once a mainstay in treating intractable cancer pain, are again on the rise. This guideline serves as a systematic review of the literature of the outcomes following neuroablative procedures. OBJECTIVE: To establish clinical practice quidelines for the use of neuroablative procedures to treat patients with cancer pain, METHODS: A systematic review of neuroablative procedures used to treat patients with cancer pain from 1980 to April 2019 was performed using the United States National Library of Medicine PubMed database, EMBASE, and Cochrane CENTRAL. After inclusion criteria were established, full text articles that met the inclusion criteria were reviewed by 2 members of the task force and the quality of the evidence was graded. RESULTS: In total, 14 646 relevant abstracts were identified by the literature search, from which 189 met initial screening criteria. After full text review, 58 of the 189 articles were included and subdivided into 4 different clinical scenarios. These include unilateral somatic nociceptive/neuropathic body cancer pain, craniofacial cancer pain, midline subdiaphragmatic visceral cancer pain, and disseminated cancer pain. Class II and III evidence was available for these 4 clinical scenarios. Level III recommendations were developed for the use of neuroablative procedures to treat patients with cancer pain. CONCLUSION: Neuroablative procedures may be an option for treating patients with refractory cancer pain. Serious adverse events were reported in some studies, but were relatively uncommon. Improved imaging, refinements in technique and the availability of new lesioning modalities may minimize the risks of neuroablation even further. The full guidelines can be accessed at https://www.cns.org/guidelines/browseguidelines-detail/guidelines-on-neuroablative-procedures-patients-wi.

## <u>Nursing</u>

**McCord J, Hana A, Cook B, Hudson MP, Miller J,** Akoegbe G, Mueller C, **Moyer M**, Jacobsen G, and **Nowak R**. The Role of Cardiac Testing with the 0/1-Hour High-Sensitivity Cardiac Troponin Algorithm Evaluating for Acute Myocardial Infarction. *Am Heart J* 2020. PMID: 33373603. Full Text

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BACKGROUND: The role of cardiac testing in the 3 zones (rule-out, observation, and rule-in) of the 0/1-hour algorithm to evaluate for acute myocardial infarction (AMI) has not been well-studied. This study evaluated the 0/1-hour algorithm with a high-sensitivity cardiac troponin (hs-cTnI) assay and investigated cardiac testing in the 3 zones. METHODS: Patients (n = 552) at a single urban center were enrolled if they were evaluated for AMI. Blood samples were obtained at presentation, 1 hour, and 3 hours for hs-cTnI. Follow-up at 30-45 days for death/AMI was done. The results of echocardiograms, stress testing, and coronary angiography were recorded. RESULTS: In total, 45 (8.2%) had AMI (27 Type 1 and 18 Type 2) during the index hospitalization while at follow-up death/AMI occurred in 11 (2.0%) of patients. The rule-out algorithm had a negative predictive value for AMI of 99.6% while the rule-in zone had a positive predictive value of 56.6%. The MACE rate at follow-up was 0.4% for those in the rule-out group. There were 6/95 (6.3%) abnormal stress tests in the rule-out zone and 4 of these were false positives. CONCLUSIONS: The 0/1-hour algorithm had high diagnostic sensitivity and negative predictive value for AMI, and adverse events were very low in patients in the rule-out zone. Noninvasive testing in rule-out zone patients had low diagnostic yield.

## Nursing

VanBlarcom AG, **Wojack CA**, and Casida J. Cardiac Tamponade Following the Removal of Epicardial Pacing Wires: Critical Care APRN Toolkit. *AACN Adv Crit Care* 2020; 31(4):410-415. PMID: 33313709. Request Article

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### Obstetrics, Gynecology, and Women's Health Services

**Briskin R**, and **Atiemo H**. Case - Unique complication of continent catheterizable stoma after bariatric surgery. *Can Urol Assoc J* 2020. PMID: 33382367. Full Text

# Obstetrics, Gynecology, and Women's Health Services

Singh PK, Singh S, Wright RE, 3rd, **Rattan R**, and Kumar A. Aging, But Not Sex and Genetic Diversity, Impacts the Pathobiology of Bacterial Endophthalmitis. *Invest Ophthalmol Vis Sci* 2020; 61(14):5. PMID: 33263715. Full Text

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PURPOSE: Age, sex, and genetics are important biological variables in determining an individual's susceptibility or response to infectious agents; however, their role has not been evaluated in intraocular

infections. In this study, we comprehensively examined the impact of these host biological factors in the pathogenesis of experimental bacterial endophthalmitis. METHODS: Endophthalmitis was induced by intravitreal injection of bacteria (Staphylococcus aureus) in the eyes of male and female C57BL/6 mice of different ages: group I (young, 6-8 weeks), group II (mid-age, 18-20 weeks), and group III (old, 1 year). Highly heterogeneous outbred J:DO mice were used for genetic diversity analysis. Eves were subjected to clinical examination, retinal function testing using electroretinography (ERG), histopathological analysis (hematoxylin and eosin staining), and bacterial burden estimation. The levels of inflammatory mediators were measured using gPCR and ELISA, and the infiltration of neutrophils was determined by flow cytometry. RESULTS: Both inbred C57BL/6 and diversity outbred (J:DO) mice were equally susceptible to S. aureus endophthalmitis, as evidenced by a time-dependent increase in clinical scores, bacterial burden, intraocular inflammation, and retinal tissue damage, in addition to decreased retinal function. However, no significant differences were observed in disease severity and innate responses in male versus female mice. Older mice (group III) exhibited higher clinical scores coinciding with increased bacterial proliferation and intraocular inflammation, resulting in enhanced disease severity. Moreover, bone-marrow-derived macrophages from old mice exhibited reduced phagocytic activity but increased inflammatory response toward S. aureus challenge. CONCLUSIONS: Age, but not sex, is an important biological variable in bacterial endophthalmitis. Identification of pathways underlying altered innate immunity and impaired bacterial clearance in aging eyes could provide new insights into the pathobiology of intraocular infections in elderly patients.

## Ophthalmology and Eye Care Services

**Zhang F**. Special communication for deaf patients during topical anesthesia cataract surgery. *American Journal of Ophthalmology Case Reports* 2020; 20. Full Text

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Purpose: To report a new method for communication with deaf patients during topical anesthetic cataract surgery. Observation: Due to communication difficulty, topical anesthesia was traditionally considered by many cataract surgeons as a contraindication for deaf patients. Retrobulbar/peribulbar-block anesthesia or general anesthesia were recommended. This paper reports a new way of communication using face-tapping and hand-pressing. It worked well with three deaf patients under conventional topical anesthetic cataract surgery. Conclusion and Importance: The face-tapping and hand-pressing communication technique with deaf patients under conventional topical anesthetic cataract surgery seemed to work well. Topical anesthesia combined with this "touching language" could be an alternative to traditional local block and general anesthesia for deaf patients undergoing cataract surgery. Large studies are recommended to confirm its safety and validation.

## Orthopaedics/Bone and Joint

Jiang Y, Chen C, Zhang X, Chen C, Zhou Y, Ni G, **Muh S**, and Lemos S. Shoulder muscle activation pattern recognition based on sEMG and machine learning algorithms. *Comput Methods Programs Biomed* 2020; 197:105721. PMID: 32882593. Full Text

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BACKGROUND AND OBJECTIVE: Surface electromyography (sEMG) has been used for robotic rehabilitation engineering for volitional control of hand prostheses or elbow exoskeleton, however, using sEMG for volitional control of an upper limb exoskeleton has not been perfectly developed. The long-term goal of our study is to process shoulder muscle bio-electrical signals for rehabilitative robotic assistive device motion control. The purposes of this study included: 1) to test the feasibility of machine learning algorithms in shoulder motion pattern recognition using sEMG signals from shoulder and upper limb muscles, 2) to investigate the influence of motion speed, individual variability, EMG recording device, and the amount of EMG datasets on the shoulder motion pattern recognition accuracy. METHODS: A novel convolutional neural network (CNN) structure was constructed to process EMG signals from 12 muscles for the pattern recognition of upper arm motions including resting, drinking, backward-forward motion, and abduction motion. The accuracy of the CNN models for pattern recognition under different motion speeds, among individuals, and by EMG recording devices was statistically analyzed using ANOVA, GLM Univariate analysis, and Chi-square tests. The influence of EMG dataset number used for CNN model training on recognition accuracy was studied by gradually increasing dataset number until the highest accuracy was obtained. RESULTS: Results showed that the accuracy of the normal speed CNN model in motion pattern recognition was 97.57% for normal speed motions and 97.07% for fast speed motions. The accuracy of the cross-subjects CNN model in motion pattern recognition was 79.64%. The accuracy of the cross-device CNN model in motion pattern recognition was 88.93% for normal speed motion and 80.87% for mixed speed. There was a statistical difference in pattern recognition accuracy between different CNN models. CONCLUSION: The EMG signals of shoulder and upper arm muscles from the upper limb motions can be processed using CNN algorithms to recognize the identical motions of the upper limb including drinking, forward/backward, abduction, and resting. A simple CNN model trained by EMG datasets of a designated motion speed accurately detected the motion patterns of the same motion speed, yielding the highest accuracy compared with other mixed CNN models for various speeds of motion pattern recognition. Increase of the number of EMG datasets for CNN model training improved the pattern recognition accuracy.

### Orthopaedics/Bone and Joint

Khalil LS, Meta FS, Tramer JS, Klochko CL, Scher C, Van Holsbeeck M, Kolowich PA, Makhni EC, Moutzouros V, and Okoroha KR. Elbow Torque is Reduced in Asymptomatic College Pitchers with Elbow Laxity: A Dynamic Ultrasound Study. *Arthroscopy* 2020. PMID: 33359823. Full Text

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PURPOSE: To determine the relationship between medial elbow torque, as measured by wearable sensor technology, and adaptations of the medial elbow structures on dynamic ultrasound imaging in asymptomatic collegiate pitchers. METHODS: Thirty-four pitchers from NCAA DII universities were eligible for preseason testing. Exclusion criteria included age <18, history of surgery, non-pitcher, or current restrictions. Pitchers were fitted with a wearable sensor sleeve which recorded elbow torque, arm slot, arm speed, and arm rotation. Pitchers threw 5 fastballs in a standardized manner off the mound at game-speed effort. Pitchers also underwent dynamic ultrasound imaging of their elbow by a musculoskeletal sonographer, with standardized valgus loading. Images were deidentified and measurements of the ulnar collateral ligament (UCL) and ulnohumeral joint space (UHJS), to assess elbow laxity, were performed by a musculoskeletal radiologist. RESULTS: Final analysis included 28 pitchers with average (standard deviation) age of 20.1(1.3) years [range 18-23] and playing experience of 15.3(1.8) years [range 11-19]. Dominant UCL thickness (p<.001), loaded UHJS (p=0.039), and delta UHJS (p<.001) were significantly greater than non-dominant. There was an inverse correlation between loaded UHJS and medial elbow torque (r =-0.4, p<.001). Additionally, every 1mm increase in UHJS significantly reduced medial elbow torque by 2.27Nm (p=0.032) and arm slot by 8.8° (p=0.019), and increased arm rotation by 5.3° (p=0.043). Pitchers with loaded UHJS ≥4.4mm and delta UHJS ≥1.25mm had significantly reduced medial elbow torque (p<.001). Pitchers with UCL thickness ≥1.65mm had significantly increased medial elbow torque (47.4 vs 44.8Nm, p=0.006). CONCLUSIONS: Pitchers with

increased dynamic elbow laxity were found to experience reduced medial elbow torque while pitching. Additionally, pitchers with greater UCL thickness on ultrasound were found to experience increased medial elbow torque while pitching. This study's findings suggest a relationship between anatomical adaptations found on ultrasound of the pitching elbow and medial elbow torque.

### Orthopaedics/Bone and Joint

**Lizzio VA**, **Smith DG**, **Guo EW**, **Cross AG**, **Gulledge CM**, **Koolmees DS**, Chalmers PN, and **Makhni EC**. The Effect of the Crow Hop on Elbow Stress During an Interval Throwing Program. *Am J Sports Med* 2020:363546520976629. PMID: 33378223. Full Text

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BACKGROUND: Postoperative rehabilitation protocols after ulnar collateral ligament (UCL) reconstruction typically involve a structured interval throwing program. In an effort to minimize torque placed on the UCL, athletes are often instructed to throw with a crow hop, even at short throwing distances. However, the effect of the crow hop on medial elbow stress is unknown, PURPOSE/HYPOTHESIS: The purpose was to determine whether elbow stress differs with and without a crow hop across the throwing distances of a typical interval throwing program. We hypothesized that crow hop throws would generate lower torque on the elbow than standing throws at each distance of the interval throwing program. STUDY DESIGN: Controlled laboratory study. METHODS: Healthy high school and collegiate pitchers and position players were recruited from the surrounding area. Each player was outfitted with a wearable athletic sleeve and device that recorded elbow torque (Newton-meters), arm slot (degrees), arm speed (revolutions per minute), and shoulder rotation (degrees). Ball velocity (miles per hour) was measured using a radar gun. Players were instructed to perform 3 crow hop throws and 3 standing throws at distances of 30, 45, 60. 90, 120, 150, and 180 feet. A repeated measures analysis of variance was used to compare ball velocity, elbow torque, arm slot, arm speed, and shoulder rotation between crow hop and standing throws at each throwing distance. RESULTS: Twenty athletes participated in this study (average age, 17.8 years; range, 15-25 years). The average medial elbow torque increased at each distance for both crow hop and standing throws at distances of 30, 45, 60, and 90 feet (P < .05), after which there were no significant increases in elbow torque (P > .05). The average torque was higher for crow hop throws than standing throws at distances of 30 feet (13.9 N·m vs 12.0 N·m; P = .002), 45 feet (21.8 N·m vs 19.3 N·m; P = .005), and 60 feet (28.0 N·m vs 24.5 N·m; P = .02). CONCLUSION: Crow hop throws generated greater medial elbow torque than standing throws at distances up to 60 feet; however, there were no differences in elbow torque at distances greater than 60 feet between the 2 throw types. For both crow hop and standing throws, elbow stress increased at each distance interval up to 90 feet before plateauing at distances greater than 90 feet. The crow hop throwing technique does not reduce medial elbow stress during a simulated interval throwing program, and it may actually increase torque at shorter throwing distances. CLINICAL RELEVANCE: The results of our study indicate that it would be prudent for players to initially perform standing throws at shorter distances and only later be allowed to employ a natural crow hop at greater distances to minimize torque placed on the medial elbow during UCL rehabilitation protocols.

### Orthopaedics/Bone and Joint

**Makhni EC**, Makhni S, and Ramkumar PN. Artificial Intelligence for the Orthopaedic Surgeon: An Overview of Potential Benefits, Limitations, and Clinical Applications. *J Am Acad Orthop Surg* 2020. PMID: 33323681. Full Text

Henry Ford Hospital (E. C. Makhni), Detroit, MI, Department of Medicine (S. Makhni), University of Chicago, Chicago, IL, and Orthopaedic Machine Learning Laboratory (Ramkumar), Cleveland Clinic, Cleveland, OH.

Artificial intelligence (AI), along with its subset technology machine learning, has transformed numerous industries through newfound efficiencies and supportive decision-making. These technologies have similarly begun to find application within United States healthcare, particularly orthopaedics. Although these modalities have the potential to similarly transform health care, there exist limitations that must also

be recognized and understood. Unfortunately, most clinicians do not have an understanding of the fundamentals of AI and therefore may have challenges in contextualizing its impact in modern healthcare. The purpose of this review was to provide an overview of the key concepts of AI and machine learning with the orthopaedic surgeon in mind. The review further highlights the potential benefits and limitations of AI, along with an overview of its applications, in orthopaedics.

### Orthopaedics/Bone and Joint

Yeni YN, Oravec D, Drost J, Bevins N, Morrison C, and Flynn MJ. Bone health assessment via digital wrist tomosynthesis in the mammography setting. *Bone* 2020; 144:115804. PMID: 33321264. Full Text

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Bone fractures attributable to osteoporosis are a significant problem. Though preventative treatment options are available for individuals who are at risk of a fracture, a substantial number of these individuals are not identified due to lack of adherence to bone screening recommendations. The issue is further complicated as standard diagnosis of osteoporosis is based on bone mineral density (BMD) derived from dual energy x-ray absorptiometry (DXA), which, while helpful in identifying many at risk, is limited in fully predicting risk of fracture. It is reasonable to expect that bone screening would become more prevalent and efficacious if offered in coordination with digital breast tomosynthesis (DBT) exams, provided that osteoporosis can be assessed using a DBT modality. Therefore, the objective of the current study was to explore the feasibility of using digital tomosynthesis imaging in a mammography setting. To this end, we measured density, cortical thickness and microstructural properties of the wrist bone, correlated these to reference measurements from microcomputed tomography and DXA, demonstrated the application in vivo in a small group of participants, and determined the repeatability of the measurements. We found that measurements from digital wrist tomosynthesis (DWT) imaging with a DBT scanner were highly repeatable ex vivo (error = 0.05%-9.62%) and in vivo (error = 0.06%-10.2%). In ex vivo trials, DWT derived BMDs were strongly correlated with reference measurements (R = 0.841-0.980), as were cortical thickness measured at lateral and medial cortices (R = 0.991 and R = 0.959, respectively) and the majority of microstructural measures (R = 0.736-0.991). The measurements were quick and tolerated by human patients with no discomfort, and appeared to be different between young and old participants in a preliminary comparison. In conclusion, DWT is feasible in a mammography setting, and informative on bone mass, cortical thickness, and microstructural qualities that are known to deteriorate in osteoporosis. To our knowledge, this study represents the first application of DBT for imaging bone. Future clinical studies are needed to further establish the efficacy for diagnosing osteoporosis and predicting risk of fragility fracture using DWT.

## Orthopaedics/Bone and Joint

Zheng JP, He X, Liu F, Yin S, Wu S, **Yang M**, Zhao J, Dai X, Jiang H, Yu L, Yin Q, Ju D, Li C, Lipovich L, Xie Y, Zhang K, Li HJ, Zhou J, and Li L. YY1 directly interacts with myocardin to repress the triad myocardin/SRF/CArG box-mediated smooth muscle gene transcription during smooth muscle phenotypic modulation. *Sci Rep* 2020; 10(1):21781. PMID: 33311559. <u>Full Text</u>

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Yin Yang 1 (YY1) regulates gene transcription in a variety of biological processes. In this study, we aim to determine the role of YY1 in vascular smooth muscle cell (VSMC) phenotypic modulation both in vivo and in vitro. Here we show that vascular injury in rodent carotid arteries induces YY1 expression along with reduced expression of smooth muscle differentiation markers in the carotids. Consistent with this finding, YY1 expression is induced in differentiated VSMCs in response to serum stimulation. To determine the underlying molecular mechanisms, we found that YY1 suppresses the transcription of CArG box-dependent SMC-specific genes including SM22α, SMα-actin and SMMHC. Interestingly, YY1 suppresses the transcriptional activity of the SM22α promoter by hindering the binding of serum response factor (SRF) to the proximal CArG box. YY1 also suppresses the transcription and the transactivation of myocardin (MYOCD), a master regulator for SMC-specific gene transcription by binding to SRF to form the MYOCD/SRF/CArG box triad (known as the ternary complex). Mechanistically, YY1 directly interacts with MYOCD to competitively displace MYOCD from SRF. This is the first evidence showing that YY1 inhibits SMC differentiation by directly targeting MYOCD. These findings provide new mechanistic insights into the regulatory mechanisms that govern SMC phenotypic modulation in the pathogenesis of vascular diseases.

### Otolaryngology – Head and Neck Surgery

Amit M, Liu C, Gleber-Netto FO, Kini S, **Tam S**, Benov A, Aashiq M, El-Naggar AK, Moreno AC, Rosenthal DI, Glisson BS, Ferrarotto R, Wong MK, Migden MR, Baruch EN, Li G, Khanna A, Goepfert RP, Nagarajan P, Weber RS, Myers JN, and Gross ND. Inclusion of extranodal extension in the lymph node classification of cutaneous squamous cell carcinoma of the head and neck. *Cancer* 2020. PMID: 33320343. Full Text

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BACKGROUND: The prognostic performance of the recently updated American Joint Committee on Cancer lymph node classification of cutaneous head and neck squamous cell carcinoma (HNSCC) has not been validated. The objective of this study was to assess the prognostic role of extranodal extension (ENE) in cutaneous HNSCC. METHODS: This was a retrospective analysis of 1258 patients with cutaneous HNSCC who underwent surgery with or without adjuvant therapy between 1995 and 2019 at The University of Texas MD Anderson Cancer Center. The primary outcome was disease-specific survival (DSS). Local, regional, and distant metastases-free survival were secondary outcomes. Recursive partitioning analysis (RPA) and a Cox proportional hazards regression model were used to assess the

fitness of staging models. RESULTS: No significant differences in 5-year DSS were observed between patients with pathologic lymph node-negative (pN0) disease (67.4%) and those with pN-positive/ENE-negative disease (68.2%; hazard ratio, 1.02; 95% CI, 0.61-1.79) or between patients with pN-positive/ENE-negative disease and those with pN-positive/ENE-positive disease (52.7%; hazard ratio, 0.57; 95% CI, 0.31-1.01). The RPA-derived model achieved better stratification between high-risk patients (category III, ENE-positive with >2 positive lymph nodes) and low-risk patients (category I, pN0; category II, ENE-positive/pN1 and ENE-negative with >2 positive lymph nodes). The performance of the RPA-derived model was better than that of the pathologic TNM classification (Akaike information criterion score, 1167 compared with 1176; Bayesian information criterion score, 1175 compared with 1195). CONCLUSIONS: The number of metastatic lymph nodes and the presence of ENE are independent prognostic factors for DSS in cutaneous HNSCC, and incorporation of these factors in staging systems improves the performance of the American Joint Committee on Cancer lymph node classification.

### Otolaryngology – Head and Neck Surgery

Amit M, Liu C, Netto Gleber FO, Kini S, **Tam S**, Benov A, Aashiq M, El-Naggar AK, Moreno AC, Rosenthal DI, Glisson BS, Ferrarotto R, Wong MK, Migden MR, Li G, Khanna A, Goepfert RP, Nagarajan P, Weber RS, Myers JN, and Gross ND. Integrating depth of invasion in T classification improves the prognostic performance of the American Joint Committee on Cancer primary tumor staging system for cutaneous squamous cell carcinoma of the head and neck. *Eur J Cancer* 2020; 144:169-177. PMID: 33352413. Full Text

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BACKGROUND: The last revision of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual included a specific system for cutaneous squamous cell carcinoma (CSCC) of the head and neck. Here, we assessed the prognostic performance of six candidate modified T-classification models in head and neck CSCC patients. METHODS: Analysis of 916 patients with head and neck CSCC given treatment with curative intent at The University of Texas MD Anderson Cancer Center between 1995 and 2019 was performed. The main outcome was disease-specific survival (DSS), and the impact of depth of invasion (DOI) was analyzed using multivariable regression models. Candidate models were developed using the optimal DOI cut points for each AJCC T classification based on goodness of fit of the model and the simplicity of the model. Staging systems were compared using Harrell's concordance index. RESULTS: Median age was 70 years (range, 19-97years) and median follow-up time of 22 months (range, 1-250months). The median DOI was 6.0 mm (range, 0.1-70.0 mm), The five-year DSS rate was 80.7% (95%CI, 77.4-83.7%). We found significant association between DOI (hazard ratio, 1.21 [95%CI: 1.01-1.43]) and DSS on multivariable analysis. Based on a low Akaike information criterion score, improvement in the concordance index, and Kaplan-Meier curves, model 6 surpassed the AJCC staging system. CONCLUSIONS: Incorporation of DOI in the current AJCC staging system improves discrimination of T classifications in head and neck CSCC patients. LAY SUMMARY: The current staging system for head and neck cutaneous squamous cell carcinoma demonstrates wide prognostic variability

and provides suboptimal risk stratification. Incorporation of depth of invasion in the T-classification system improves risk prediction and patient counseling. PRECIS: We propose improved head and neck cutaneous squamous cell carcinoma T staging that will include depth of invasion and should be considered in future versions of the American Joint Committee on Cancer after external validation.

### Otolaryngology – Head and Neck Surgery

Bauer AM, **Angster K**, Schuman AD, Thompson BG, and Telian SA. Aberrant AICA Injury During Translabyrinthine Approach. *Otol Neurotol* 2020; 41(10):1423-1426. PMID: 33003181. <u>Full Text</u>

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OBJECTIVE: To define a complication of the translabyrinthine surgical approach to the posterior fossa related to a rare variant of the anterior inferior cerebellar artery (AICA) that penetrated into the petrous temporal bone. PATIENT: A healthy 59-year-old male with a unilateral sporadic vestibular schwannoma. INTERVENTION: The patient elected to undergo a translabyrinthine approach for resection of a vestibular schwannoma. An aberrant loop of AICA was encountered during the temporal bone dissection within the petrous portion of the temporal bone. OUTCOMES: The patient suffered a presumed ischemic insult resulting in a fluctuating ipsilateral facial paresis and atypical postoperative nystagmus. RESULTS: MRI demonstrated an ischemic lesion in the vascular distribution of the right anterior-inferior cerebellar artery, including the lateral portion of the right cerebellar hemisphere, middle cerebellar peduncle, and bordering the right cranial nerve VII nucleus. His functional recovery was excellent, essentially identical to the anticipated course in an otherwise uncomplicated surgery. CONCLUSIONS: This case highlights the irregular anatomy of the AICA as well as the importance of thorough neurological exams in the postsurgical lateral skull base patient.

### Otolaryngology – Head and Neck Surgery

**Craig JR**, and **Deeb RH**. Reconstruction of Anterior Table Frontal Sinus Defects with Pericranial Flap and Titanium Mesh. *Laryngoscope* 2020. PMID: 33258483. Full Text

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#### Pathology and Laboratory Medicine

**Alhamar M**, **Ahsan B**, **Hogan K**, and **Raoufi M**. Appendiceal intussusception presenting as a caecal mass. *Malays J Pathol* 2020; 42(3):483-486. PMID: 33361733. Request Article

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INTRODUCTION: The differential diagnosis of caecal mass is broad and the inclusion of appendiceal pathologies is an important element. CASE REPORT: We report a 37-year-old woman with recurrent right iliac fossa pain. Computed tomography scan revealed a caecal mass suggesting complete inversion or intussusception of the appendix, which was confirmed by pathologic microscopic examination. This case report discusses appendiceal intussusception with emphasis on diagnosis and treatment options. DISCUSSION: Appendiceal intussusception is a rare entity and the complete type typically presents as a polypoid lesion located at the appendiceal orifice in the caecum. It is imperative to include this entity in the differential diagnosis of caecal mass, especially during colonoscopy, as the removal of this polypoid lesion can result in a devastating caecal perforation or haemorrhage.

## Pathology and Laboratory Medicine

Das R, McGrath K, Seiser N, Smith K, Uttam S, Brand RE, Fasanella KE, Khalid A, Chennat JS, Sarkaria S, Singh H, Slivka A, Zeh HJ, Zureikat AH, Hogg ME, Lee K, Paniccia A, Ongchin MC, Pingpank JF, Boone BA, Dasyam AK, Bahary N, Gorantla VC, Rhee JC, Thomas R, Ellsworth S, Landau MS, Ohori

NP, Henn P, Shyu S, **Theisen BK**, and Singhi AD. Tumor Size Differences Between Preoperative Endoscopic Ultrasound and Postoperative Pathology for Neoadjuvant-Treated Pancreatic Ductal Adenocarcinoma Predict Patient Outcome. *Clin Gastroenterol Hepatol* 2020. PMID: 33278573. Full Text

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BACKGROUND & AIMS: The assessment of therapeutic response after neoadjuvant treatment and pancreatectomy for pancreatic ductal adenocarcinoma (PDAC) has been an ongoing challenge. Several limitations have been encountered when employing current grading systems for residual tumor. Considering endoscopic ultrasound (EUS) represents a sensitive imaging technique for PDAC, differences in tumor size between preoperative EUS and postoperative pathology after neoadjuvant therapy was hypothesized to represent an improved marker of treatment response. METHODS: For 340 treatment-naïve and 365 neoadjuvant-treated PDACs, EUS and pathologic findings were analyzed and correlated with patient overall survival (OS). A separate group of 200 neoadjuvant-treated PDACs served as a validation cohort for further analysis. RESULTS: Among treatment-naïve PDACs, there was a moderate concordance between EUS imaging and postoperative pathology for tumor size (r = 0.726, p<0.001) and AJCC 8(th) edition T-stage (r = 0.586, p<0.001). In the setting of neoadjuvant therapy, a decrease in T-stage correlated with improved 3-year OS rates (50% vs. 31%, p<0.001). Through recursive partitioning, a cutoff of ≥47% tumor size reduction was also found to be associated with improved OS (67% vs. 32%, p<0.001). Improved OS using a ≥47% threshold was validated using a separate cohort of neoadiuvant-treated PDACs (72% vs. 36%, p<0.001). By multivariate analysis, a reduction in tumor size by ≥47% was an independent prognostic factor for improved OS (p=0.007). CONCLUSIONS: The difference in tumor size between preoperative EUS imaging and postoperative pathology among neoadjuvant-treated PDAC patients is an important prognostic indicator and may guide subsequent chemotherapeutic management.

## Pathology and Laboratory Medicine

**Friedman BJ**, **Robinson G**, and **Kohen L**. Dermoscopic Features of Spitz Tumor With LMNA-NTRK1 Fusion. *Dermatol Pract Concept* 2021; 11(1):e2020101. PMID: 33354405. Request Article

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## Pathology and Laboratory Medicine

Li P, Zhang D, Zhou J, Li P, **Shen Y**, Pan Z, Evans AG, and Liao X. Hepatic involvement by T-cell neoplasms: a clinicopathologic study of 40 cases. *Hum Pathol* 2020; 106:1-12. PMID: 33010300. <u>Full Text</u>

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Hepatic involvement by a T-cell neoplasm is rare and often challenging to diagnose in liver biopsies. We collected 40 cases of T-cell neoplasms diagnosed in the liver from five large academic institutions to assess the clinicopathologic features. The patients included 11 women and 29 men, with a median age of 54 (range: 2-75) years and a high mortality rate (31/37, 83.8%). Fourteen (35%) patients were diagnosed with hepatosplenic T-cell lymphoma (HSTCL), 13 (32.5%) peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS), and 13 (32.5%) other types of T-cell neoplasms. Patients with HSTCL were much younger and had worse survival than PTCL-NOS and other T-cell neoplasms (P < 0.05). On imaging studies, 20 cases (50%) showed abnormalities, including 10 with mass lesions that correlated with normal or cholestatic pattern enzyme elevation. Histomorphological analysis revealed four main patterns: with the exception of mass forming lesions (pattern 4; n = 8), cases with sinusoidal predominant (pattern 1; n = 12), portal predominant with sinusoidal infiltrates (pattern 2; n = 13) or lobular aggregates (pattern 3; n = 5) demonstrated small to medium lymphocytes resembling a reactive/inflammatory process. In addition, we described two cases of T-cell large granular lymphocytic leukemia that mimicked HSTCL, and a case of aggressive post-transplant lymphoproliferative disorder that developed after chronic Epstein-barr virus (EBV) infection, suggesting the importance of EBV testing in some lymphoma cases. As the largest cohort of T-cell neoplasms in liver, our study provides critical data on disease frequency, distribution, and clinicopathologic features that are essential for accurate diagnosis.

## Pathology and Laboratory Medicine

**McCord J**, **Hana A**, **Cook B**, **Hudson MP**, **Miller J**, Akoegbe G, Mueller C, **Moyer M**, Jacobsen G, and **Nowak R**. The Role of Cardiac Testing with the 0/1-Hour High-Sensitivity Cardiac Troponin Algorithm Evaluating for Acute Myocardial Infarction. *Am Heart J* 2020. PMID: 33373603. Full Text

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BACKGROUND: The role of cardiac testing in the 3 zones (rule-out, observation, and rule-in) of the 0/1-hour algorithm to evaluate for acute myocardial infarction (AMI) has not been well-studied. This study evaluated the 0/1-hour algorithm with a high-sensitivity cardiac troponin (hs-cTnI) assay and investigated cardiac testing in the 3 zones. METHODS: Patients (n = 552) at a single urban center were enrolled if they were evaluated for AMI. Blood samples were obtained at presentation, 1 hour, and 3 hours for hs-cTnI. Follow-up at 30-45 days for death/AMI was done. The results of echocardiograms, stress testing, and coronary angiography were recorded. RESULTS: In total, 45 (8.2%) had AMI (27 Type 1 and 18 Type 2) during the index hospitalization while at follow-up death/AMI occurred in 11 (2.0%) of patients. The rule-out algorithm had a negative predictive value for AMI of 99.6% while the rule-in zone had a positive predictive value of 56.6%. The MACE rate at follow-up was 0.4% for those in the rule-out group. There were 6/95 (6.3%) abnormal stress tests in the rule-out zone and 4 of these were false positives. CONCLUSIONS: The 0/1-hour algorithm had high diagnostic sensitivity and negative predictive value for AMI, and adverse events were very low in patients in the rule-out zone. Noninvasive testing in rule-out zone patients had low diagnostic yield.

## Pathology and Laboratory Medicine

**Samuel L**. Point-of-Care Testing in Microbiology. *Clin Lab Med* 2020; 40(4):483-494. PMID: 33121617. Full Text

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Point-of-care (POC) or near patient testing for infectious diseases is a rapidly expanding space that is part of an ongoing effort to bring care closer to the patient. Traditional POC tests were known for their limited utility, but advances in technology have seen significant improvements in performance of these assays. The increasing promise of these tests is also coupled with their increasing complexity, which requires the oversight of qualified laboratory-trained personnel.

### Pathology and Laboratory Medicine

Sardana R, Mishra SK, **Williamson SR**, Mohanty A, and Mohanty SK. Immune checkpoints and their inhibitors: Reappraisal of a novel diagnostic and therapeutic dimension in the urologic malignancies. *Semin Oncol* 2020; 47(6):367-379. PMID: 33160642. Full Text

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Advances in molecular immunology have unveiled some of the complexity of the mechanisms regulating cellular immune responses and led to the successful targeting of immune checkpoints in attempts to enhance antitumor T cell responses. Surgery, chemotherapy, and radiation therapy have been the mainstay of treatment in urologic malignancies. Immune checkpoint molecules such as cytotoxic Tlymphocyte associated protein-4, programmed cell death protein-1, and programmed death-ligand 1 have been shown to play central roles in evading cancer immunity. Thus these molecules have been targeted by inhibitors for the management of cancers forming the basis of immunotherapy. Immunotherapy is now among the first line therapeutic options for metastatic renal cell carcinomas. In advanced bladder cancer, immunotherapy is the standard of care in the second line and the first line for cisplatin ineligible patients. There continues to be ongoing research to identify the role if any of immunotherapy in testicular, prostatic. and penile cancers. The ideal biomarker for response to immunotherapy is still elusive. Although programmed death-ligand 1 immunohistochemical testing has been widely used across the globe as a biomarker for immunotherapy, companion diagnostic tests have inherent issues with testing and reporting and cannot have universal applicability. Additional biomarkers including, tumor mutational burden, deficient mismatch repair, high microsatellite instability, and immune gene expression profiling are being evaluated in various clinical trials. This review appraises the data of immunotherapy in the management of urologic malignancies.

### **Pharmacy**

Liu J, Mercuro NJ, **Davis SL**, Palmo T, Kashyap S, Patel TS, Petty LA, Yarnold PR, Kaye KS, and Scheetz MH. Antimicrobial never events: Objective application of a framework to assess vancomycin appropriateness. *Infect Control Hosp Epidemiol* 2020:1-3. PMID: 33371928. Full Text

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To address appropriateness of antibiotic use, we implemented an electronic framework to evaluate antibiotic "never events" (NEs) at 2 medical centers. Patient-level vancomycin administration records were classified as NEs or non-NEs. The objective framework allowed capture of true-positive vancomycin NEs in one-third of patients identified by the electronic strategy.

### **Public Health Sciences**

Garman L, Pelikan RC, Rasmussen A, Lareau CA, Savoy KA, Deshmukh US, Bagavant H, **Levin AM**, Daouk S, Drake WP, and Montgomery CG. Single Cell Transcriptomics Implicate Novel Monocyte and T Cell Immune Dysregulation in Sarcoidosis. *Front Immunol* 2020; 11:567342. PMID: 33363531. Full Text

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Sarcoidosis is a systemic inflammatory disease characterized by infiltration of immune cells into granulomas. Previous gene expression studies using heterogeneous cell mixtures lack insight into celltype-specific immune dysregulation. We performed the first single-cell RNA-sequencing study of sarcoidosis in peripheral immune cells in 48 patients and controls. Following unbiased clustering, differentially expressed genes were identified for 18 cell types and bioinformatically assessed for function and pathway enrichment. Our results reveal persistent activation of circulating classical monocytes with subsequent upregulation of trafficking molecules. Specifically, classical monocytes upregulated distinct markers of activation including adhesion molecules, pattern recognition receptors, and chemokine receptors, as well as enrichment of immunoregulatory pathways HMGB1, mTOR, and ephrin receptor signaling. Predictive modeling implicated TGFβ and mTOR signaling as drivers of persistent monocyte activation, Additionally, sarcoidosis T cell subsets displayed patterns of dysregulation, CD4 naïve T cells were enriched for markers of apoptosis and Th17/T(reg) differentiation, while effector T cells showed enrichment of anergy-related pathways. Differentially expressed genes in regulatory T cells suggested dysfunctional p53, cell death, and TNFR2 signaling. Using more sensitive technology and more precise units of measure, we identify cell-type specific, novel inflammatory and regulatory pathways. Based on our findings, we suggest a novel model involving four convergent arms of dysregulation: persistent hyperactivation of innate and adaptive immunity via classical monocytes and CD4 naïve T cells, regulatory T cell dysfunction, and effector T cell anergy. We further our understanding of the immunopathology of sarcoidosis and point to novel therapeutic targets.

## Public Health Sciences

**Maahs L**, **Tang A**, **Saheli ZA**, Jacob B, Polasani R, and **Hwang C**. Real-world effectiveness of the pegfilgrastim on-body injector in preventing severe neutropenia. *J Oncol Pharm Pract* 2020:1078155220980517. PMID: 33323023. Full Text

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INTRODUCTION: Granulocyte colony-stimulating factors are used in medical oncology for the prevention of neutropenia. On-body injectors (OBI) have an advantage over the traditional injection (TI) method of

not requiring a second visit to the clinic, but these devices are subject to failure. The objective of this study was to assess the efficacy of OBIs in the real-world. METHODS: Women with breast cancer diagnosed between June 2015 and June 2016 treated with cytotoxic chemotherapy and a granulocyte colony-stimulating factor were retrospectively identified from the medical records of Henry Ford Hospital. The primary outcome was the incidence of severe neutropenia (SN), defined as an absolute neutrophil count (ANC) ≤500. Secondary outcomes included incidence of neutropenia (ANC ≤ 1500), neutropenic fever, and mortality. A secondary analysis of the data was performed to identify predictors of SN. RESULTS: A total of 837 cycles of chemotherapy were analyzed. The OBI was used in 395 cycles and the TI in 442. The OBI group had patients that were older, had higher baseline ANC, and were more often white. The incidences of SN, neutropenic fever and neutropenia were not different between groups. Patients with a lower baseline ANC and white ethnicity were at a higher risk for SN. AC (doxorubicin and cyclophosphamide) was the most commonly used chemotherapy regimen (38% of total cycles). CONCLUSIONS: There was no difference in the efficacy of the OBI and TI methods for preventing SN, neutropenic fever and neutropenia.

#### Public Health Sciences

Miller CJ, Runge-Morris M, **Cassidy-Bushrow AE**, **Straughen JK**, Dittrich TM, Baker TR, Petriello MC, Mor G, Ruden DM, O'Leary BF, Teimoori S, Tummala CM, Heldman S, Agarwal M, Roth K, Yang Z, and Baker BB. A Review of Volatile Organic Compound Contamination in Post-Industrial Urban Centers: Reproductive Health Implications Using a Detroit Lens. *Int J Environ Res Public Health* 2020; 17(23). PMID: 33255777. Full Text

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Volatile organic compounds (VOCs) are a group of aromatic or chlorinated organic chemicals commonly found in manufactured products that have high vapor pressure, and thus vaporize readily at room temperature. While airshed VOCs are well studied and have provided insights into public health issues, we suggest that belowground VOCs and the related vapor intrusion process could be equally or even more relevant to public health. The persistence, movement, remediation, and human health implications of subsurface VOCs in urban landscapes remain relatively understudied despite evidence of widespread contamination. This review explores the state of the science of subsurface movement and remediation of VOCs through groundwater and soils, the linkages between these poorly understood contaminant exposure pathways and health outcomes based on research in various animal models, and describes the role of these contaminants in human health, focusing on birth outcomes, notably low birth weight and preterm birth. Finally, this review provides recommendations for future research to address knowledge gaps that are essential for not only tackling health disparities and environmental injustice in post-industrial cities, but also protecting and preserving critical freshwater resources.

#### Public Health Sciences

Park P, Chang V, Yeh HH, Schwalb JM, Nerenz DR, Schultz LR, Abdulhak MM, Easton R, Perez-Cruet M, Kashlan ON, Oppenlander ME, Szerlip NJ, Swong KN, and Aleem IS. Impact of Michigan's new opioid prescribing laws on spine surgery patients: analysis of the Michigan Spine Surgery Improvement Collaborative. *J Neurosurg Spine* 2020:1-6. PMID: 33307531. Full Text

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OBJECTIVE: In 2017, Michigan passed new legislation designed to reduce opioid abuse. This study evaluated the impact of these new restrictive laws on preoperative narcotic use, short-term outcomes, and readmission rates after spinal surgery. METHODS: Patient data from 1 year before and 1 year after initiation of the new opioid laws (beginning July 1, 2018) were queried from the Michigan Spine Surgery Improvement Collaborative database. Before and after implementation of the major elements of the new laws, 12,325 and 11,988 patients, respectively, were treated. RESULTS: Patients before and after passage of the opioid laws had generally similar demographic and surgical characteristics. Notably, after passage of the opioid laws, the number of patients taking daily narcotics preoperatively decreased from 3783 (48.7%) to 2698 (39.7%; p < 0.0001). Three months postoperatively, there were no differences in minimum clinically important difference (56.0% vs 58.0%, p = 0.1068), numeric rating scale (NRS) score of back pain (3.5 vs 3.4, p = 0.1156), NRS score of leg pain (2.7 vs 2.7, p = 0.3595), satisfaction (84.4% vs 84.7%, p = 0.6852), or 90-day readmission rate (5.8% vs 6.2%, p = 0.3202) between groups. Although there was no difference in readmission rates, pain as a reason for readmission was marginally more common (0.86% vs 1.22%, p = 0.0323). CONCLUSIONS: There was a meaningful decrease in preoperative narcotic use, but notably there was no apparent negative impact on postoperative recovery, patient satisfaction, or short-term outcomes after spinal surgery despite more restrictive opioid prescribing. Although the readmission rate did not significantly increase, pain as a reason for readmission was marginally more frequently observed.

#### Pulmonary and Critical Care Medicine

**Lazar MH**, **Fadel R**, **Gardner-Gray J**, **Tatem G**, **Caldwell MT**, **Swiderek J**, and **Jennings JH**. Racial Differences in a Detroit, MI, ICU Population of Coronavirus Disease 2019 Patients. *Crit Care Med* 2020. PMID: 33372746. Full Text

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OBJECTIVES: To investigate the potential influence of racial differences in outcomes of patients infected by coronavirus disease 2019-positive patients who require intensive care in an urban hospital. DESIGN: Retrospective cohort study. SETTING: Henry Ford Health System Multidisciplinary ICU, a total of 156 beds spread throughout the hospital in Detroit, MI. PATIENTS: We obtained data from the electronic medical record of all adult severe acute respiratory syndrome coronavirus-2-positive patients managed in the ICU of Henry Ford Hospital in Detroit, MI, between March 13, 2020, and July 31, 2020. Included patients were divided into two groups: people of color (including Black, Asian, Hispanic/Latino, and Arab) and White. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: A total of 365 patients were evaluated: 219 were Black (60.0%), 129 were White (35.3%), two were Asian (0.6%), eight were Hispanic/Latino (2.2%), and seven were Arab (1.9%). People of color were younger (62.8 vs 67.1; p = 0.007), with equal distribution of sex, People of color had less coronary artery disease (34 [14,4%] vs 35 [27.1%]; p =0.003) and less self-reported use of regular alcohol consumption (50 [21.2%] vs 12 [9.3%]; p = 0.004) than Whites, with no differences in diabetes (125 [53.0%] vs 66 [51.2%]; p = 0.742), hypertension (188 [79.7%] vs 99 [76.8%]; p = 0.516), congestive heart failure (41 [17.4%] vs 32 [24.8%]; p = 0.090), or chronic kidney disease (123 [54.1%] vs 55 [42.6%]; p = 0.083). There was no difference in ICU length of stay between people of color (18 d [CI, 7-47 d]) and Whites (18 d [CI, 6-48 d]; p = 0. 0.979). Neither frequency (72.5% vs 71.3%; p = ns) nor median time to mechanical ventilation between people of color (9 d [CI, 6-15 d]) and Whites (10 d [CI, 5-16 d]; p = 0.733) was different. Overall, 188 patients (51.5 %) died in the hospital. The 28-day mortality was lower in people of color (107/236; 45.3%) versus Whites (73/129; 56.6%) (adjusted odds ratio 0.60; p = 0.034), and there was an increased median survival time in people of color (20 d) versus Whites (13.5 d; hazard ratio 0.62; p = 0.002). The inhospital mortality was lower in people of color versus White, but the difference was not statistically significant (113 [47.9%] vs 75 [58.1%], respectively; p = 0.061). Finally, there was no significant difference in days of symptoms prior to admission, frequency of presenting symptoms, or frequency or severity of acute respiratory distress syndrome between the two groups. CONCLUSIONS: In critically ill patients infected with coronavirus disease 2019, people of color had a lower 28-day mortality than Whites with no difference in hospital mortality, ICU length of stay, or rates of intubation. These findings are contrary to previously held beliefs surrounding the pandemic.

### Pulmonary and Critical Care Medicine

Zhang Y, Shi L, **Simoff MJ**, Wagner OJ, and Lavin J. Biopsy frequency and complications among lung cancer patients in the United States. *Lung Cancer Management* 2020; 9(4). Full Text

Objective: This study aimed to describe the frequency and distribution of biopsy procedures for patients diagnosed and treated for primary lung cancer. Study design: Retrospective cohort study within an administrative database. Materials & methods: This observational study used data from the IBM MarketScan® Databases between 2013 and 2015. Results: The total number of lung biopsies performed among eligible subjects was 32,814; an average of 1.7 biopsies per patient. Bronchoscopy and percutaneous approaches accounted for 95% of all procedures. Complication rates by procedure are remarkably similar irrespective of biopsy frequency. Conclusion: Nearly half (46%) of patients in this population experienced multiple biopsies prior to diagnosis. Further, biopsy choice or sequence in patients receiving multiple procedures was unpredictable.

### Radiation Oncology

Jagsi R, Griffith KA, Vicini F, Boike T, Burmeister J, Dominello MM, Grills I, Hayman JA, Moran JM, Paximadis P, Radawski JD, **Walker EM**, and Pierce LJ. Toward Improving Patients' Experiences of Acute Toxicity From Breast Radiotherapy: Insights From the Analysis of Patient-Reported Outcomes in a Large Multicenter Cohort. *J Clin Oncol* 2020; 38(34):4019-4029. PMID: 32986529. Full Text

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PURPOSE: Understanding acute toxicities after whole-breast radiotherapy is important to inform patients, guide treatment decisions, and target supportive care. We evaluated patient-reported outcomes prospectively collected from a cohort of patients with breast cancer. METHODS: We describe the maximal toxicity reported by 8,711 patients treated between 2012 and 2019 at 27 practices. Multivariable models identified characteristics associated with (1) breast pain, (2) bother from itching, stinging/burning, swelling, or hurting of the treated breast, and (3) fatigue within 7 days of completing whole-breast radiotherapy. RESULTS: Moderate or severe breast pain was reported by 3,233 (37.1%): 1,282 (28.9%) of those receiving hypofractionation and 1,951 (45.7%) of those receiving conventional fractionation. Frequent bother from at least one breast symptom was reported by 4,424 (50.8%): 1,833 (41.3%) after hypofractionation and 2.591 (60.7%) after conventional fractionation. Severe fatigue was reported by 2,008 (23.1%): 843 (19.0%) after hypofractionation and 1,165 (27.3%) after conventional fractionation. Among patients receiving hypofractionated radiotherapy, younger age (P < .001), higher body mass index (BMI; P < .001), Black (P < .001) or other race (P = .002), smoking status (P < .001), larger breast volume (P = .002), lack of chemotherapy receipt (P = .004), receipt of boost treatment (P < .001), and treatment at a nonteaching center predicted breast pain. Among patients receiving conventionally fractionated radiotherapy, younger age (P < .001), higher BMI (P = .003), Black (P < .001) or other race (P = .002), diabetes (P = .001), smoking status (P < .001), and larger breast volume (P < .001) predicted breast pain. CONCLUSION: In this large observational data set, substantial differences existed according to radiotherapy dose fractionation. Race-related differences in pain existed despite controlling for multiple

other factors; additional research is needed to understand what drives these differences to target potentially modifiable factors. Intensifying supportive care may be appropriate for subgroups identified as being vulnerable to greater toxicity.

### Radiation Oncology

Keall PJ, Sawant A, Berbeco RI, Booth JT, Cho B, Cerviño LI, Cirino E, Dieterich S, Fast MF, Greer PB, Munck Af Rosenschöld P, **Parikh PJ**, Poulsen PR, Santanam L, Sherouse GW, Shi J, and Stathakis S. AAPM Task Group 264: The Safe Clinical Implementation of MLC Tracking in Radiotherapy. *Med Phys* 2020. PMID: 33260251. Full Text

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The era of real-time radiotherapy is upon us. Robotic and gimbaled linac tracking are clinically established technologies with the clinical realization of couch tracking in development. Multileaf collimators (MLCs) are standard equipment for most cancer radiotherapy systems, and therefore MLC tracking is a potentially widely available technology. MLC tracking has been the subject of theoretical and experimental research for decades and was first implemented for patient treatments in 2013. The AAPM Task Group 264-Safe Clinical Implementation of MLC Tracking in Radiotherapy Report was charged to proactively provide the broader radiation oncology community with 1) clinical implementation guidelines including hardware, software, and clinical indications for use, 2) commissioning and quality assurance recommendations based on early user experience, as well as guidelines on Failure Mode and Effects Analysis, and 3) a discussion of potential future developments. The deliverables from this report include: an explanation of MLC tracking and its historical development; terms and definitions relevant to MLC tracking; the clinical benefit of, clinical experience with and clinical implementation guidelines for MLC tracking; quality assurance guidelines, including example quality assurance worksheets; a clinical decision pathway, future outlook and overall recommendations.

#### Rheumatology

Ortiz-Fernández L, Saruhan-Direskeneli G, Alibaz-Oner F, Kaymaz-Tahra S, Coit P, Kong X, Kiprianos AP, Maughan RT, Aydin SZ, Aksu K, Keser G, Kamali S, Inanc M, Springer J, Akar S, Onen F, Akkoc N, Khalidi NA, Koening C, Karadag O, Kiraz S, Forbess L, Langford CA, McAlear CA, Ozbalkan Z, Yavuz S, Çetin GY, Alpay-Kanitez N, Chung S, Ates A, Karaaslan Y, **McKinnon-Maksimowicz K**, Monach PA, Ozer HTE, Seyahi E, Fresko I, Cefle A, Seo P, Warrington KJ, Ozturk MA, Ytterberg SR, Cobankara V, Onat AM, Duzgun N, Bıcakcıgil M, Yentür SP, Lally L, Manfredi AA, Baldissera E, Erken E, Yazici A,

Kısacık B, Kaşifoğlu T, Dalkilic E, Cuthbertson D, Pagnoux C, Sreih A, Reales G, Wallace C, Wren JD, Cunninghame-Graham DS, Vyse TJ, Sun Y, Chen H, Grayson PC, Tombetti E, Jiang L, Mason JC, Merkel PA, Direskeneli H, and Sawalha AH. Identification of susceptibility loci for Takayasu arteritis through a large multi-ancestral genome-wide association study. *Am J Hum Genet* 2020. PMID: 33308445. Request Article

Takayasu arteritis is a rare inflammatory disease of large arteries. We performed a genetic study in Takayasu arteritis comprising 6,670 individuals (1,226 affected individuals) from five different populations. We discovered HLA risk factors and four non-HLA susceptibility loci in VPS8, SVEP1, CFL2, and chr13q21 and reinforced IL12B, PTK2B, and chr21q22 as robust susceptibility loci shared across ancestries. Functional analysis proposed plausible underlying disease mechanisms and pinpointed ETS2 as a potential causal gene for chr21q22 association. We also identified >60 candidate loci with suggestive association (p <  $5 \times 10(-5)$ ) and devised a genetic risk score for Takayasu arteritis. Takayasu arteritis was compared to hundreds of other traits, revealing the closest genetic relatedness to inflammatory bowel disease. Epigenetic patterns within risk loci suggest roles for monocytes and B cells in Takayasu arteritis. This work enhances understanding of the genetic basis and pathophysiology of Takayasu arteritis and provides clues for potential new therapeutic targets.

#### Surgery

Brescia AA, Clark MJ, Theurer PF, Lall SC, **Nemeh HW**, Downey RS, Martin DE, Dabir RR, Asfaw ZE, Robinson PL, **Harrington SD**, Gandhi DB, Waljee JF, Englesbe MJ, Brummett CM, Prager RL, Likosky DS, Kim KM, and Lagisetty KH. Establishment and Implementation of Evidence-Based Opioid Prescribing Guidelines in Cardiac Surgery. *Ann Thorac Surg* 2020. PMID: 33285132. <u>Full Text</u>

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BACKGROUND: Despite the risk of new persistent opioid use after cardiac surgery, post-discharge opioid use has not been quantified and evidence-based prescribing guidelines have not been established. METHODS: Opioid-naïve patients undergoing primary cardiac surgery via median sternotomy between January-December 2019 at 10 hospitals participating in a statewide collaborative were selected. Clinical data were linked to patient-reported outcomes collected at 30-day follow-up. An opioid prescribing

recommendation stratified by inpatient opioid use on the day before discharge (0, 1-3, or ≥4 pills) was implemented in July 2019. Interrupted time-series analyses were performed for prescription size and post-discharge opioid use before (January-June) and after (July-December) guideline implementation. RESULTS: Among 1495 patients (729 pre- and 766 post-recommendation), median prescription size decreased from 20 to 12 pills after recommendation release (p<0.001), while opioid use decreased from 3 to 0 pills (p<0.001). Change in prescription size over time was +0.6 pills/month before and -0.8 pills/month after the recommendation (difference: -1.4 pills/month, p=0.036). Change in patient use was +0.6 pills/month before and -0.4 pills/month after the recommendation (difference: -1.0 pills/month, p=0.017). Pain levels during the first week after surgery and refills were unchanged. Patients using 0 pills before discharge (n=710) were prescribed a median of 0 pills and used 0, while those using 1-3 pills (n=536) were prescribed 20 and used 7, and those using ≥4 pills (n=249) were prescribed 32 and used 24. CONCLUSIONS: An opioid prescribing recommendation was effective, and prescribing after cardiac surgery should be guided by inpatient use.

### Surgery

Idowu OA, **Boyajian HH**, Lindsay-Rivera K, Lee CS, Lee MJ, Shi LL, and Athiviraham A. Trends of Ulnar Collateral Ligament Reconstruction in the United States from 2003 to 2014: Analysis of 3,133 Patients. *Arthrosc Sports Med Rehabil* 2020; 2(6):e705-e710. PMID: 33364608. Full Text

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PURPOSE: The purpose of this study is to investigate the trends concerning ulnar collateral ligament (UCL) reconstruction (UCLR) for athletic injuries within the United States over the years 2003 to 2014. METHODS: A retrospective review of the Truven Health Marketscan® Commercial Database was conducted for patients undergoing UCLR. Data was reviewed for patients treated between 2003 and 2014, and the cohort of patients undergoing UCLR was queried using Common Procedural Terminology code 24346. Patients ages 11 to 40 years were included and divided into 6 different age groups, with the rate of UCLR calculated for each group. RESULTS: The overall rate of UCLR increased from 4.4 per million in 2003 to 11.9 per million in 2014 (p < .01). Throughout the same time period, the rate per million increased from 3.3 to 22.1 in 11- to 15-year-olds (p < .01), from 105.4 to 293.2 in 16- to 20-year-olds (p < .01), from 23.1 to 67.0 in 21- to 25-year-olds (p < .01), and from 2.1 to 5.7 in 31- to 35-year-olds (p < .01). There was no significant increase in the rate of UCLR in the age groups of 26 to 30 and 36 to 40 years. CONCLUSION: UCLR was mostly performed in patients aged 11 to 25 years (96.6%), and specifically most common in those patients aged 16 to 20 years (67.4%). The rate of UCLR procedures increased over time for younger age groups significantly more than for their older counterparts. CLINICAL RELEVANCE: UCLR rates are increasing in young patients despite efforts addressing injury risk reduction strategies and education for coaches, players, and parents regarding risk factors for UCL injury.

## Surgery

Ivanics T, Nasser H, Kandagatla P, Leonard-Murali S, Jones A, Abouljoud M, Gupta AH, and Woodward A. Prescribing Habits of Providers and Risk Factors for Nonadherence to Opioid Prescribing Guidelines. *Am Surg* 2020:3134820956332. PMID: 33295200. Full Text

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Department of Transplantation Surgery, Henry Ford Hospital, Detroit MI, USA.

BACKGROUND: The Michigan Opioid Prescribing Engagement Network introduced guidelines in October 2017 to combat opioid overprescription following various surgical procedures. We sought to evaluate changes in opioid prescribing at our academic center and identify factors associated with nonadherence to recently implemented opioid prescribing guidelines. METHODS: This retrospective review analyzed opioid prescribing data for appendectomy, cholecystectomy, and hernia repair from January 2015 through September 2017 (pre-guidelines group) and November 2017 through December 2018 (post-guidelines

group). October 2017 data were excluded to allow for guideline implementation. Opioid prescribing data were recorded as total morphine equivalents (TMEs). RESULTS: Of 1493 cases (903 pre-vs. 590 post-guidelines), the mean TME prescribed significantly decreased post-guidelines (231.9  $\pm$  108.6 vs. 112.7  $\pm$  73.9 mg; P < .01). More providers prescribed within recommended limits post-guidelines (2.8% vs. 44.8%; P < .01). On multivariable analysis, independent risk factors for guideline nonadherence were the American Society of Anesthesiologists class > 2 (adjusted odds ratio [AOR]:1.65, 95% confidence interval[CI] 1.09-2.49; P = .02), general surgery vs. acute care surgery service (AOR 1.89, 95% CI 1.15-3.10; P = .01), oxycodone vs. hydrocodone (AOR:1.90, 95% CI:1.06-3.41; P = .03), and nonphysician provider vs. resident prescriber (AOR:2.10, 95% CI:1.14-3.11; P < .01). CONCLUSIONS: Opioid prescribing significantly reduced after the adoption of opioid prescribing guidelines at our institution. Numerous factors associated with provider guideline nonadherence may identify actionable targets to minimize opioid overprescribing further.

## Surgery

VanBlarcom AG, **Wojack CA**, and Casida J. Cardiac Tamponade Following the Removal of Epicardial Pacing Wires: Critical Care APRN Toolkit. *AACN Adv Crit Care* 2020; 31(4):410-415. PMID: 33313709. Request Article

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### Urology

Alanee S, **Peabody J**, and **Menon M**. Prostate Cancer Undetected by mpMRI: Tumour Conspicuity is Reliant Upon Optimal Scan Timing and Quality. *Urology* 2020. PMID: 33279614. Full Text

Detroit Medical Center, Detroit, MI. Electronic address: salanee@dmc.org. Vattikuti Urology Institute, Henry Ford Health System, Detroit, MI.

#### Urology

Alanee S, **Peabody J**, and **Menon M**. AUTHOR REPLY. *Urology* 2020; 146:188. PMID: 33272426. Full Text

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#### Uroloay

**Briskin R**, and **Atiemo H**. Case - Unique complication of continent catheterizable stoma after bariatric surgery. *Can Urol Assoc J* 2020. PMID: 33382367. Full Text

Henry Ford Health System, Detroit, MI, United States.

### **Conference Abstracts**

### Dermatology

Bissonnette R, **Gold LS**, Kircik L, Tyring SK, Tallman A, and Armstrong A. 16392 Efficacy of tapinarof cream by body region in subjects with plaque psoriasis in a phase 2b randomized controlled study. *Journal of the American Academy of Dermatology* 2020; 83(6):AB62.

Tapinarof is a therapeutic arvl hydrocarbon receptor modulating agent (TAMA) in development for treatment of psoriasis and atopic dermatitis. In a phase 2b study, Physician Global Assessment (PGA) and Psoriasis Area and Severity Index (PASI) responses at week 12 were significantly higher in all tapinarof groups vs vehicle. Higher responses in tapinarof groups were maintained for 4 weeks after treatment versus vehicle. This post hoc analysis evaluated mean change in PASI from baseline by body region. Overall (n = 175), mean baseline PASI score was 8.8 and most subjects (80%) had a PGA score of 3 (moderate). Mean PASI improvements at week 12 were significantly greater in tapinarof 1% twicedaily (bid), 1% once-daily (qd), 0.5% bid, and 0.5% qd groups vs vehicle bid and qd, overall: -8.70, -6.62, -6.30, and -5.41 vs -2.77 and -1.54, respectively (all P <.001); in the upper extremities: -9.65, -9.05, -8.70, and -6.04 vs -4.88 and -1.61 (all P <.05); and lower extremities: -8.74, -8.19, -7.16, and -6.33 vs -2.47 and -2.0 (all P <.001). In the trunk and head/neck, PASI improvements were significantly greater in all tapinarof groups vs vehicle except the 0.5% bid group: -11.94, -9.13, -9.0, and -8.25 vs -4.08 and -1.85 (P <.01); and -9.0, -7.40, -5.0, and -9.0 vs -1.75 and -2.50 (P <.05), respectively. Tapinarof cream was generally well tolerated; most adverse events were mild or moderate. Tapinarof cream demonstrated consistent efficacy across body regions as measured by PASI and was generally well tolerated. A phase 3 study of tapinarof cream 1% gd in psoriasis is ongoing (NCT03956355).

#### Dermatology

**Braunberger TL**, Vakharia P, **Narla S**, Nicholson C, **Parks-Miller A**, and **Hamzavi IH**. 15821 Efficacy and safety of carbon dioxide laser excision in hidradenitis suppurativa: Experience from an urban academic medical center. *Journal of the American Academy of Dermatology* 2020; 83(6):AB47.

Background: Hidradenitis suppurativa (HS) is often refractory to standard medical and surgical interventions. Carbon dioxide (CO2) laser excision has demonstrated promising results, yet little evidence exists to expand and support previous studies. Objective: To examine the efficacy and safety of CO2 laser excision for HS. Methods: A retrospective review was performed at Henry Ford Hospital of patients with refractory hidradenitis suppurativa who underwent CO2 laser excision with secondary intention healing from August 2014 to May 2017. Outcomes included wound healing status, time to healing. recurrence, and postoperative complication rates. Results: Overall, 71 total sites in 48 patients underwent CO2 laser excision. Of patients with Hurley stage data available, 25 had Hurley stage 3, 16 had Hurley stage 2, and 1 had Hurley stage 1 disease. Of 57 treated sites (n = 40) with wound healing information available, 50 had documented full healing (87.7%) with a median time to healing of 5 months (interquartile range 3-7). Four patient had recurrence at an average of 5.2 months post-operatively, and 8 cases had complications (infection n = 4, contracture n = 2, dehiscence n = 1, nerve entrapment n = 1). Conclusions: While our cohort exhibited a recurrence rate of 7.9%, others have reported recurrence rates of 1.1% and 29.3%. One study found post-operative healing time following CO2 excision to be 8.8 weeks, but our average healing time was prolonged in comparison. Our study on CO2 excision found satisfactory healing rates and time to healing with reduced recurrence and complication rates in hidradenitis suppurativa patients, and this modality should be further investigated.

### **Dermatology**

Dermer SJ, Maeglin JM, and **Gold LS**. 16520 Continuing medical education on acne improves dermatologists' knowledge and competence on patient management. *Journal of the American Academy of Dermatology* 2020; 83(6):AB180.

Background: Although acne is fairly common, clinicians are not aware of its impact on QoL and how to best prevent acne scars. Methods: Dermatologists participated in online CME activities on diagnosis and treatment of acne. CME formats were a 30-minute panel discussion, and two 15-minute 2-person video conversations, with synchronized slides. Effectiveness was analyzed using 3 multiple-choice and 1 self-

efficacy question for each activity, presented as pre-/post-CME repeated pairs. Activities posted from December 2018 through March 2019; data were collected for 30 days after launch. Chi-square test assessed changes in responses to questions from pre- to post-CME. P values measured significance; P <.05 = statistically significant. Results: In pre- to post-CME for all activities combined, average correct responses improved from 43% (pre) to 59% (post); n = 379, P <.05. Post-CME, there was a 15% absolute improvement in knowledge on the impact of acne on QoL (36% to 51% pre/post; P <.05); a 33% overall increase in confidence assessing the impact of acne on QoL; and an overall 26% increase in confidence in the ability to ameliorate the psychosocal impact of acne with treatment. Post-CME, there was a 17% absolute improvement in knowledge on the risk for acne scars and scar prevention (36% to 51% pre/post; P <.05); a 27% overall increase in confidence in individualizing treatment in adults. Conclusions: Online CME consisting of video-based discussions with synchronized slides improved dermatologists' knowledge relating to the impact of acne on QoL and on the preventing acne scars.

### Dermatology

**Gold LS**, Del Rosso JQ, Kircik L, Bhatia N, Hooper D, and Nahm WK. 13509 Integrated safety analysis of FMX103 1.5% topical minocycline foam for the treatment of moderate to severe papulopustular rosacea: Results from two phase 3 studies. *Journal of the American Academy of Dermatology* 2020; 83(6):AB119.

Objective: To evaluate the safety of FMX103 1.5% topical minocycline foam for adults with moderate to severe papulopustular rosacea, using pooled data from 2 phase 3 studies. Methods: Two phase 3 randomized, multicenter, double-blind, vehicle-controlled, 2-arm, 12-week studies (FX2016-11 and FX2016-12) evaluated efficacy, safety, and tolerability of FMX103 vs vehicle foam. Eligible subjects (based on lesion count and IGA score for rosacea severity) were randomly assigned in a 2:1 ratio (FMX103: vehicle). Subjects returned for visits at weeks 2, 4, 8, and 12. Results: The safety population included 1521 subjects (FMX103, n = 1008; vehicle, n = 513). Treatment emergent adverse events (TEAEs) were experienced by 341 subjects (22.4%), with the incidence balanced between treatment groups (FMX103, 21.7%; vehicle, 23.8%). The most frequently reported TEAEs, in the FMX103 and vehicle groups, respectively, were viral upper respiratory tract infection (2.4% vs 2.3%) and upper respiratory tract infection (1.9% vs 2.5%). Most TEAEs were mild or moderate in severity (FMX103, 98.6%; vehicle, 96.7%). Serious TEAEs were reported in 8 subjects (FMX103, n = 3, 0.3%; vehicle, n = 5, 1.0%); all were unrelated to treatment. TEAEs leading to drug withdrawal occurred in 9 subjects (FMX103, n = 7, 0.7%; vehicle, n = 2, 0.4%); 1 TEAE was considered to be related to FMX103 (moderate pruritus). At week 12, all facial tolerability assessments in both groups had higher percentages of subjects reporting "none" compared with baseline and the assessments trended toward improving scores. Conclusions: This integrated safety analysis demonstrated that FMX103 1.5% is well tolerated, with a favorable safety profile.

### **Dermatology**

**Gold LS**, Del Rosso JQ, Kircik L, Bhatia N, Hooper D, Nahm WK, and Stuart I. 17800 Open-label extension study evaluating the long-term safety, efficacy, and tolerability of FMX103 1.5% topical minocycline foam in the treatment of moderate to severe facial papulopustular rosacea. *Journal of the American Academy of Dermatology* 2020; 83(6):AB199.

Objective: To assess the long-term safety, efficacy, and tolerability of FMX103 1.5% in moderate to severe facial papulopustular rosacea. Methods: Eligible subjects were enrolled in a 40-week open-label extension (OLE) study at the final study visit of 2 identical phase 3, randomized, double-blind, vehicle-controlled, 12-week studies. Subjects initially enrolled in the FMX103 group continued to receive active treatment, while those previously in the vehicle group crossed over to receive active treatment in the OLE. Safety and efficacy and tolerability were assessed over 40 weeks. Results: Of the 504 subjects enrolled, 81.3% of subjects completed the OLE. The majority of TEAEs were mild to moderate in severity (overall 94.0%). Except for one case of severe pruritus (probably related), all severe TEAEs and all serious adverse events were considered to be unrelated to the study treatment. At week 40, most subjects from both groups reported no symptoms or only mild symptoms of burning/stinging (100%), flushing/blushing (94.5%), dryness/xerosis (98.5%), itching (99.5%), peeling/desquamation (99.0%), or hyperpigmentation (99.3%). Overall, the mean reduction from baseline in absolute inflammatory lesion count, and the percent change at week 40 was 22.8 and 82.3%, respectively. The IGA treatment success

rate from baseline of the double-blind study to week 40 was 79.8%. Conclusions: FMX103 1.5% demonstrated efficacy in the treatment of moderate to severe facial papulopustular rosacea and appeared to be safe and well tolerated for up to an additional 40 weeks of treatment.

#### Dermatology

**Gold LS**, Weiss JS, Green LJ, Kircik L, PharMd TL, and Harris S. 15324 Long-term management of moderate to severe plaque psoriasis: Maintenance of treatment success following cessation of fixed combination halobetasol propionate 0.01% and tazarotene 0.045% lotion in patients with baseline body surface area of 6%-12%. *Journal of the American Academy of Dermatology* 2020; 83(6):AB36.

Topical therapy is the mainstay of treatment for patients with localized psoriasis. The objective was to investigate maintenance of effect with halobetasol propionate 0.01%/tazarotene 0.045% (HP/TAZ) lotion. In this 1-year open-label study, patients with moderate to severe psoriasis applied HP/TAZ once-daily. At week 8. HP/TAZ was stopped for treatment success (Investigator Global Assessment IIGA) score of 'clear' or 'almost clear'); participants not reaching treatment success were treated for an additional 4 weeks. At week 12, any patient demonstrating ≥1-grade IGA improvement continued and was managed in 4-week cycles (no treatment success; continued HP/TAZ; achieved treatment success; no treatment until next evaluation). Maximum continuous exposure was 24 weeks. This post hoc analysis evaluated maintenance in participants with high baseline Body Surface Area (BSA) 6%-12% (n = 210). At week 8, 50% achieved, BSA ≤5%. For patients participating at least 1 year in the study, 50.0% and 21.4% maintained, BSA ≤5% and ≤3%, respectively. At time of treatment success (n = 102), BSA was ≤5%, ≤3%, ≤2%, and ≤1% in 74.5%, 59.8%, 46.1%, and 33.3% of participants, respectively. Of participants who stopped therapy after treatment success: 5.7% did not require retreatment, 12.9% did not require retreatment for ≥3 months, 21.4% did not require retreatment for ≥2 months, and 44.3% did not require retreatment for ≥1 month. HP/TAZ lotion provides rapid and sustained treatment success in patients with moderate to severe psoriasis with baseline, BSA 6%-12% when followed for 1 year, with nearly half of participants not requiring retreatment for ≥1 month. Funding: Ortho Dermatologics.

#### Dermatology

**Hamzavi I**, Harris JE, Rosmarin D, Grimes PE, Pandya A, Gottlieb AB, Butler KA, Kuo IFI, Sun K, and Lebwohl M. 17753 Analysis of 24-week response to ruxolitinib cream for the treatment of vitiligo based on patient demographics and clinical characteristics. *Journal of the American Academy of Dermatology* 2020; 83(6):AB86.

Ruxolitinib cream, a Janus kinase inhibitor, is under investigation for vitiligo treatment. Factors including skin type and disease duration may contribute to treatment efficacy. This 24-week component of a 104week, phase 2, randomized, double-blind study (NCT03099304) enrolled adult patients with vitiligo that included depigmentation ≥0.5% of body surface area (BSA) on the face and ≥3% of BSA on nonfacial areas. 157 patients were equally randomized to receive ruxolitinib cream (1.5% twice daily [bid], 1.5% once daily [QD], 0.5% QD, or 0.15% QD) or vehicle bid for 24 weeks. The primary end point was the proportion of patients achieving ≥50% improvement in facial Vitiligo Area Scoring Index (F-VASI50) at week 24. This subgroup analysis investigated response by patient demographics and baseline characteristics; results were generally similar across treatment groups at week 24. Among patients who received ruxolitinib cream 1.5% BID (n = 33; F-VASI50 responders, 45.5%), a larger proportion of patients in the following subgroups were F-VASI50 responders: patients ≤50 years old (58.8%); female patients (60.0%); patients with skin type I–III (50.0%), ≤1.5% affected baseline facial, BSA (52.6%), baseline F-VASI scores of 0.75 to 20 years (60.0%); and previous recipients of topical corticosteroids (50.0%). There were no substantial differences between responders who were white (44.8%) vs nonwhite (50.0%), who had stable (46.2%) vs progressive disease (45.0%), or those with total, BSA ≤20% (45.0%) vs >20% (46,2%). Ruxolitinib cream was effective for the treatment of vitiligo across demographics and clinical characteristics, including in patients with longstanding and extensive disease.

## **Dermatology**

**Kohli I**, Nicholson C, Williams JD, Seo I, Tian X, Atillasoy E, **Lim HW**, and **Hamzavi IH**. 17955 Comparison of SPF50+ and SPF100+ sunscreens on the induction of cutaneous pigmentation over

multiple days: A real-world, single-center, randomized, double-blinded evaluation. *Journal of the American Academy of Dermatology* 2020; 83(6):AB203.

Recently, a study evaluating the difference in sunburn protection offered by SPF 50+ and SPF 100+ sunscreens over the course of 5 consecutive days in a beach environment facilitated a unique opportunity to evaluate the protection sunscreens provide against the induction of cutaneous pigmentation. A randomized, double-blinded, split body/face study assessing the efficacy of two broad spectrum sunscreens (SPF50+ and 100+) was conducted in the beach setting of St Petersburg, Florida, Fifty-five healthy subjects (1 phototype I, 22 phototype II, and 32 phototype III; average age 45.2 years [range: 19-59]) were enrolled. Subjects were permitted unrestricted access to test sunscreens and instructed to apply to the designated side as they normally would. Objective assessments of daily and cumulative changes in cutaneous pigmentation were conducted by colorimetry (ΔL\*, Δb\*, ΔITA°) and diffuse reflectance spectroscopy (DRS) (Δ melanin). SPF 100+ sunscreen offered greater protection against pigmentation induction as determined by a lower ΔL\* and an increased Δb\* on the SPF 50+ treated side (P < .001), which resulted in a mean  $\Delta ITA^{\circ}$  of -7.57 on the SPF 50+ side and -5.78 on the SPF 100+ side. This pigmentation differential was supported by DRS assessments indicating greater melanin induction on the SPF 50+ side,  $\Delta$  melanin (SPF50+ 0.18 ± 0.09 vs SPF100+ 0.15 ± 0.09, P =.01). Although pigment formation occurred on both sides, compared with SPF 50+ sunscreen, objective assessments show that the SPF 100+ sunscreen offered significantly greater protection against the induction of cutaneous pigmentation in actual use.

#### Dermatology

**Lyons AB**, Zubair R, **Miller AP**, **Kohli I**, and **Hamzavi IH**. 15485 Evaluating the safety and efficacy of intense pulsed light with radiofrequency in US patients with hidradenitis suppurativa: A split-body study. *Journal of the American Academy of Dermatology* 2020; 83(6):AB154.

Laser and light-based treatments for hidradenitis suppurativa (HS) have gained popularity and are thought to work by: targeting melanin in the hair follicle leading to laser-induced hair removal, debulking, sebaceous gland reduction, or bacterial load reduction. Laight therapy (Lenicura, Germany) is a European Union approved, treatment for HS and acne, utilizing intense pulsed light (IPL) with radiofrequency (RF). IPL is believed to cause photothermolysis, where the absorption of light by chromophores in the skin creates heat to target the blood vessels that supply sebaceous glands to reduce sebum production and cause thermal damage to hair follicles. Similarly, it is hypothesized that RF causes thermal damage, inhibits sebaceous gland activity, and induces collagen production and collagen fiber remodeling in the dermis. The objective of this study was to determine the safety and efficacy of IPL+RF in US patients with HS. Two subjects (Hurley Stage II and III) underwent IPL+RF treatments every 2 weeks for a total of 10 treatments to a randomized half of the body. Clinical assessments and patient reported outcomes were obtained at each visit. One patient had a 3-point improvement in the Dermatology Life Quality Index (DLQI) and the other had a 1-point worsening in DLQI, but no improvement in clinical outcomes (Hurley Staging-Physician Global Assessment [HSPGA], Hidradenitis Suppurativa Clinical Response [HiSCR], International Hidradenitis Suppurativa Severity Score System [IHS4]) were observed for either patient. No adverse events were reported. While this study is ongoing, larger studies are needed to further evaluate the safety and efficacy of this treatment.

## Dermatology

**Mohammad T**, Hamel R, Chahine A, Vick GL, Boh E, Alora MBT, Mistur R, Baron ED, Cooper K, and Lim HW. 13303 Prevalence of photodermatoses in the general dermatology clinic of four academic medical centers: A multicenter retrospective analysis of 1080 patients over a 10-year period. *Journal of the American Academy of Dermatology* 2020; 83(6):AB117.

Background: Previous studies have examined the prevalence of photodermatoses among racial groups in academic institutions. Because of an insufficient amount of patients, various racial differences were not statistically significant. Objective: Assess the prevalence of photodermatoses in four academic medical centers and compare the frequency of photodermatoses among racial groups. Methods: A retrospective review of dermatology clinic medical records was performed at 4 institutions. Charts documenting a diagnosis consistent with the International Classification of Disease, Ninth and Tenth Revisions, codes

related to photodermatoses between August 2006 and August 2016 were selected for further individual evaluation. A total of 9736 charts were manually reviewed and classified. Results: There were 1080 patients with photodermatoses identified: 572 (53%) African American/Black, 378 (35%) White, and 130 (12%) of other races. Statistically significant differences in the distribution between Whites and Blacks were identified for polymorphous light eruption (more common in Blacks), as well as for photoallergic contact dermatitis, phototoxic drug eruption, phytophotodermatitis, porphyria, and solar urticaria (more common in Whites). The most commonly diagnosed photodermatoses were polymorphous light eruption (total 672), photodermatitis not otherwise specified (total 189), and phototoxic drug eruption (total 73). Discussion: Comparing Blacks and Whites, our study demonstrated significantly higher proportions of polymorphous light eruption in Blacks, and higher proportions of photoallergic contact dermatitis, phototoxic drug eruptions, phytophotodermatitis, porphyrias, and solar urticaria in Whites.

#### Dermatology

**Narla S**, and Silverberg JI. 15838 Autoimmune comorbidities of psoriasis in US adults and children. *Journal of the American Academy of Dermatology* 2020; 83(6):AB48.

Background: Psoriasis is a chronic inflammatory skin disease affecting >7 million persons in the US. Few comprehensive large-scale and controlled studies examined the spectrum of autoimmune diseases occurring in psoriasis. Objective: To determine the autoimmune disorders associated with psoriasis in US adults and children, and the excess payer costs related to care for these autoimmune comorbidities. Methods: Data from the 2002-2012 National Inpatient Sample were analyzed, including a representative 20% sample of all US hospitalizations. Results: In adults, psoriasis was associated with ≥1 autoimmune disease (adjusted odds ratio [95% confidence interval]: 1.90 [1.86-1.94]), including 28 of 35 autoimmune disorders examined. Autoimmune disorders with the largest effect-size included including alopecia areata (8.61 [4.95-14.98]), vitiligo (5.88 [4.91-7.03]), erythema nodosum (3.59 [2.43-5.29]), ankylosing spondylitis (3.31 [2.86-3.83]), primary biliary cirrhosis (2.68 [2.21-3.25]), nonalcoholic steatohepatitis (2.71 [2.57-2.86]), and autoimmune hepatitis (2.88 [2.22-3.73]). In children, psoriasis was associated with increased odds of type 1 diabetes (1.68 [1.14-2.49]), rheumatoid arthritis (6.45 [2.65-15.69]), systemic lupus erythematosus (2.66 [1.18-5.99]), alopecia areata (49.11 [7.05-341.94]), vitiligo (23.11 [7.46-71.66]), autoimmune hemolytic anemia (7.23 [2.35-22.21]), and unspecified autoimmune disease [29.08 [8.23-102.83]). There were significant differences of geometric-mean cost of care among adult (\$8168 [\$8017-\$8322] vs \$7888 [\$7780-\$7997], P <.0001) and pediatric (\$6842 [5808-8060] vs \$5761 [5375-6176]), P = .0392) inpatients with psoriasis, with \$76,120 and \$49,991,534 in excess annual costs of inpatient care attributed to autoimmune disorders, respectively. Conclusions: Psoriasis was associated with hospitalization for multiple cutaneous and extracutaneous autoimmune disorders in adults and children, which contributed to substantial excess costs.

### **Dermatology**

Oska S, **Yeager DG**, **Zarbo A**, **Friedman BJ**, and **Shwayder T**. 18303 Ataxia telangiectasia and melanoma: The role of dermatology in ataxia telangiectasia. *Journal of the American Academy of Dermatology* 2020; 83(6):AB209.

Presentation: A 28-year-old Caucasian woman with ataxia telangiectasia (AT), hypothyroidism, diabetes, uterine leiomyomas, liver adenoma, and hypogammaglobulinemia presented with a 6-month history of growth of melanocytic lesion which had previously been stable for the 4-5 years. Physical examination revealed a large, dark brown macule on the right lateral foot. Course and Therapy: Shave biopsy revealed a broad, uneven proliferation of atypical, pleomorphic melanocytes with prominent nucleoli with cleaved nuclei. Breslow thickness was 1.4 mm with positive margins, 1 mitosis/mm2, and no ulceration. Immunohistochemical staining revealed diffusely positive HMB45, MIB-1 present in >10% of dermal melanocytes in some foci, preservation of p16, no mutation in BRAFV600E nor loss of BAP1. Wide local excision of 2 cm margins revealed invasive melanoma with Breslow thickness of 0.81 mm and melanoma in situ. Sentinel lymph node biopsy revealed incidental nodal nevus. Discussion: Ataxia telangiectasia (AT) is an autosomal recessive mutation in the ATM gene on chromosome 11 characterized by early onset cerebellar ataxia, oculocutaneous telangiectasias, immunodeficiency, and progressive respiratory failure. Incidence of malignancy is 37-fold in AT compared with the general population, as the ATM mutation impedes the ability of the tumor suppressor protein p53 to halt the cell cycle for DNA repair

causing cells to accumulate damaged DNA. Approximately 85% of malignancies are hematopoietic. The incidence of melanoma in AT has not yet been characterized; however, the incidence of melanoma, like other malignancies, is increased in AT relatives. In the general population, 5%-10% of melanomas have been associated with somatic ATM mutations.

## Dermatology

Rosso JD, Tan J, Weiss JS, **Gold LS**, Cook-Bolden F, Eichenfield L, Tanghetti E, Graeber M, Saenz AA, and Ahmad F. 13882 Trifarotene 50 µg/g cream: An effective and safe treatment for moderate facial and truncal acne. *Journal of the American Academy of Dermatology* 2020; 83(6):AB14.

Introduction: While ~50% of patients with facial acne have truncal acne, data concerning treatment of truncal acne has been lacking. Three recent studies evaluated the efficacy and safety of a new retinoid, trifarotene 50 µg/g cream (trifarotene), for facial and truncal acne. Methods: Two multicenter, randomized. double-blind, vehicle controlled, 12-week phase 3 studies ("Perfect" 1+2) and 1 multicenter, open-label, non-comparative 52-week study ("Satisfy") investigated trifarotene once-daily in moderate facial and truncal acne. Efficacy end points included the Investigator's Global Assessment (IGA 0-4, face), the Physician Global Assessment (PGA 0-4, trunk), and the change in facial/truncal inflammatory and noninflammatory lesions. Safety assessments included adverse events and local tolerance (erythema, scaling, drvness and stinging/burning). Results: The "Perfect" studies recruited 2420 subjects, and 1214 were treated with trifarotene. "Satisfy" enrolled 455 subjects, and 348 (76.5%) completed the 52-week study. All three studies met all efficacy end points, and both IGA and PGA successes (score 0-1, and 2grade improvement) continued to increase throughout the full 52 weeks of the "Satisfy" study. There was a 29.4% IGA success rate with trifarotene compared with 19.5% for vehicle in "Perfect 1," and 42.3% trifarotene IGA success rate compared with 25.7% for vehicle in "Perfect 2." Signs/symptoms of local tolerability were mostly mild/moderate. Local irritation increased during week 1 on the face, up to week 2-4 on the trunk, decreasing thereafter, and was managed with moisturizers and/or regimen (application frequency) adjustment. Summary: Trifarotene was effective and safe in 3 phase 3 studies of moderate facial and truncal acne.

#### Dermatology

Veverka KA, Hansen JB, Yaloumis M, Kircik L, and **Gold LS**. 17754 Treatment success in mild psoriasis patients with fixed-combination calcipotriene and betamethasone dipropionate foam: Results from the PSO-FAST trial. *Journal of the American Academy of Dermatology* 2020; 83(6):AB198.

Background: Numerous topical and systemic therapies are available for the treatment of cutaneous psoriasis: very few have been demonstrated effective for mild psoriasis. We evaluated efficacy in a mild patient cohort with once-daily application of Cal/BD foam for 4 weeks in a post hoc analysis. Methods: Adults with mild-severe plaque psoriasis (IGA ≥2;, BSA 2%-30%) were randomized 3:1 to Cal/BD foam (n = 323) or vehicle (n = 103) once daily for up to 4 weeks (Leonardi et al. J Drugs Dermatol 2015:14:1468-77). Patient characteristics and IGA 'treatment success' was determined for patients with mild psoriasis (IGA = 2 according to 5-point IGA). 'Treatment success' for mild patients required a 2-grade IGA improvement with a rating of 'clear' (IGA = 0) at week 4 (Mantel-Haenszel). Results: At baseline, 65/426 patients in PSO-FAST had mild psoriasis; mean duration was 14 years, BSA% = 4.8 and mPASI = 4.7. After 4 weeks, significantly more patients with mild psoriasis achieved treatment success with Cal/BD foam than foam vehicle with 30.6% versus 0.0% [P = .019] being clear of visible psoriasis lesions. Similarly, reductions in mPASI from baseline were -35.5, -55.3, and -71.9, respectively for Cal/BD foam at week 1, 2, and 4 vs vehicle -15.2, -25.0, and -27.7. PASI-75 at week 4 was 49.0% in the mild Cal/BD foam group and 7.1% in the mild vehicle group (P = .023). Conclusions: These important results establish treatment success for Cal/BD foam in mild psoriasis, a population in which efficacy is difficult to demonstrate since the treatment must completely clear visible disease to be considered effective.

#### Dermatology

Weiss JS, Bhatia N, **Gold LS**, Martin G, Pillai R, and Guenin E. 15211 Treatment of moderate to severe acne with once-daily tazarotene 0.045% lotion in males: Pooled analysis of two phase 3 studies. *Journal of the American Academy of Dermatology* 2020; 83(6):AB144.

Acne vulgaris has been reported in 85% of adolescents, with moderate to severe acne occurring more frequently in adolescent/adult males than females. Tazarotene is a potent topical retinoid for acne treatment, but irritation with existing formulations may limit its use. An innovative tazarotene 0.045% lotion formulation was developed by utilizing polymeric emulsion technology. In two phase 3, double-blind. vehicle-controlled 12-week studies, eligible patients aged ≥9 years with moderate to severe acne were randomized (1:1) to receive once-daily tazarotene 0.045% lotion or vehicle. Data for male patients were summarized descriptively at week 12 in this analysis. Efficacy assessments included reductions in inflammatory/noninflammatory lesion counts and percent of patients achieving ≥2-grade reduction in Evaluator Global Severity Scores (EGSS) and a clear/almost clear score (treatment success). Adverse events (AEs) and cutaneous safety/tolerability were also assessed. Of 1614 total pooled participants, 550 were males (n = 268 tazarotene 0.045%; n = 282 vehicle). Changes from baseline in absolute lesion counts were higher with tazarotene (least-squares mean [standard deviation] inflammatory: -15.9 [10.5]; noninflammatory -22.4 [16.1]) versus vehicle (-11.3 [10.5]; -14.4 [17.8]). More patients achieved treatment success with tazarotene (25.1%) versus vehicle (12.7%). The percent of males reporting treatment-emergent AEs (TEAEs) was similar between tazarotene (19.0%; 50/263) and vehicle (19.3%; 53/275). In both groups, most TEAEs were of mild-moderate severity. Serious AEs occurred in 1 patient in each group (not treatment-related). The most common administration-related TEAE was application site pain (2.7% tazarotene; 0% vehicle). The novel tazarotene 0.045% lotion was efficacious and well tolerated in male patients with moderate to severe acne.

#### Dermatology

Yosipovitch G, Bieber T, **Gold LS**, Kwatra S, Tatulych S, Nduaka C, Cameron MC, Williams D, Biswas P, and Valdez H. 15517 Eczema Area and Severity Index 90 (EASI-90) responder rates with abrocitinib and relationship with quality of life (QoL) and itch in patients with moderate to severe atopic dermatitis: Results from a randomized phase 3 clinical trial. *Journal of the American Academy of Dermatology* 2020; 83(6):AB41.

Introduction: Abrocitinib is an oral Janus kinase 1 inhibitor under investigation for the treatment of moderate to severe AD. Design: Randomized, double-blind, placebo-controlled phase 3 trial (NCT03349060; JADE MONO-1). Methods: Patients ≥12 years old with clinical diagnosis of moderate to severe AD were randomly assigned (2:2:1) to once-daily abrocitinib 200 mg, abrocitinib 100 mg, or placebo for 12 weeks. Eczema Area and Severity Index 90 (EASI-90), Dermatology Life Quality Index (DLQI), Children's DLQI (CDLQI), and peak pruritus numeric rating scale (PP NRS; 0-10) were measured at baseline and weeks 2, 4, 8, and 12. Results: 154, 156, and 77 patients were treated with abrocitinib 200 mg, abrocitinib 100 mg, or placebo, respectively. Proportions of patients achieving ≥ 90% improvement in EASI-90 overall were 38.6% and 18.6% versus 5.3% at week 12 (difference from placebo [95% CI], 33.4% [24.3%-42.5%] and 13.3% [5.4%-21.2%]), with little difference between those with moderate baseline IGA (42.9% and 18.5% vs 6.7%; 36.2% [23.7%-48.7%] and 11.8% [1.0%-22.6%]) and severe baseline IGA (32.3% and 18.8% vs 3.2%; 29.0% [15.8%-42.2%] and 15.5% [4.1%-26.9%]). Greater proportions of week-12 EASI-90 responders versus nonresponders achieved no/mild alteration in QoL (89.0% vs 46.6%; per published [C]DLQI severity bands), ≥4-point improvement in PP-NRS (88.4% vs 25.1%; among those with baseline PP-NRS ≥4), and PP-NRS <2 (70.0% vs 10.2%; among those with baseline PP-NRS ≥2). Conclusions: Abrocitinib therapy was associated with significantly greater EASI-90 responder rates versus placebo, regardless of baseline AD severity. EASI-90 response at week 12 corresponded with patients experiencing low impairment in QoL, clinically meaningful improvement in itch, and/or little-to-no itch.

### <u>Dermatology</u>

**Zarbo A**, **Luk KM**, **Friedman BJ**, and **Shwayder T**. 18618 A differential diagnosis for the congenital midline mass: Striated muscle hamartoma. *Journal of the American Academy of Dermatology* 2020; 83(6):AB216.

History: A 5-day-old black male full-term neonate born via vacuum-assisted delivery for non-reassuring fetal heart rate presented with congenital presentation of two asymptomatic midline lesions which appeared asymptomatic. There was no history of seizures, ophthalmologic findings, abnormalities in head

circumference, height, weight, or limb size. Newborn screening examination was unremarkable. Examination: On the midline submental chin there was a soft, brown dome-shaped plaque measuring 0.8 cm with a circumferential ring of light brown pigmentation; on the midline upper chest there was a light brown 2-mm dome-shaped papule. Course and Therapy: Ultrasound of the submental chin lesion revealed a 0.5 × 0.8 × 0.4-cm heterogeneously hypoechoic structure with a peripheral soft tissue rind. Punch biopsies of the submental chin and the midline upper chest revealed haphazardly arranged striated muscle fibers in the dermis, some of which inserted directly into the epidermis. The muscle fibers were highlighted by Masson trichrome and myogenin. Alcian blue revealed increased dermal mucin. Discussion: Striated muscle hamartomas (SMH) are rare, benign congenital skin tumors characterized by haphazard arrangement of mature striated skeletal muscle, collagen, nerve bundles, and adipose tissue in the dermal and subcutaneous tissue. Although a rare entity, it is important to recognize this benign hamartoma as a congenital midline defect. Conservative management with clinical monitoring is recommended if cosmetically acceptable, as spontaneous regression over a period of years has been reported. Surgical excision may be pursued; however, the hamartoma may recur.

### Public Health Sciences

McAllister P, Casciano J, Cohen J, Thompson S, Krasenbaum L, Dotiwala Z, Tangirala K, and **Lamerato** L. PND98 Real World IMPACT of Fremanezumab Treatment on Headache Frequency and Healthcare Resource Use Among US Patients with Episodic or Chronic Migraine. *Value in Health* 2020; 23:S640.

Objectives: Fremanezumab, a fully-humanized monoclonal antibody (IgG2Da) that selectively targets the calcitonin gene-related peptide (CGRP) pathway, has demonstrated efficacy in adults with episodic or chronic migraine in clinical trials and has been approved for migraine prevention in adults. However, realworld data on the effectiveness of fremanezumab are limited. This retrospective, observational cohort study assessed patient-reported headache frequency and healthcare resource utilization (HCRU) before and after fremanezumab treatment initiation. Methods: Data were extracted from September 2018 through June 2020 from the EMRClaims+®, an integrated health services database containing over 20 million medical records from national commercial insurance claims, Medicare claims, and regional electronic medical records. Patients included in the cohort analysis were aged ≥18 years and were administered fremanezumab, with enrollment or treatment history for ≥6 months prior to initiating fremanezumab (index date), and enrollment or treatment encounter for ≥1 month after the index date. Headache frequency was assessed at baseline and ≥1 month after fremanezumab initiation. Wilcoxonsigned rank tests were used to compare means of headache frequencies before and after fremanezumab initiation. Results: A total of 54 patients were eligible for analysis of headache frequency. Overall headache frequency decreased by 63% after fremanezumab initiation; mean (standard deviation [SDI) headache frequency was 22.24 (9.29) days per month pre-index versus 8.24 (7.42) days per month postindex (P <0.0001). Mean ER visits per month decreased from 0.72 to 0.54 (P = 0.003), and mean outpatient visits per month decreased from 1.04 to 0.81 (P = 0.0004). While mean hospitalizations per month also decreased, the result did not reach statistical significance (P = 0.095). Conclusions: Significant reductions in headache frequency and HCRU were observed after fremanezumab initiation overall and across episodic and chronic migraine groups in a real-world setting.

## Public Health Sciences

McAllister P, **Lamerato L**, Casciano J, Cohen JM, Thompson S, Krasenbaum L, Dotiwala Z, Tangirala K, and Mauskop A. PND109 Improvements in Patient-Reported Migraine PAIN Intensity and Composite Migraine Symptoms with Fremanezumab in the Real World. *Value in Health* 2020; 23:S642.

Objectives: Fremanezumab, a fully-humanized monoclonal antibody (IgG2∆a) that selectively targets the calcitonin gene-related peptide (CGRP) pathway, has been approved for migraine prevention in adults with episodic migraine (EM) or chronic migraine (CM). However, little data exists on the effectiveness of fremanezumab in a real-world setting. This retrospective, observational cohort study assessed real-world patient-reported changes in migraine pain intensity (MPI) and composite migraine symptoms (headache frequency/symptoms) after starting fremanezumab therapy. Methods: Data were extracted from September 2018 through June 2020 from the Midwest component of EMRClaims+®, an integrated health services database containing >20 million medical records from national commercial insurance claims, Medicare claims, and regional electronic medical records. Patients included were aged ≥18 years and

were administered fremanezumab, with enrollment or treatment history ≥6 months prior to initiating fremanezumab (index date) and enrollment or treatment encounter ≥1 month after the index date. MPI (10-point visual analog scale [VAS; 0=no pain, 10=worst pain]) and patient-reported change in headache frequency/symptoms were assessed pre-index and ≥1 month after fremanezumab initiation. Wilcoxon signed-rank tests were used to compare MPI and headache frequency/symptoms before and after fremanezumab initiation. Results: Seventy-four patients (EM, n=21; CM, n=49) were eligible for analysis of MPI. MPI decreased significantly by 18% after fremanezumab initiation in the overall population: mean (standard deviation [SD]) VAS pain score was 5.47 (3.19) pre-index versus 4.51 (3.34) post-index (P=0.014). After fremanezumab initiation, pain levels decreased significantly by 45% in patients with EM (mean [SD] VAS pain score: pre-index, 5.57 [3.56]; post-index, 3.04 [3.37]; P=0.002) and decreased non-significantly by 10% in patients with CM after fremanezumab initiation (pre-index, 5.61 [2.99]; post-index, 5.06 [3.16]; P=0.203). Among patients who self-reported changes in headache frequency/symptoms (n=129), 83.7% reported improvement after fremanezumab initiation. Conclusions: After fremanezumab initiation, MPI decreased significantly and the majority of patients reported an improvement in headache frequency/symptoms.

## **Books and Book Chapters**

## Surgery

**Nahirniak P**, and Tuma F. "Adhesiolysis". <u>StatPearls</u>. Treasure Island (FL), StatPearls Publishing Copyright © 2020, StatPearls Publishing LLC. PMID: 33085366. <u>Full Text</u>

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Adhesions are fibrous tissue connections (adherence tissues) between various tissue planes or organs usually caused by inflammatory causes, most commonly surgery. Fibrin deposition leads to fibrous connections between organs or tissues. These adhesions are part of the internal healing process and inflammatory reactions. They participate in the body's defense mechanisms against the causes of inflammation (physical, chemical, infections, etc.). Adhesions can occur in any organ or part of the body, e.g., abdomen, pelvis, thorax, intraocular space, joint spaces. Depending on the cause and location of adhesions, they can be beneficial (in tissue healing) or harmful (causing complications). They can cause chronic pain, infertility, bowel obstruction, or diminished range of joint range of motion, for example. Intra-abdominal and pelvic adhesions and adhesiolysis are by far the most common of all adhesions; therefore, they will be the focus of this article. Abdominal adhesions form after any surgery or inflammatory cause, including trauma or bleeding. The most common known cause of adhesions is surgery, especially open procedures. They heal, seal, and repair sites of injury and inflammation to protect and limit further damage. But, the formation of adhesions is not without unfavorable consequences. Bowel obstruction is a common complication of post-operative adhesions. Occasional, this mandates surgical adhesiolysis - lysing cutting the adhesions to resolve the obstruction. Adhesiolysis is performed much less frequently for other reasons like pain or compression of other structures.

### **HFHS Publications on COVID-19**

## Cardiology/Cardiovascular Research

Jain V, **Gupta K**, Bhatia K, Bansal A, Arora S, **Khandelwal AK**, Rosenberg JR, Levisay JP, Tommaso CL, Ricciardi MJ, and Qamar A. Management of STEMI during the COVID-19 pandemic: Lessons learned in 2020 to prepare for 2021. *Trends Cardiovasc Med* 2020. PMID: 33338636. Full Text

#### Dermatology

Lyons AB, Narla S, Torres AE, Parks-Miller A, Kohli I, Ozog DM, Lim HW, and Hamzavi IH. Skin and eye protection against ultraviolet C from ultraviolet germicidal irradiation devices during the COVID-19 pandemic. *Int J Dermatol* 2020. PMID: 33259055. Full Text

## **Diagnostic Radiology**

**Poyiadji N, Klochko C, Palazzolo J, Brown ML**, and **Griffith B**. Impact of the COVID-19 pandemic on radiology physician work RVUs at a large subspecialized radiology practice. *Clin Imaging* 2020; 73:38-42. PMID: 33302235. Full Text

### **Emergency Medicine**

**Lazar MH**, **Fadel R**, **Gardner-Gray J**, **Tatem G**, **Caldwell MT**, **Swiderek J**, and **Jennings JH**. Racial Differences in a Detroit, MI, ICU Population of Coronavirus Disease 2019 Patients. *Crit Care Med* 2020. PMID: 33372746. Full Text

### Infectious Diseases

Heldman MR, Kates OS, Haydel BM, Florman SS, Rana MM, **Chaudhry ZS**, **Ramesh MS**, Safa K, Kotton CN, Blumberg EA, Besharatian BD, Tanna SD, Ison MG, Malinis M, Azar MM, Rakita RM, Morillas JA, Majeed A, Sait AS, Spaggiari M, Hemmige V, Mehta SA, Neumann H, Badami A, Jeng A, Goldman JD, Lala A, Hemmersbach-Miller M, McCort ME, Bajrovic V, Ortiz-Bautista C, Friedman-Moraco R, Sehgal S, Lease ED, Limaye AP, and Fisher CE. Healthcare resource use among solid organ transplant recipients hospitalized with COVID-19. *Clin Transplant* 2020:e14174. PMID: 33349940. <u>Full Text</u>

### Infectious Diseases

Lundgren JD, Grund B, Barkauskas CE, Holland TL, Gottlieb RL, Sandkovsky U, Brown SM, Knowlton KU, Self WH, Files DC, Jain MK, Benfield T, Bowdish ME, Leshnower BG, Baker JV, Jensen JU, Gardner EM, Ginde AA, Harris ES, Johansen IS, **Markowitz N**, Matthay MA, Østergaard L, Chang CC, Davey VJ, Goodman A, Higgs ES, Murray DD, Murray TA, Paredes R, Parmar MKB, Phillips AN, Reilly C, Sharma S, Dewar RL, Teitelbaum M, Wentworth D, Cao H, Klekotka P, Babiker AG, Gelijns AC, Kan VL, Polizzotto MN, Thompson BT, Lane HC, and Neaton JD. A Neutralizing Monoclonal Antibody for Hospitalized Patients with Covid-19. *N Engl J Med* 2020. PMID: 33356051. Full Text

### Infectious Diseases

McCullough PA, Alexander PE, Armstrong R, Arvinte C, Bain AF, Bartlett RP, Berkowitz RL, Berry AC, Borody TJ, Brewer JH, Brufsky AM, Clarke T, Derwand R, Eck A, Eck J, Eisner RA, Fareed GC, Farella A, Fonseca SNS, Geyer CE, Jr., Gonnering RS, Graves KE, Gross KBV, Hazan S, Held KS, Hight HT, Immanuel S, Jacobs MM, Ladapo JA, Lee LH, Littell J, Lozano I, Mangat HS, Marble B, **McKinnon JE**, Merritt LD, Orient JM, Oskoui R, Pompan DC, Procter BC, Prodromos C, Rajter JC, Rajter JJ, Ram CVS, Rios SS, Risch HA, Robb MJA, Rutherford M, Scholz M, Singleton MM, Tumlin JA, Tyson BM, Urso RG, Victory K, Vliet EL, Wax CM, Wolkoff AG, Wooll V, and Zelenko V. Multifaceted highly targeted sequential multidrug treatment of early ambulatory high-risk SARS-CoV-2 infection (COVID-19). *Rev Cardiovasc Med* 2020; 21(4):517-530. PMID: 33387997. Request Article

#### Internal Medicine

Jain V, **Gupta K**, Bhatia K, Bansal A, Arora S, **Khandelwal AK**, Rosenberg JR, Levisay JP, Tommaso CL, Ricciardi MJ, and Qamar A. Management of STEMI during the COVID-19 pandemic: Lessons learned in 2020 to prepare for 2021. *Trends Cardiovasc Med* 2020. PMID: 33338636. Full Text

## Internal Medicine

Lazar MH, Fadel R, Gardner-Gray J, Tatem G, Caldwell MT, Swiderek J, and Jennings JH. Racial Differences in a Detroit, MI, ICU Population of Coronavirus Disease 2019 Patients. *Crit Care Med* 2020. PMID: 33372746. Full Text

## Internal Medicine

Piscoya A, **Ng-Sueng LF**, Parra Del Riego A, Cerna-Viacava R, Pasupuleti V, Roman YM, Thota P, White CM, and Hernandez AV. Efficacy and harms of remdesivir for the treatment of COVID-19: A systematic review and meta-analysis. *PLoS One* 2020; 15(12):e0243705. PMID: 33301514. Full Text

# Pulmonary and Critical Care Medicine

**Lazar MH**, **Fadel R**, **Gardner-Gray J**, **Tatem G**, **Caldwell MT**, **Swiderek J**, and **Jennings JH**. Racial Differences in a Detroit, MI, ICU Population of Coronavirus Disease 2019 Patients. *Crit Care Med* 2020. PMID: 33372746. Full Text