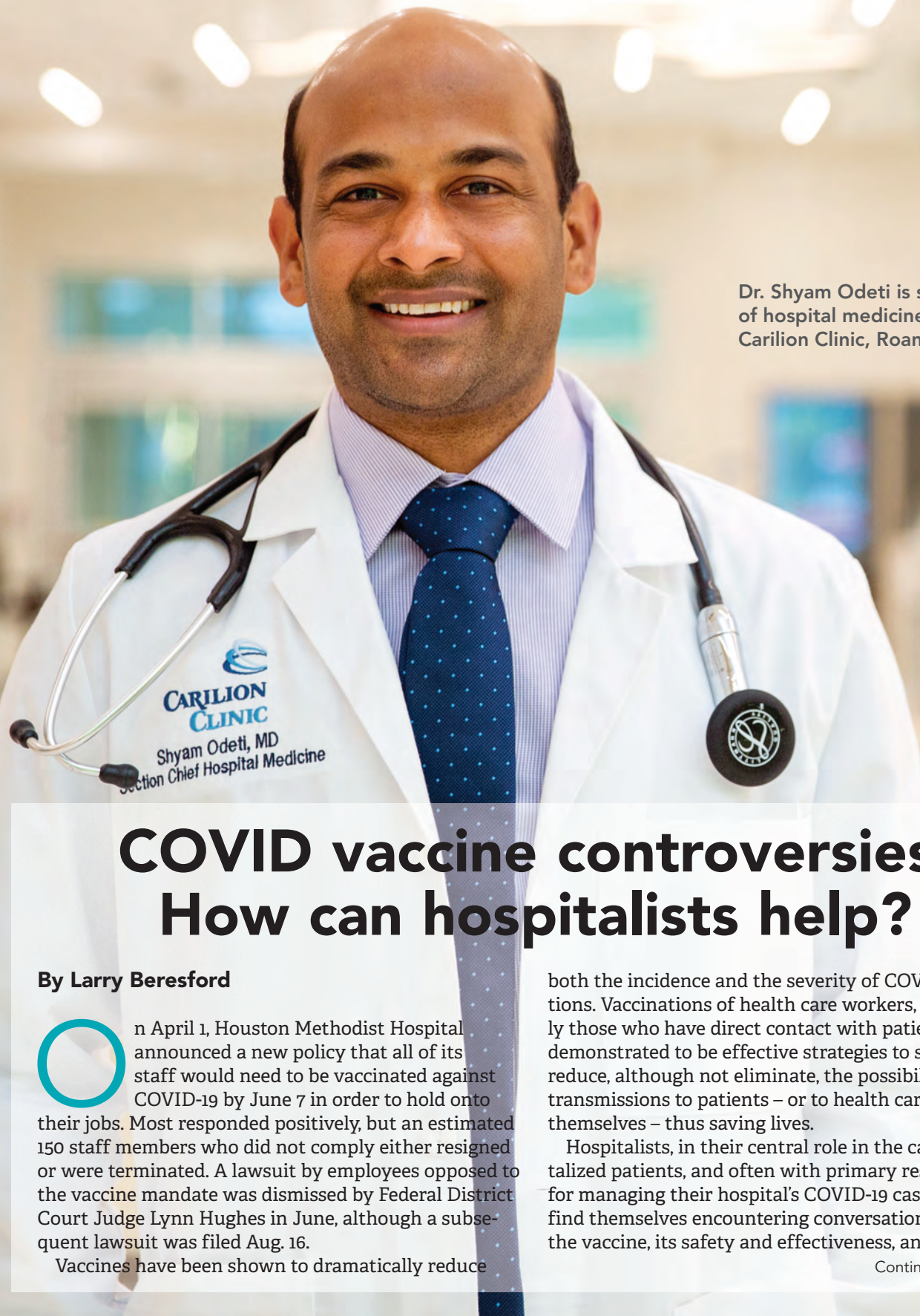


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Dr. Shyam Odeti is section chief of hospital medicine at Carilion Clinic, Roanoke, Va.

## COVID vaccine controversies: How can hospitalists help?

By Larry Beresford

**O**n April 1, Houston Methodist Hospital announced a new policy that all of its staff would need to be vaccinated against COVID-19 by June 7 in order to hold onto their jobs. Most responded positively, but an estimated 150 staff members who did not comply either resigned or were terminated. A lawsuit by employees opposed to the vaccine mandate was dismissed by Federal District Court Judge Lynn Hughes in June, although a subsequent lawsuit was filed Aug. 16.

Vaccines have been shown to dramatically reduce

both the incidence and the severity of COVID infections. Vaccinations of health care workers, especially those who have direct contact with patients, are demonstrated to be effective strategies to significantly reduce, although not eliminate, the possibility of viral transmissions to patients – or to health care workers themselves – thus saving lives.

Hospitalists, in their central role in the care of hospitalized patients, and often with primary responsibility for managing their hospital's COVID-19 caseloads, may find themselves encountering conversations about the vaccine, its safety and effectiveness, and mandates

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# Tolerance in medicine

Overcoming frustration and fatigue

By Ronald Matuszak, MD

There is a narrative being pushed now about health care professionals being “frustrated” and “tired” in the midst of this current Delta COVID wave. This stems from the idea that this current wave was potentially preventable if everyone received the COVID vaccines when they were made available.

I certainly understand this frustration and am tired of dealing with COVID restrictions and wearing masks. Above all I’m tired of talking about it. But frustration and fatigue are nothing new for those in the health care profession. Part of our training is that we should care for everyone, no matter what. Compassion for the ill should not be restricted to patients with a certain financial status, immigration status, race, gender, sexual orientation, or education level. Socially and polit-

*“I urge people to remember that in the business of health care we deal with preventable diseases all the time, every day.”*

ically, we are having a reckoning with how we treat people and how we need to do better to create a more just society. A key virtue in all of this is tolerance.

If we are going to have a free society, tolerance is essential. This is because in a free society people are going to, well, be free. In medicine we tolerate people who are morbidly obese, drink alcohol excessively, smoke, refuse to take their medications, won’t exercise, won’t sleep,



*Dr. Matuszak works for Sound Physicians and is a nocturnist at a hospital in the San Francisco Bay Area.*

and do drugs. The overwhelming majority of these people know that what they are doing is bad for their health. Not only do we tolerate them, we are taught to treat them indiscriminately. When someone who is morbidly obese has a heart attack, we treat them, give them medicine, and tell them the importance of losing weight. We do not tell them, “you shouldn’t have eaten so much and gotten so fat,” or “don’t you wish you didn’t get so fat?”

What I am trying to circle back to here is that, if you could force people into doing everything they could for their health and eliminate all “preventable” diseases, then the need for health care in this country – including doctors, nurses, hospitals, and pharmaceuticals, just to name a few – would be cut dramatically. While the frustration for the continued COVID surges is understandable, I urge people to remember that in the business of health care we deal with preventable diseases all the time, every day. We are taught to show compassion for everyone, and for good reason. We have no idea what many people’s backstories are; we just know that they are sick and need help.

I urge everyone to put the unvaccinated under the same umbrella you put other people with preventable diseases, which, sadly, is a lot of patients. Continue to educate those about the vaccine as you should about every other aspect of their health. Education is part of our job as health care professionals but judgment is not.

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THE HOSPITALIST (ISSN 1553-085X) is published monthly for the Society of Hospital Medicine by Frontline Medical Communications Inc., 7 Century Drive, Suite 302, Parsippany, NJ 07054-4609. Print subscriptions are free for Society of Hospital Medicine members. Annual paid subscriptions are available to all others for the following rates:

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In the Literature

# Clinician reviews of HM-centric research

By Maryann T. Ally, MD, MPH, FACP, FHM; Joseph Avalos, MD, FHM; Jessica Bazick, MD; Catherine E. Firestein, MD, MPH, FHM; Bryan Huang, MD, FHM; Milla Kviatkovsky, DO; Kevin Kwak, MD; Jonathan McIntyre, MD; Sandeep Segar, MD

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By Maryann T. Ally, MD, MPH, FACP, FHM

### 1 The clinical use of lung MRI in cystic fibrosis

**CLINICAL QUESTION:** What impact does lung MRI have on the management of patients with cystic fibrosis?

**BACKGROUND:** Patients with cystic fibrosis (CF) are living longer thanks to advances in medical pharmacotherapy, but pulmonary exacerbations still contribute to significant morbidity and mortality. Pulmonologists use a combination of pulmonary function tests or lung clearance index, radiographic imaging, and respiratory culture results to guide management of patients with CF. Currently, CT scan and chest x-ray are the most utilized radiographic studies to evaluate lung disease, since historically MRI of the lung is more expensive and less accessible, has longer acquisition time, and is affected by respiratory motion. Chest x-rays are inexpensive, accessible, and quick to perform, but there is risk of radiation exposure with repeated chest x-rays performed over time. Chest x-rays can miss 91% of mucus plugs and 44% of bronchiectasis when compared with CT scans. New technical developments of lung MRI, however, can aid in the diagnosis between lung inflammation and scar tissue.

**STUDY DESIGN:** Review article.

**SETTING:** National and international

peer-reviewed articles, position papers, and review articles.

**SYNOPSIS:** There have been several advancements in MRI techniques that can be used to detect reversible



Dr. Ally

lung architecture in patients with CF, and CF-specific MRI scoring systems have been developed. Novel MRI techniques known as ultrashort echo-time can show pulmonary structures, including mucus plugs and bronchial dilation, to a submillimeter spatial resolution, though they are inferior to CT scan in detecting normal airways. Three-dimensional, ultrashort echo-time MRI of the lungs with new respiratory synchronization systems has shorter acquisition times and is not affected by respiratory motion artifact. MRI T2-weighted images can capture reversible changes caused by a pulmonary exacerbation, such as edema, infiltrate, and mucus plugs. When there is lung inflammation, the T2-weighted images are increased and, after completion of antibiotics when the inflammation subsides, the signals decrease. For example, when patients with CF have allergic bronchopulmonary aspergillosis, it is diagnosed using radiographic imaging. CT scans have a 100% specificity for ABPA, but using both MRI

T1-weighted and T2-weighted sequences in a technique called the inverted mucoid impaction signal can also diagnose this disease process, as shown in one study showing a 94% sensitivity and 100% specificity using this approach.

Functional MRIs, such as contrast-enhanced MRI of ventilation and MRI of perfusion, aim to assess small airways, which other imaging modalities cannot assess. Contrast-enhanced MRI of lung ventilation using Xenon gas is sensitive to early airway obstruction in patients with CF with normal spirometry and is more sensitive than pulmonary function tests or lung clearance index. The use of Xenon gas is pending approval from the Food and Drug Administration and is already clinically being used in the United Kingdom. Additionally, this type of contrast-enhanced MRI requires expensive hardware and skilled personnel.

Contrast-enhanced MRI of perfusion is another technique to assess severity of disease. There are additional developments being investigated that would increase the size of the MRI machine, improve image resolution, decrease acquisition times and noise, and automate quantification. The benefits of using lung MRI for annual follow-up, emergent cases, and research purposes in patients with CF include no radiation exposure, high-resolution scoring of structural abnormalities, and characterization of airway inflammation, whereas the disadvantages are that MRIs are more expensive, not as accessible, and currently take longer to complete when compared with CT imaging.

Hospitalists should continue to collaborate with pulmonologists to determine the best combination of diagnostic modalities to evaluate a CF patient's pulmonary exacerbation, including which radiographic study is most appropriate, especially as lung MRI continues to improve.

**BOTTOM LINE:** With advances in new techniques, lung MRI can assess the severity of lung architecture of patients with CF during

a pulmonary exacerbation and for routine monitoring of their pulmonary status, with the added benefit of being free of radiation exposure. **CITATION:** Dournes G et al. The clinical use of lung MRI in cystic fibrosis. *Chest*. 2020 Dec 17; 159(6):2205-17. doi: 10.1016/j.chest.2020.12.008.

*Dr. Ally is associate clinical professor of medicine in the Division of Hospital Medicine and a physician adviser at the University of California, San Diego.*

By Joseph Avalos, MD, FHM

### 2 Management of diabetes and hyperglycemia in the hospital

**CLINICAL QUESTION:** What are the best practices for controlling hyperglycemia in the inpatient setting?

**BACKGROUND:** Diabetes mellitus and hyperglycemia are associated with higher mortality, increased length of stay, and hospital-associated complications. Inappropriate treatment methods can increase risk for hypoglycemia, also associated with poor inpatient outcomes.



Dr. Avalos

**STUDY DESIGN:** Meta-analysis of randomized clinical trials.

**SETTING:** Multiple hospitals including medicine and surgery patients with type 2 diabetes mellitus.

**SYNOPSIS:** How hyperglycemia is treated or prevented in the hospital will depend on the clinical setting of the patient but will largely utilize insulin as the mainstay of therapy. Primary glucose targets for fasting (less than 140 mg/dL) and random (less than 180 mg/dL); for critically ill patients, the target glucose is 140-180 mg/dL. Continuous intravenous insulin is the preferred regimen for critically ill patients, but patients should be monitored for hypokalemia, a common side effect. For non-critically ill patients, insulin therapy

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will vary: Subcutaneous sliding scale–correctional insulin is most appropriate for dietary-controlled, insulin-naïve type 2 diabetes or patients with only mild hyperglycemia. It is inappropriate for type 1 diabetes. Basal-bolus insulin (long-acting insulin plus rapid-acting mealtime insulin) and correctional is recommended for type 1 diabetes or established type 2 diabetes and patients with moderate-severe hyperglycemia. It has better control of hyperglycemia but increased risk of iatrogenic hypoglycemia. Long-acting insulin plus rapid-acting correctional is preferred for patients with decreased oral intake or while fasting or undergoing a procedure.

Noninsulin diabetes medications have not been widely used in the hospital, but recent studies show there are upcoming opportunities for their utilization in certain circumstances. Metformin, in general, should be avoided in the inpatient setting, as there can be increased risk of lactic acidosis in certain patients. Sulfonylureas, more popular in the United Kingdom, may have utility treating steroid-induced hyperglycemia but has a higher risk for hypoglycemia in the hospital setting. Thiazolidinediones, in general, should be avoided because they carry a risk of fluid retention and heart failure. Sodium-glucose cotransporter 2 inhibitors have been shown to be safe in patients with heart failure or diabetic kidney disease and are currently being studied in hospitalized patients with heart failure. dipeptidyl peptidase-4 inhibitors have lower hypoglycemia risk, and studies are favoring increased utilization, effective alone, as well as in combination with basal insulin. glucagonlike peptide receptor-1 agonists, especially used with basal insulin, have shown good glucose control but are accompanied with GI side effects; more studies are needed to show efficacy.

Patients requiring parenteral nutrition should have insulin mixed in with the formula, with glucose monitored every 6 hours. Patients with hyperglycemia on continuous enteral nutrition should receive basal insulin with correctional rapid-acting insulin every 6 hours. Steroid-induced hyperglycemia is best treated by targeting prandial glucose with higher mealtime insulin dosages or using a higher correctional insulin sliding scale. An appropriate insulin tapering plan should accompany steroid cessation plans, as well.

**BOTTOM LINE:** Insulin remains the cornerstone of diabetes and

hyperglycemia treatment in the hospital. Depending on the clinical setting – based on severity of illness, long-term diabetes control (based on hemoglobin A1c), and nutritional status – the insulin regimen will vary, with goals to target glucose 140-180 mg/dL and avoid hypoglycemia. Oral diabetes regimens will have a future role as more studies evaluate best clinical applications.

**CITATION:** Pasquel FJ et al. Management of diabetes and hyperglycaemia in the hospital. *Lancet Diabetes Endocrinol.* 2021 Mar;9(3):174-88. doi: 10.1016/S2213-8587(20)30381-8.

*Dr. Avalos is assistant clinical professor of medicine in Division of Hospital Medicine at the University of California, San Diego.*

By Jessica Bazick, MD

### 3 Impact of zinc on mortality risk and HIV disease progression among heavy alcohol users

**CLINICAL QUESTION:** Is there benefit to zinc supplementation on mortality for HIV-positive adults with heavy alcohol use?

**BACKGROUND:** Zinc deficiency is a common condition among HIV-positive people and those with alcohol-use disorders. Zinc supplementation is generally widely available and well tolerated, so it was proposed as a potential intervention to improve outcomes in HIV-positive people with heavy alcohol use. Infection with HIV, heavy alcohol use, and zinc deficiency are associated with negative health outcomes by mechanisms that result in increased microbial translocation and inflammation. The benefits of addressing zinc deficiency among people living with HIV/AIDS who are also heavy users of alcohol is unclear.

**STUDY DESIGN:** Double-blinded, placebo-controlled clinical trial.

**SETTING:** HIV clinics and nonclinical addiction care sites in St. Petersburg, Russia.

**SYNOPSIS:** This study recruited 254 participants from 2013 to 2015 for a double-blinded, placebo-controlled randomized clinical trial of zinc supplementation. The intervention group received zinc gluconate supplementation (15 mg for men and 12 mg for women, taken daily by mouth) vs. the placebo group, over a period of 18 months. The primary outcome measured was mortality risk based on a change in the Veterans Aging Cohort Study (VACS) index score from baseline and 18 months. The VACS index scores

range from 0 to 164, with higher scores associated with higher mortality risk. The secondary outcomes were changes in CD4 cell count, assessment of cardiovascular disease risk (using the Reynolds Risk Score), and changes in inflammatory biomarkers at baseline and 18 months later. Statistical analysis used adjusted linear regression analyses. Study participants were aged 18-70 years, had documented HIV infection and were naïve to antiretroviral therapy at baseline, and had heavy alcohol consumption for the past 30 days prior to enrollment. Heavy alcohol use was defined as more than 4 standard drinks per day (or more than 14 standard drinks per week) for men and more than 3 drinks per day (or more than 7 drinks per week) for women.

Zinc supplementation in this study was not associated with a reduced VACS index score or reduced cardiovascular disease risk for people with HIV and heavy alcohol use. The study also did not find a significant impact in CD4 cell counts, biomarkers of inflammation, or microbial translocation. However, the study was limited by small size and low adherence. Further trials with greater statistical power may be warranted to determine the impact zinc supplementation has on HIV-positive people who are heavy alcohol users.

**BOTTOM LINE:** Zinc supplementation was not proven to improve health outcomes in HIV-positive adults who are heavy alcohol users.

**CITATION:** Freiberg M et al. Effect of zinc supplementation vs placebo on mortality risk and HIV disease progression among HIV-positive adults with heavy alcohol use. *JAMA Netw Open.* 2020;3(5):e204330. doi: 10.1001/jamanetworkopen.2020.4330.

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By Catherine E. Firestein, MD, MPH, FHM

### 4 Non-vitamin K oral anticoagulants linked with lower fracture risk than warfarin

**CLINICAL QUESTION:** Is there a difference in fracture risk associated with non-vitamin K oral anticoagulants vs. warfarin?

**BACKGROUND:** Oral anticoagulants are frequently prescribed for patients with atrial fibrillation or venous thromboembolism. It has been suggested that warfarin might

increase fracture risk because of its mechanism of action, and vitamin K antagonists can impair bone mineralization. Prior studies have shown conflicting evidence regarding the fracture risk associated with warfarin and non-vitamin K oral anticoagulants (NOACs).

**STUDY DESIGN:** Systematic review and meta-analysis.

**SETTING:** Meta-analysis.

**SYNOPSIS:** The authors searched multiple sites for studies published through May 19, 2020, using a combination of terms including NOAC, fracture, and vitamin K antagonist. The meta-analysis included clinical trials, cohort studies, and case-control studies but excluded case reports, review articles, editorials, and letters to the editor. With 388,209 individual patients, 29 studies were analyzed, including 5 cohort studies and 24 randomized controlled trials, which translates to 388,209 individual patients.

Patients treated with NOACs had a lower fracture risk than those treated with warfarin (pooled risk ratio, 0.84; 95% confidence interval, 0.77-0.91; *P* less than .001). For risk of hip fracture in particular, the subgroup analyses using 17 studies of individual anticoagulants found the risk to be lower in patients taking apixaban but not other NOACs (pooled RR, 0.68; 95% CI, 0.52-0.89; *P* = .006). For vertebral fractures, the subgroup analyses using 11 studies demonstrated lower risk in patients taking rivaroxaban (pooled RR, 0.73; 95% CI, 0.63-0.85; *P* less than .001) or apixaban (pooled RR, 0.47; 95% CI, 0.23-0.95; *P* = .035). One limitation is that none of the trials were explicitly designed to assess fracture risk; additionally, the calculated number of fractures was a sum of events at each site rather than the number of patients with a fracture, so a patient with multiple fractures might have accounted for multiple data points.

**BOTTOM LINE:** When prescribing oral anticoagulants, consider using NOACs over warfarin in patients at increased risk of fractures.

**REFERENCE:** Huang H et al. Fracture risks in patients treated with different oral anticoagulants: A systematic review and meta-analysis. *J Am Heart Assoc.* 2021 Apr 6;10(7):e019618. doi: 10.1161/JAHA.120.019618.

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Continued from page 4

By Bryan Huang, MD, FHM

## 5 Transition from IV to oral antibiotics for *S. aureus* bacteremia

**CLINICAL QUESTION:** Can patients with *Staphylococcus aureus* bacteremia be successfully treated with transition from IV to oral antibiotics?

**STUDY DESIGN:** Retrospective cohort study.

**SETTING:** Single medical center in the Netherlands.

**SYNOPSIS:** Of patients with complicated *S. aureus* bacteremia with metastatic infection (osteomyelitis, abscess, joint infection) but without endovascular infection (no evidence of endocarditis or other endovascular infection on echocardiogram or PET/CT), 106 were enrolled. Of those



Dr. Huang

enrolled, 45 patients received IV antibiotics only, predominantly flucloxacillin, for a median of 45 days and 61 were transitioned from IV to oral antibiotics, predominantly clindamycin, after a median of 16 days. No relapses of bacteremia were found in a 3-month follow-up period in either group. In the prolonged IV group, 3-month mortality was 13.3% vs. 6.6% in the IV-oral switch group ( $P = .242$ ). Median hospital admission duration was 29 days in the prolonged IV group vs. 17 days in the IV-oral switch group ( $P = .001$ ).

Limitations include that this was a single-center study done in a foreign hospital, the incidence of methicillin-resistant *S. aureus* (MRSA) was low (4 of 106 patients), flucloxacillin is not commonly used in the United States, and PET/CT is rarely used to assess for endovascular infection in the United States.

**BOTTOM LINE:** There is growing evidence that, in select patients, *S. aureus* bacteremia may be treated with a transition from IV to oral antibiotics.

**CITATION:** Kouijzer IJE et al. Intravenous to oral switch in complicated *Staphylococcus aureus* bacteremia without endovascular infection: A retrospective single-center cohort study. *Clin Infect Dis*. 2021 Feb 19;73(5):895-8. doi: 10.1093/cid/ciab156.

*Dr. Huang is physician adviser and clinical professor of medicine in the Division of Hospital Medicine at the University of California, San Diego.*

By Milla Kviatkovsky, DO

## 6 Impact of IV iron in iron-deficient patients with CKD

**CLINICAL QUESTION:** Does IV iron improve exercise capacity in patients with chronic kidney disease who are iron deficient but not anemic?

**BACKGROUND:** Patients with chronic kidney disease (CKD) have significant excess mortality, many from cardiac-related causes including heart failure. Studies have shown that, for patients with CKD and heart failure, survival is worse in those with iron deficiency. Other



Dr. Kviatkovsky

studies specific to patients with heart failure have shown benefit of IV iron, demonstrating reduced cardiovascular events, improved functional capacity, and decreased symptom burden. The authors hypothesized that a single dose of 1,000 mg of IV iron would benefit functional capacity in nonanemic patients with CKD.

**STUDY DESIGN:** Prospective randomized, controlled, double-blinded trial.

**SETTING:** Three sites in the United Kingdom.

**SYNOPSIS:** Adults with CKD stages 3b-5 with ferritin less than 100 mcg/L or transferrin saturation less than 20% but without anemia were randomly assigned in a 1:1 ratio to receive 1,000 mg IV iron or placebo of clear saline solution. Patients underwent assessments at 1 and 3 months, including a 6-minute walk test (6MWT), basic metabolic panel, full blood count, hemoglobin, and serum ferritin. New York Heart Association Functional Classification, ECG, and 2D echo were performed at baseline and at 1 and 3 months. The primary endpoint was functional capacity at 1 and 3 months as assessed by the 6MWT.

Secondary endpoints included adverse events such as death, infections, and hospitalization. A total of 54 patients were randomized, and mean age was 61.6 years in the treatment group and 57.8 years in the placebo group. Study results suggested that there was no statistically significant difference in the 6MWT between the treatment and placebo group at 1 and 3 months, although the mean increase in 6MWT at 3 months for the treatment group was 6.0 meters, compared with 1.9 meters

in the placebo group. Subjective assessment of quality of life was not significantly different between the two groups at 1 and 3 months. There was no change in NYHA category of heart failure or echo findings between groups. There were no adverse events related to the treatment arm.

**BOTTOM LINE:** In contrast with the results of IV infusion of iron in heart failure patients, this study did not show benefit of a single dose of 1,000 mg IV iron infusion in patients with CKD and iron deficiency but no anemia with regards to the 6MWT or quality of life scores.

**CITATION:** Bhandari S et al. A multicentre prospective double blinded randomised controlled trial of intravenous iron (ferric Derisomaltose (FDI)) in iron deficient but not anaemic patients with chronic kidney disease on functional status. *BMC Nephrol*. 2021 Mar 30;22(1):115. doi: 10.1186/s12882-021-02308-y.

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By Kevin Kwak, MD

## 7 Cryoballoon ablation superior to drug therapy as initial treatment for paroxysmal AFib

**CLINICAL QUESTION:** Is cryoballoon ablation more effective than

antiarrhythmic agents, and is it safe as an initial treatment option for symptomatic paroxysmal atrial fibrillation?

**BACKGROUND:** Recent studies have shown the superiority of



Dr. Kwak

catheter ablation in treatment of paroxysmal atrial fibrillation (AFib) over drug therapy in lowering the risk of recurrence and preventing progression to persistent AFib.

Despite these studies, the current guidelines for treatment of paroxysmal AFib recommend the use of antiarrhythmic agents prior to ablation. This study aims to assess the treatment success and safety profile of ablation as the first-line therapy.

**STUDY DESIGN:** Randomized, controlled trial.

**SETTING:** A set of 24 U.S. medical centers.

**SYNOPSIS:** Patients who had symptomatic, paroxysmal AFib and had

never received antiarrhythmic agents were randomized to either undergo cryoballoon ablation or receive a class I/III antiarrhythmic agent. These patients were followed for 12 months to monitor treatment success, as well as any procedure-related serious adverse events.

Approximately 75% of patients in the ablation therapy group achieved treatment success at 12 months, compared with 45% of patients in the drug therapy group. The study was revealed a similar safety profile between patients in both groups, with serious adverse events – clinically significant pericardial effusion, transient ischemic attack, MI, and major bleeding – occurring in approximately 14% of the patients.

**BOTTOM LINE:** Cryoballoon ablation is superior to antiarrhythmic agents as first-line therapy for prevention of recurrence of atrial arrhythmias. In addition, there were few serious adverse events associated with cryoablation.

**CITATION:** Oussama MW et al. Cryoballoon ablation as initial therapy for atrial fibrillation. *N Engl J Med*. 2021 Jan 28;384(4):316-24. doi: 10.1056/NEJMoa2029554.

*Dr. Kwak is assistant professor of medicine at the University of California, San Diego.*

By Jonathan McIntyre, MD

## 8 No need to adjust PAUSE protocol for bleeding risk

**CLINICAL QUESTION:** Are there clinically significant modifiable risk factors for perioperative bleeding within the PAUSE protocol, a perioperative direct oral anticoagulant (DOAC) interruption strategy for patients with nonvalvular atrial fibrillation?

**BACKGROUND:** The perioperative management of anticoagulation, either a DOAC or warfarin, in patients with atrial fibrillation (AFib) has implications on the risk of bleeding and thromboembolism. Advanced age, heparin bridging, renal failure, aspirin coadministration, and Charlson comorbidity score were predictive of major bleeding in patients treated with warfarin. Only recently have strategies for perioperative DOAC management been published. The PAUSE study (Perioperative Anticoagulant Use for Surgery Evaluation) demonstrated that a standardized perioperative interruption scheme, driven by surgery/procedure-associated bleeding

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# Candida auris transmission can be contained in post-acute care settings

By Judy Stone, MD

**A** new study from Orange County, Calif., shows how *Candida auris*, an emerging pathogen, was successfully identified and contained in long-term acute care hospitals (LTACHs) and ventilator-capable skilled-nursing facilities (vSNFs).

Lead author Ellora Karmarkar, MD, MSc, formerly an epidemic intelligence service officer with the Centers for Disease Control and Prevention and currently with the California Department of Public Health, said in an interview that the prospective surveillance of urine cultures

for *C. auris* was prompted by “seeing what was happening in New York, New Jersey, and Illinois [being] pretty alarming for a lot of the health officials in California, [who] know that LTACHs are high-risk facilities because they take care of really sick people. Some of those people are there for a very long time.”

Therefore, the study authors decided to focus their investigations there, rather than in acute care hospitals, which were believed to be at lower risk for *C. auris* outbreaks.

The Orange County Health Department, working with the California Department of Health and the CDC, asked labs to prospectively identify all

*Candida* isolates in urines from LTACHs between September 2018 and February 2019. Normally, labs do not speciate *Candida* from nonsterile body sites.

Dan Diekema, MD, an epidemiologist and clinical microbiologist at the University of Iowa, Iowa City, who was not involved in the study, told this news organization, “Acute care hospitals really ought to be moving toward doing species identification of *Candida* from nonsterile sites if they really want to have a better chance of detecting this early.”

The OCHD also screened LTACH and vSNF

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risk, conferred low rates of major bleeding (1.5%) and arterial thromboembolism (0.3%) in 3,007 enrolled patients. This subanalysis of the PAUSE data set aimed to identify clinically significant, modifiable risk factors for perioperative bleeding within the context of the PAUSE anticoagulation interruption protocol. **STUDY DESIGN:** Prospective management study.

**SETTING:** Twenty-three clinical centers in Canada, United States, and Europe enrolled patients. Enrollment dates were Aug. 1, 2014, through July 31, 2018.

**SYNOPSIS:** The PAUSE study recruited adults 18 years or older with AFib on dabigatran, rivaroxaban, or apixaban into three cohorts, and interruption of anticoagulation was executed based on approximated surgical/procedural bleeding risk. For apixaban and rivaroxaban, high-bleeding risk procedures had an interruption and resumption interval of 2 days, whereas for lower-bleeding risk procedures, it was 1 day. For dabigatran, creatinine clearance (CrCl) 50 or greater, or less than 50 mL/min, was included in the interruption protocol. DOAC interruption was 1 day for patients on dabigatran and with a CrCl of 50 mL/min or greater, 2 days for patients with a CrCl of 30-50 mL/min undergoing a low-bleeding risk procedure, and 4 days in patients undergoing a high-bleeding risk procedure. The primary outcome was clinically relevant nonmajor bleeding (CRNM) and/or major bleeding (MB). Presumed predictors of bleeding include age, sex, comorbidities, medications, the clinical variables of the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, renal disease CrCl less than

50 mL/min, prior history of major bleeding, and protocol interruption compliance. This subanalysis measured the association of each of the presumed risk factors with CRNM+MB using logistic regression for univariate analysis. A Forest plot was created to report the odds ratio. Additionally, a multivariate logistic regression was completed to control for geographical confounding.

The multivariate regression analysis stratified by region found that hypertension and prior bleeding were significantly associated with CRNM/MB (odds ratio, 1.79; 95% confidence interval, 1.07-2.99 and OR, 1.71; 95% CI, 1.08-2.71, respectively). Additionally, the DOAC level (greater than 50 ng/mL vs. 50 ng/mL or less) had no significant association with CRNM/MB.

**BOTTOM LINE:** The PAUSE protocol provides an effective strategy for DOAC interruption anchored on surgery/procedure-related bleeding risk, DOAC half-life, and CrCl for dabigatran. This subanalysis of the PAUSE data demonstrated that hypertension and a prior history of bleeding were the only independent determinants of perioperative bleeding. Therefore, augmentation of the PAUSE management protocol to mitigate against bleeding is not needed.

**CITATION:** Tafur AJ et al. Predictors of bleeding in the perioperative anticoagulant use for surgery evaluation study. *J Am Heart Assoc.* 2020 Oct 20;9(19):e017316. doi: 10.1161/JAHA.120.017316.

*Dr. McIntyre is assistant clinical professor of medicine in the Division of Hospital Medicine at the University of California, San Diego.*

By Sandeep Segar, MD

## 9 Increased infliximab clearance associated with higher colectomy rates in acute severe ulcerative colitis

**CLINICAL QUESTION:** What is the optimal dosing of infliximab in patients with acute severe ulcerative colitis?

**BACKGROUND:** Patients hospitalized with acute severe ulcerative colitis (ASUC) often require colectomy. Infliximab (IFX) is a tumor necrosis factor- $\alpha$  antagonist that is an effective salvage therapy against ASUC and to prevent colectomy; however, optimal



Dr. Segar

IFX dosing is unclear. Higher baseline IFX drug clearance is associated with worsened clinical outcomes and higher levels of antibodies to IFX. This study aims to assess the relationship between IFX drug clearance and rate of colectomy in ASUC to help offer a framework for individualized clearance-based dosing for IFX. **STUDY DESIGN:** Retrospective, observational study.

**SETTING:** Tertiary care teaching hospital in San Diego.

**SYNOPSIS:** With use of chart review of hospitalized patients from July 2014 to May 2018, data were obtained on 39 patients with clinically documented ASUC who had been initiated on IFX as rescue therapy. Calculated baseline IFX clearance was calculated for subjects with a pre-established formula using data prior to IFX administration:  $0.407 \times (\text{albumin concentration}/4.1) - 1.54 \times (1.471) \text{IFX Antibody} \times (0.764) \text{sex}$ , where IFX Antibody status

is 0 (not present) at baseline, and sex is 1 for females and 0 for males.

The primary endpoint compared baseline infliximab clearance between patients requiring colectomy at 1 month, 6 months, and 12 months with those not requiring colectomy. The median calculated infliximab clearance was higher in patients who required colectomy at 6 months (0.733 L/day vs. 0.569;  $P = .005$ ) compared with those who did not. An IFX clearance greater than 0.627 L/day identified patients requiring colectomy with 80% sensitivity and 82.8% specificity. Patients with IFX clearance of 0.627 L/day or more underwent colectomy within 6 months, compared with patients with lower IFX clearance values (61.5% vs. 7.7%;  $P = .001$ ). Of note, the total administered IFX doses were higher among patients who required colectomy at 6 months, compared with those who did not; however, serum IFX concentrations were not assessed. Similar correlations were noted at 1-month and 12-month endpoints.

**BOTTOM LINE:** In hospitalized patients with ASUC, who were receiving IFX as salvage therapy, higher baseline IFX clearance is associated with higher rates of colectomy. Future studies are warranted to compare outcomes in clearance-based dosing vs. standard dosing of IFX. **CITATION:** Battat R et al. Baseline clearance of infliximab is associated with requirement for colectomy in patients with acute severe ulcerative colitis. *Clin Gastroenterol Hepatol.* 2021 Mar;19(3):511-8.e6. doi: 10.1016/j.cgh.2020.03.072.

*Dr. Segar is assistant clinical professor of medicine in the Division of Hospital Medicine at the University of California, San Diego.*

# Health care–associated infections spiked in 2020 in U.S. hospitals

By Lucy Hicks

Several health care-associated infections in U.S. hospitals spiked in 2020 compared to the previous year, according to a Centers for Disease Control and Prevention analysis published Sept. 2 in *Infection Control and Hospital Epidemiology* (2021. doi: 10.1017/ice.2021.362). Soaring hospitalization rates, sicker patients who required more frequent and intense care, and staffing and supply shortages caused by the COVID-19 pandemic are thought to have contributed to this increase.

This is the first increase in health care–associated infections since 2015.

These findings “are a reflection of the enormous stress that COVID has placed on our health care system,” Arjun Srinivasan, MD (Capt., U.S. Public Health Service), the associate director of the CDC’s Health Care–Associated Infection Prevention Programs, Atlanta, told this news organization. He was not an author of the article, but he supervised the research. “We don’t want anyone to read this report and think that it represents a failure of the individual provider or a failure of health care providers in this country in their care of COVID patients,” he said. He noted that health care professionals have provided “tremendously good care to patients under extremely difficult circumstances.”

“People don’t fail – systems fail – and that’s what happened here,”

he said. “Our systems that we need to have in place to prevent health care–associated infection simply were not as strong as they needed to be to survive this challenge.”

In the study, researchers used data reported to the National Healthcare Safety Network, the CDC’s tracking system for health care–associated infections. The team compared national standard infection ratios – calculated by dividing the number of reported infections by the number of predicted infections – between 2019 and 2020 for six routinely tracked events:

- Central line–associated bloodstream infections
- Catheter-associated urinary tract infections (CAUTIs)
- Ventilator-associated events (VAEs)
- Infections associated with colon surgery and abdominal hysterectomy
- *Clostridioides difficile* infections
- Methicillin-resistant *Staphylococcus aureus* (MRSA) infections

Infections were estimated using regression models created with baseline data from 2015.

“The new report highlights the need for health care facilities to strengthen their infection prevention programs and support them with adequate resources so that they can handle emerging threats to public health, while at the same time ensuring that gains made in combating HAIs [health care–associated infections] are not lost,” said the Association for Professionals in

Infection Control and Epidemiology in a statement.

The analysis revealed significant national increases in central line–associated bloodstream infections, CAUTIs, VAEs, and MRSA infections in 2020 compared to 2019. Among all infection types, the greatest increase was in central-line infections, which

*The influx of sicker patients in hospitals throughout 2020 led to more frequent and longer use of medical devices.*

were 46%–47% higher in the third quarter and fourth quarter (Q4) of 2020 relative to the same periods the previous year. VAEs rose by 45%, MRSA infections increased by 34%, and CAUTIs increased by 19% in Q4 of 2020 compared to 2019.

The influx of sicker patients in hospitals throughout 2020 led to more frequent and longer use of medical devices such as catheters and ventilators. The use of these devices increases risk for infection, David P. Calfee, MD, chief medical epidemiologist at the New York–Presbyterian/Weill Cornell Medical Center, said in an interview. He is an editor of *Infection Control and Hospital Epidemiology* and was not involved with the study. Shortages in personal protective equipment and crowded intensive care units could also have affected how care

was delivered, he said. These factors could have led to “reductions in the ability to provide some of the types of care that are needed to optimally reduce the risk of infection.”

There was either no change or decreases in infections associated with colon surgery or abdominal hysterectomy, likely because there were fewer elective surgeries performed, said Dr. Srinivasan. *C. difficile*–associated infections also decreased throughout 2020 compared to the previous year. Common practices to prevent the spread of COVID-19 in hospitals, such as environmental cleaning, use of personal protective equipment, and patient isolation, likely helped to curb the spread of *C. difficile*. Although these mitigating procedures do help protect against MRSA infection, many other factors, notably, the use of medical devices such as ventilators and catheters, can increase the risk for MRSA infection, Dr. Srinivasan added.

Although more research is needed to identify the reasons for these spikes in infection, the findings help quantify the scope of these increases across the United States, Dr. Calfee said. The data allow hospitals and health care professionals to “look back at what we did and then think forward in terms of what we can do different in the future,” he added, “so that these stresses to the system have less of an impact on how we are able to provide care.”

Dr. Srinivasan and Dr. Calfee report no relevant financial relationships.

Continued from previous page

patients with composite cultures from the axilla-groin or nasal swabs. Screening was undertaken because 5%–10% of colonized patients later develop invasive infections, and 30%–60% die.

The first bloodstream infection was detected in May 2019. Per the report, published online Sept. 7 in *Annals of Internal Medicine* (2021. doi: 10.7326/M21-2013), “As of 1 January 2020, of 182 patients, 22 (12%) died within 30 days of *C. auris* identification; 47 (26%) died within 90 days. One of 47 deaths was attributed to *C. auris*.” Whole-genome sequencing showed that the isolates were all closely related in clade III.

Experts conducted extensive education in infection control at the LTACHs, and communication among the LTACHs and between the long-term facilities and acute care hospitals was improved. As a result, receiving facilities accepting transfers began culturing their newly

admitted patients and quickly identified 4 of 99 patients with *C. auris* who had no known history of colonization. By October 2019, the outbreak was contained in two facilities, down from the nine where *C. auris* was initially found.

Dr. Diekema noted, “The challenge, of course, for a new emerging MDRO [multidrug-resistant organism] like *Candida auris*, is that the initial approach, in general, has to be almost passive, when you have not seen the organism. ... Passive surveillance means that you just carefully monitor your clinical cultures, and the first time you detect the MDRO of concern, then you begin doing the point prevalence surveys. ... This [prospective] kind of approach is really good for how we should move forward with both initial detection and containment of MDRO spread.”

Many outbreak studies are confined to a particular institution. Authors of an accompanying editorial (*Ann Intern Med*. 2021 Sep 7. doi: 10.7326/

M21-3456) commented that this study “underlines the importance of proactive protocols for outbreak investigations and containment measures across the entirety of the health care network serving at-risk patients.”

In her research, Dr. Karmarkar observed that “some of these facilities don’t have the same infrastructure and infection prevention and control that an acute care hospital might.”

She said in an interview that “one of the challenges was that people were so focused on COVID that they forgot about the MDROs. ... Some of the things that we recommend to help control *Candida auris* are also excellent practices for every other organism including COVID care. ... What I appreciated about this investigation is that every facility that we went to was so open to learning, so happy to have us there. They’re very interested in learning about *Candida auris* and understanding what they could do to control it.”



# Leading through adversity

Resilience and positive change

By Erin E. King, MD

**PHM 2021 session**

Leading through adversity

**Presenter**

Ilan Alhadeff, MD, MBA, SFHM, CLHM

**Session summary**

As the VP of hospitalist services and a practicing hospitalist in Boca Raton, Fla., Dr. Alhadeff shared an emotional journey where the impact of lives lost has led to organizational innovation and advocacy. He started this journey on the date of the Parkland High School shooting, Feb. 14, 2018. On this day, he lost his 14-year-old daughter Alyssa and described subsequent emotions of anger, sadness, hopelessness, and the pressure to be the protector of his family.

Despite receiving an outpouring of support through memorials, texts, letters, and social media posts, he was immersed in “survival mode.” He likens this to the experience many of us may be having during

the pandemic. He described caring for patients with limited empathy and the impact this likely had on patient care. During this challenging time, the strongest supports became those that stated they couldn’t imagine how this event could have impacted Dr. Alhadeff’s life but offered support in any way needed – true empathic communication.

He and his wife founded Make Our Schools Safe (MOSS), a student-forward organization that promotes a culture of safety. This organization supports efforts for silent safety alerts in schools and fencing around schools to allow for 1-point entry. Lessons Dr. Alhadeff learned that might impact any pediatric hospitalist include the knowledge that mental health concerns aren’t going away; for example, after a school shooting any student affected should be provided counseling services as needed, and turning grief into action can help.

Dr. Alhadeff describes resiliency as the ability to bounce back from adversity, with components includ-

ing self-awareness, mindfulness, self-care, positive relationships, and purpose. While many of us have not had the great personal losses experienced by Dr. Alhadeff, we all are experiencing an once-in-a-lifetime transformation of health care with political and social interference. It is up to each of us to determine our role and how we can use our influence for positive change.

As noted by Dr. Alhadeff, “We are not all in the same boat. We ARE in the same storm.”

**Key takeaways**

- How PHM can promote MOSS: Allow children to be part of the work to keep schools safe. Advocate for local MOSS chapters. Support legislative advocacy for school safety.
- Despite adversity, we have the ability to demonstrate resilience. We do so through development of self-awareness, mindfulness, engagement in self-care, nurturing positive relationships, and continuing to pursue our greater purpose.



*Dr. King is a pediatric hospitalist at Children’s Minnesota, Minneapolis, and the director of medical education, an associate program director for the Pediatrics Residency program at the University of Minnesota. She received her medical degree from Wright State University Boonshoft School of Medicine and completed pediatric residency and chief residency at the University of Minnesota.*



Rupesh Prasad, MD, MPH, CPE, SFHM  
SHM Member - 16 years

“Joining SHM provided me with not only the resources to be a successful hospitalist, but also a strong platform to share my experiences and learn from pioneers in this field. Being part of the Hospital Medicine community, and being involved in many different committees, Special Interest Groups, and the HMX portal, has been a wonderful learning and enlightening experience. The ongoing COVID-19 pandemic highlights the value of being engaged with peers in SHM, where we have been able to share our challenges and successes dealing with this crisis, while also helping support and strengthen each other as we try to build resilience and combat burnout in this field.”

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# Febrile infant guideline allows wiggle room on hospital admission, testing

By Heidi Splete

MDedge News

The long-anticipated American Academy of Pediatrics guidelines for the treatment of well-appearing febrile infants have arrived, and key points include updated guidance for cerebrospinal fluid testing and urine cultures, according to Robert Pantell, MD, and Kenneth Roberts, MD, who presented the guidelines at the virtual Pediatric Hospital Medicine annual conference.

The AAP guideline was published in the August 2021 issue of *Pediatrics* (doi: 10.1542/peds.2021-052228). The guideline includes 21 key action statements and 40 total recommendations, and describes separate management algorithms for three age groups: infants aged 8-21 days, 22-28 days, and 29-60 days.

Dr. Roberts, of the University of North Carolina at Chapel Hill, and Dr. Pantell, of the University of California, San Francisco, emphasized that all pediatricians should read the full guideline, but they offered an overview of some of the notable points.

Some changes that drove the development of evidence-based guideline included changes in technology, such as the increased use of procalcitonin, the development of large research networks for studies of sufficient size, and a need to reduce the costs of unnecessary care and unnecessary trauma for infants, Dr. Roberts said. Use of data from large networks such as the Pediatric Emergency Care Applied Research Network provided enough evidence to support dividing the aged 8- to 60-day population into three groups.

The guideline applies to well-appearing term infants aged 8-60 days and at least 37 weeks' gestation, with fever of 38° C (100.4° F) or higher in the past 24 hours in the home or clinical setting. The decision to exclude infants in the first week of life from the guideline was because at this age, infants "are sufficiently different in rates and types of illness, including early-onset bacterial infection," according to the authors.

Dr. Roberts emphasized that the guidelines apply to "well-appearing infants," which is not always obvious. "If a clinician is not confident an infant is well appearing, the clinical practice guideline should not be applied," he said.

The guideline also includes a visual algorithm for each age group.

Dr. Pantell summarized the key action statements for the three age groups, and encouraged pediatricians to review the visual algorithms and footnotes available in the full text of the guideline.

The guideline includes seven key action statements for each of the three age groups. Four of these address evaluations, using urine, blood culture, inflammatory markers (IM), and cerebrospinal fluid (CSF). One action statement focuses on initial treatment, and two on management: hospital admission versus monitoring at home, and treatment cessation.

## Infants aged 8-21 days

The key action statements for well-appearing infants aged 8-21 days are similar to what clinicians likely would do for ill-appearing infants, the authors noted, based in part on the challenge of assessing an infant this age as "well appearing," because they don't yet have the ability to interact with the clinician.

For the 8- to 21-day group, the first two key actions are to obtain a urine specimen and blood culture, Dr. Pantell said. Also, clinicians "should" obtain a CSF for analysis and culture. "We recognize that the ability to get CSF quickly is a chal-

*Some changes that drove the development of evidence-based guideline included a need to reduce the costs of unnecessary care and unnecessary trauma for infants.*

lenge," he added. However, for the 8- to 21-day age group, a new feature is that these infants may be discharged if the CSF is negative. Evaluation in this youngest group states that clinicians "may assess inflammatory markers" including height of fever, absolute neutrophil count, C-reactive protein, and procalcitonin.

Treatment of infants in the 8- to 21-day group "should" include parenteral antimicrobial therapy, according to the guideline, and these infants "should" be actively monitored in the hospital by nurses and staff experienced in neonatal care, Dr. Pantell said. The guideline also includes a key action statement to stop antimicrobials at 24-36 hours if cultures are negative, but to treat identified organisms.

## Infants aged 22-28 days

In both the 22- to 28-day-old and 29- to 60-day-old groups, the guideline offers opportunities for less testing and treatment, such as avoiding a lumbar puncture, and fewer hospitalizations. The development of a separate guideline for the 22- to 28-day group is something new, said Dr. Pantell. The guideline states that clinicians should obtain urine specimens and blood culture, and should assess IM in this group. Further key action statements note that clinicians "should obtain a CSF if any IM is positive," but "may" obtain CSF if the infant is hospitalized, if blood and urine cultures have been obtained, and if none of the IMs are abnormal.

As with younger patients, those with a negative CSF can go home, he said. As for treatment, clinicians "should" administer parenteral antimicrobial therapy to infants managed at home even if they have a negative CSF and urinalysis (UA), and no abnormal inflammatory markers. Other points for management of infants in this age group at home include verbal teaching and

written instructions for caregivers, plans for a re-evaluation at home in 24 hours, and a plan for communication and access to emergency care in case of a change in clinical status, Dr. Pantell explained. The guideline states that infants "should" be hospitalized if CSF is either not obtained or not interpretable, which leaves room for clinical judgment and individual circumstances. Antimicrobials "should" be discontinued in this group once all cultures are negative after 24-36 hours and no other infection requires treatment.

## Infants aged 29-60 days

For the 29- to 60-day group, there are some differences, the main one is the recommendation of blood cultures in this group, said Dr. Pantell. "We are seeing a lot of UTIs [urinary tract infections], and we would like those treated." However, clinicians need not obtain a CSF if other IMs are normal, but may do so if any IM is abnormal. Antimicrobial therapy may include ceftriaxone or cephalexin for UTIs, or vancomycin for bacteremia.

Although antimicrobial therapy is an option for UTIs and bacterial meningitis, clinicians "need not" use antimicrobials if CSF is normal, if UA is negative, and if no IMs are abnormal, Dr. Pantell added. Overall, further management of infants in this oldest age group should focus on discharge to home in the absence of abnormal findings, but hospitalization in the presence of abnormal CSF, IMs, or other concerns.

During a question-and-answer session, Dr. Roberts said that, while rectal temperature is

*The guideline recommends factoring family values and preferences into any treatment decisions:*

*"Variations, taking into account individual circumstances, may be appropriate."*

preferable, any method is acceptable as a starting point for applying the guideline. Importantly, the guideline still leaves room for clinical judgment. "We hope this will change some thinking as far as whether one model fits all," he noted. The authors tried to temper the word "should" with the word "may" when possible, so clinicians can say: "I'm going to individualize my decision to the infant in front of me."

Ultimately, the guideline is meant as a guide, and not an absolute standard of care, the authors said. The language of the key action statements includes the words "should, may, need not" in place of "must, must not." The guideline recommends factoring family values and preferences into any treatment decisions: "Variations, taking into account individual circumstances, may be appropriate."

The guideline received no outside funding. The authors had no financial conflicts to disclose.

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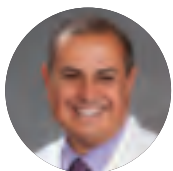


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# Fauci says 'unprecedented' conditions could influence COVID vaccine approval for kids

By Heidi Splete  
MDedge News

“From a public health standpoint, I think we have an evolving situation,” said Anthony S. Fauci, MD, director of the National Institute of Allergy and Infectious Diseases, in a moderated session with Lee Beers, MD, president of the American Academy of Pediatrics, at the virtual Pediatric Hospital Medicine annual conference.

Early in the COVID-19 pandemic, the data suggested that children could become infected, but that serious outcomes were unlikely, said Dr. Fauci. Now, with the Delta variant surging in the United States and globally, “what we are seeing is really quite disturbing,” as more children are impacted and hospitalized with serious illness, he noted.

The reasons for this shift remain unclear, he said.

Dr. Beers emphasized the ability of pediatric hospitalists to be flex-



Dr. Anthony S. Fauci

ible in the face of uncertainty and the evolving virus, and asked Dr. Fauci to elaborate on the unique traits of the Delta variant that make it especially challenging.

“There is no doubt that Delta transmits much more efficiently than the Alpha variant or any other variant,” Dr. Fauci said. The transmissibility is evident in comparisons of the level of virus in the nasophar-

*“If I were a [non-COVID] virus looking for a niche, I would be really confused. I don’t know what will happen this winter, but if we get good control over COVID-19 by winter, we could have a very vengeful influenza season.”*

ynx of the Delta variant, compared with the original Alpha COVID-19 virus – Delta is as much as 1,000 times higher, he explained.

In addition, the level of virus in the nasopharynx of vaccinated individuals who develop breakthrough infections with the Delta variant is similar to the levels in unvaccinated individuals who are infected with the Delta variant.

The Delta variant is “the tough guy on the block” at the moment, Dr. Fauci said.

Dr. Fauci also responded to a question on the lack of winter viruses, such as respiratory syncytial virus and the flu, last winter, but the surge in these viruses over the summer.

This winter’s activity remains uncertain, Dr. Fauci said. However, he speculated “with a strong dose of humility and modesty” that viruses tend to have niches, some are seasonal, and the winter viruses that were displaced by COVID-19 hit harder in the summer instead. “If I were a [non-COVID] virus looking for a niche, I would be really confused,” he said. “I don’t know what will happen this winter, but if we get good control over COVID-19 by winter, we could have a very vengeful influenza season,” he said. “This is speculation; I don’t have any data for this,” he cautioned.

Dr. Beers raised the issue of back-to-school safety, and the updated AAP guidance for universal masking for K-12 students. “Our guidance about return to school gets updated as the situation changes and we gain a better understanding of how kids can get to school safely,” she said. A combination of factors affect back-to-school guidance, including the ineligibility of children younger

than 12 years to be vaccinated, the number of adolescents who are eligible but have not been vaccinated, and the challenge for educators to navigate which children should wear masks, Dr. Beers said.

“We want to get vaccines for our youngest kids as soon as safely possible,” Dr. Beers emphasized. She noted that the same urgency is needed to provide vaccines for children as for adults, although “we have to do it safely, and be sure and feel confident in the data.”

When asked to comment about the status of FDA authorization of COVID-19 vaccines for younger children, Dr. Fauci described the current situation as one that “might require some unprecedented and unique action” on the part of the FDA, which tends to move cautiously because of safety considerations. However, concerns about adverse events might get in the way of protecting children against what “you are really worried about,” in this case COVID-19 and its variants, he said. Despite the breakthrough infections, “vaccination continues to very adequately protect people from getting severe disease,” he emphasized.

*“We want to get vaccines for our youngest kids as soon as safely possible. ... We have to do it safely, and be sure and feel confident in the data.”*

Dr. Fauci also said that he believes the current data support boosters for the immune compromised; however, “it is a different story about the general vaccinated population and the vaccinated elderly,” he said. Sooner or later most people will likely need boosters; “the question is who, when, and how soon,” he noted.

Dr. Fauci wrapped up the session with kudos and support for the pediatric health care community. “As a nonpediatrician, I have a great deal of respect for the job you are doing,” he said. “Keep up the great work.”

Dr. Beers echoed this sentiment, saying that she was “continually awed, impressed, and inspired” by how the pediatric hospitalists are navigating the ever-changing pandemic environment.

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# Choosing Wisely campaign targets waste and overuse in hospital pediatrics

By Heidi Splete  
MDedge News

“Health care spending and health care waste is a huge problem in the U.S., including for children,” Vivian Lee, MD, of Children’s Hospital, Los Angeles, said in a presentation at the annual virtual Pediatric Hospital Medicine conference.

Data from a 2019 study suggested that approximately 25% of health care spending in the United States qualifies as “wasteful spending,” in categories such as overtesting, and unnecessary hospitalization, Dr. Lee said. “It is essential for physicians in hospitals to be stewards of high-value care,” she emphasized.



Dr. Lee

To combat wasteful spending and control health care costs, the Choosing Wisely campaign was created in 2012 as an initiative from the American Board of Internal Medicine Foundation. An ongoing goal of the campaign is to raise awareness among physicians and patients about potential areas of low-value services and overuse. The overall campaign includes clinician-driven recommendations from multiple medical organizations.

The PHM produced its first set of five recommendations in 2012, Dr. Lee said. These recommendations, titled “Five Things Physicians and Patients Should Question,” have been updated for 2021. The updated recommendations were created as a partnership among the Academic Pediatric Association, the American Academy of Pediatrics, and the Society of Hospital Medicine. A joint committee reviewed the latest evidence, and the updates were approved by the societies and published by the ABIM in January 2021.

“We think these recommendations truly reflect an exciting and evolving landscape for pediatric hospitalists,” Dr. Lee said. “There is a greater focus on opportunities to transition out of the hospital sooner, or avoid hospitalization altogether. There is an emphasis on antibiotic stewardship and a growing recognition of the impact that overuse may have on our vulnerable neonatal population,” she said. Several members of the Choosing Wisely panel presented the recommendations during the virtual presentation.

## Revised recommendations

The new “Five Things Physicians and Patients Should Question” are as follows:

**1. Do not prescribe IV antibiotics for predetermined durations for patients hospitalized with infections such as pyelonephritis, osteomyelitis, and complicated pneumonia. Consider early transition to oral antibiotics.**

Many antibiotic doses used in clinical practice are preset durations that are not based on

high-quality evidence, said Mike Tchou, MD, of Children’s Hospital of Colorado in Aurora. However, studies now show that earlier transition to enteral antibiotics can improve a range of outcomes including neonatal urinary tract infections, osteomyelitis, and complicated pneumonia, he said. Considering early transition based on a patient’s response can decrease adverse events, pain, length of stay, and health care costs, he explained.

*“We think these recommendations truly reflect an exciting and evolving landscape for pediatric hospitalists. ... There is a greater focus on opportunities to transition out of the hospital sooner.”*

**2. Do not continue hospitalization in well-appearing febrile infants once bacterial cultures (i.e., blood, cerebrospinal, and/or urine) have been confirmed negative for 24-36 hours, if adequate outpatient follow-up can be ensured.**

Recent data indicate that continuing hospitalization beyond 24-36 hours of confirmed negative bacterial cultures does not improve clinical outcomes for well-appearing infants admitted for concern of serious bacterial infection, said Paula Soung, MD, of Children’s Wisconsin in Milwaukee. In fact, “blood culture yield is highest in the first 12-36 hours after incubation with multiple studies demonstrating >90% of pathogen cultures being positive by 24 hours,” Dr. Soung said. “If adequate outpatient follow-up can be assured, discharging well-appearing febrile infants at 24-36 hours after confirming cultures are negative has many positive outcomes,” she said.

**3. Do not initiate phototherapy in term or late preterm well-appearing infants with neonatal hyperbilirubinemia if their bilirubin is below levels at which the AAP guidelines recommend treatment.**

In making this recommendation, “we considered that the risk of kernicterus and cerebral palsy is extremely low in otherwise healthy term and late preterm newborns,” said Allison Holmes, MD, of Children’s Hospital at Dartmouth-Hitchcock, Manchester, N.H. “Subthreshold phototherapy leads to unnecessary hospitalization and its associated costs and harms,” and data show that kernicterus generally occurs close to 40 mg/dL and occurs most often in infants with hemolysis, she added.

The evidence for the recommendations included data showing that, among other factors, 8.6 of 100,000 babies have a bilirubin greater than 30 mg/dL, said Dr. Holmes. Risks of using sub-

threshold phototherapy include increased length of stay, increased readmissions, and increased costs, as well as decreased breastfeeding and bonding with parents, and increased parental anxiety. “Adding prolonged hospitalization for an intervention that might not be necessary can be stressful for parents,” she said.

**4. Do not use broad-spectrum antibiotics such as ceftriaxone for children hospitalized with uncomplicated community-acquired pneumonia. Use narrow-spectrum antibiotics such as penicillin, ampicillin, or amoxicillin.**

Michelle Lossius, MD, of the Shands Hospital for Children at the University of Florida, Gainesville, noted that the recommendations reflect Infectious Diseases Society of America guidelines from 2011 advising the use of ampicillin or penicillin for this population of children. More recent studies with large populations support the ability of narrow-spectrum antibiotics to limit the development of resistant organisms while achieving the same or better outcomes for children hospitalized with CAP, she said.

**5. Do not start IV antibiotic therapy on well-appearing newborn infants with isolated risk factors for sepsis such as maternal chorioamnionitis, prolonged rupture of membranes, or untreated group B streptococcal colonization. Use clinical tools such as an evidence-based sepsis risk calculator to guide management.**

“This recommendation combines other recommendations,” said Prabi Rajbhandari, MD, of Akron (Ohio) Children’s Hospital. The evidence is ample, as the Centers for Disease Control and Prevention recommends the use of sepsis calculators to guide clinical management in sepsis patients, she said.

Data comparing periods before and after the adoption of a sepsis risk calculator showed a significant reduction in the use of blood cultures and antibiotics, she noted. Other risks of jumping to IV antibiotics include increased hospital stay, increased parental anxiety, and decreased parental bonding, Dr. Rajbhandari added.

Next steps include how to prioritize implementation, as well as deimplementation of outdated practices, said Francisco Alvarez, MD, of Lucile Packard Children’s Hospital, Palo Alto, Calif. “A lot of our practices were started without good evidence for why they should be done,” he said. Other steps include value improvement research; use of dashboards and benchmarking; involving other stakeholders including patients, families, and other health care providers; and addressing racial disparities, he concluded.

The presenters had no financial conflicts to disclose. The conference was sponsored by the Academic Pediatric Association, the American Academy of Pediatrics, and the Society of Hospital Medicine.



Dr. Alvarez



Dr. Rajbhandari

# Move from awareness to action to combat racism in medicine

By Heidi Splete  
MDedge News

Structural racism and implicit bias are connected, and both must be addressed to move from awareness of racism to action, said Nathan Chomilo, MD, of HealthPartners/Park Nicollet, Brooklyn Center, Minn., in a presentation at the virtual Pediatric Hospital Medicine annual conference.

“We need pediatricians with the courage to address racism head on,” he said.

One step in moving from awareness to action against structural and institutional racism in medicine is examining policies, Dr. Chomilo said. He cited the creation of Medicare and Medicaid in 1965 as examples of how policy changes can make a difference, illustrated by data from 1955 to 1975 that showed a significant decrease in infant deaths among Black infants in Mississippi after 1965.

Medicaid expansion has helped to narrow, but not eliminate, racial

disparities in health care, Dr. Chomilo said. The impact of Medicare and Medicaid is evident in the current COVID-19 pandemic, as county-level data show that areas where more than 25% of the population are



Dr. Chomilo

*“Racial identity is informed by racial socialization. All of us are socialized along the lines of race; it happens in conversations with parents, family, peers, community.”*

uninsured have higher rates of COVID-19 infections, said Dr. Chomilo. Policies that impact access to care also impact their incidence of chronic diseases and risk for severe disease, he noted.

“If you don’t have ready access to a health care provider, you don’t have access to the vaccine, and you don’t have information that would inform your getting the vaccine,” he added.

**Prioritizing the power of voting**  
“Voting is one of many ways we can impact structural racism in health care policy,” Dr. Chomilo emphasized.

However, voting inequity remains

a challenge, Dr. Chomilo noted. Community-level disparities lead to inequity in voting access and subsequent disparities in voter participation, he said. “Leaders are less responsive to nonvoting constituents,” which can result in policies that impact health inequitably, and loop back to community-level health disparities, he explained.

Historically, physicians have had

an 8%-9% lower voter turnout than the general public, although this may have changed in recent elections, Dr. Chomilo said. He encouraged all clinicians to set an example and vote, and to empower their patients to vote. Evidence shows that enfranchisement of Black voters is associated with reductions in education gaps for Blacks and Whites, and that enfranchisement of women is associated with increased spending on children and lower child mortality, he said. Dr. Chomilo encouraged pediatricians and all clinicians to take advantage of the resources on voting available from the American Academy of Pediatrics ([aap.org/votekids](http://aap.org/votekids)).

“When we see more people in a community vote, leaders are more responsive to their needs,” he said.

**Informing racial identity**  
“Racial identity is informed by racial socialization,” Dr. Chomilo said. “All of us are socialized along the lines of race; it happens in conversations

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# PHM 2021 plenary: Achieving gender equity in medicine

By **Carlos (Tony) Casillas, MD, MPH;**  
**Jennifer K. O'Toole, MD, MEd**

## PHM 2021 session

Accelerating Patient Care and Healthcare Workforce Diversity and Inclusion

## Presenter

Julie Silver, MD

## Session summary

Gender inequity in medicine has been well documented and further highlighted by the tremendous impact of the COVID-19 pandemic on women in medicine. While more women than men are entering medical schools across the United States, women still struggle to reach the highest levels of academic rank, achieve leadership positions of power and influence, receive fair equitable pay, attain leadership roles in national societies, and receive funding from national agencies. They also continue to face discrimination and implicit and explicit biases. Women of color or from other minority backgrounds face even greater barriers and biases. Despite being a specialty in which women represent almost 70% of the workforce, pediatrics is not immune to these disparities.

In her PHM21 plenary on Aug. 3, 2021, Dr. Silver, a national expert in gender equity disparities, detailed the landscape for women in medicine and proposed some solutions to accelerate systemic change for gender equity. In order to understand and mitigate gender inequity, Dr. Silver encouraged the PHM community to identify influential “gatekeepers” of promotion, advancement, and salary compensation. In academic medicine medical schools, funding agencies, professional societies, and journals are the gatekeepers to advancement and compensation for women. Women are traditionally underrepresented as

members and influential leaders of these gate-keeping organizations and in their recognition structures; therefore their advancement, compensation, and well-being are hindered.

## Key takeaways

- Critical mass theory will not help alleviate gender inequity in medicine, as women make up a critical mass in pediatrics and are still experiencing stark inequities. Critical actor leaders are needed to highlight disparities and drive change even once a critical mass is reached.
- Our current diversity, equity, and inclusion (DEI) efforts are ineffective and are creating an “illusion of fairness that causes majority group members to become less sensitive to recognizing discrimination against minorities.” Many of the activities that are considered citizenship, including committees focused on DEI efforts, should be counted as scholarship, and appropriately compensated to ensure promotion of our women and minority colleagues.
- Male allies are critical to documenting, disseminating, and addressing gender inequality. Without the support of men in the field, we will see little progress.
- While there are numerous advocacy angles we can take when advocating for gender equity, the most effective will be the financial angle. Gender pay gaps at the start of a career can lead to roughly 2 million dollars of salary loss for a woman over the course of her career. In order to alleviate those salary pay gaps our institutions must not expect women to negotiate for fair pay, make salary benchmarks transparent, continue to monitor and conduct research on compensation disparities, and attempt to alleviate the weight of educational debt.
- COVID-19 is causing immense stress on women in medicine, and the impact could be disastrous. We must recognize and reward the “4th



*Dr. Casillas is the internal medicine–pediatric chief resident for the University of Cincinnati/ Cincinnati Children’s Internal Medicine–Pediatric program. His career goal is to serve as a hospitalist for children and adults, and he is interested in health equity and Latinx health. Dr. O’Toole is a pediatric and adult hospitalist at Cincinnati Children’s Hospital Medical Center and University of Cincinnati Medical Center, and a professor of pediatrics and internal medicine at the University of Cincinnati College of Medicine. She serves as program director of Cincinnati’s Combined Internal Medicine and Pediatrics Residency Program.*

shift” women are working for COVID-19–related activities at home and at work, and put measures in place to #GiveHerAReasonToStay in health care.

- Men and other women leaders have a responsibility to sponsor the many and well-qualified women in medicine for awards, committees, and speaking engagements. These opportunities are key markers of success in academic medicine and are critical to advancement and salary compensation.

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with parents, family, peers, community.” Another point in moving from awareness to action in eliminating structural racism is recognizing that children are not too young to talk about race, Dr. Chomilo emphasized.

Children start to navigate racial identity and to take note of other differences at an early age. For example, a 3-year-old might ask, “why does that person talk funny; why is that person being pushed in a chair?” Dr. Chomilo said, and it is important for parents and as pediatricians to be prepared for these questions, which are part of normal development. As children get older, they start to reflect on what differences mean for them, which is not rooted in anything negative, he noted.

Children first develop racial identity at home, but children solidify their identities in child care and school settings, Dr. Chomilo said. The American Academy of Pediatrics has acknowledged the potential for racial bias in education and child care, and said in a statement that, “it is critical for pediatricians to recognize the institutional personally mediated, and internalized levels of racism that occur in the educational setting, because education is a critical social determinant of health for children.” In fact, data from children in preschool show that they use racial categories to identify themselves and others, to include or exclude children from activities, and to negotiate power in their social and play networks.

Early intervention matters in educating children about racism, Dr. Chomilo said. “If we were not taught to talk about race, it is on us to learn about it ourselves as well,” he said.

Ultimately, the goal is to create active antiracism among adults and children, said Dr. Chomilo. He encouraged pediatricians and parents not to shut down or discourage children when they raise questions of race, but to take the opportunity to teach. “There may be hurt feelings around what a child said, even if they didn’t mean to offend someone,” he noted. Take the topic seriously, and make racism conversations ongoing; teach children to safely oppose negative messages and behaviors in others, and replace them with something positive, he emphasized.

## Addressing bias in clinical settings

Dr. Chomilo also encouraged hospitalists to consider internalized racism in clinical settings and take action to build confidence and cultural pride in all patients by ensuring that a pediatric hospital unit is welcoming and representative of the diversity in a given community, with appropriate options for books, movies, and toys. He also encouraged pediatric hospitalists to assess children for experiences of racism as part of a social assessment. Be aware of signs of posttraumatic stress, anxiety, depression, or grief that might have a racial component, he said.

Dr. Chomilo had no financial conflicts to disclose.

# MedEd must take broader view of disabilities

By Heidi Splete  
MDedge News

“All physicians, regardless of specialty, will work with patients with disabilities,”

Corrie Harris, MD, of the University of Louisville (Ky.), said in a plenary session presentation at the virtual Pediatric Hospital Medicine conference.

Disabilities vary in their visibility, from cognitive and sensory impairments that are not immediately obvious to an obvious physical disability, she said.

One in four adults and one in six children in the United States has a disability, said Dr. Harris. The prevalence of disability increases with age, but occurs across the lifespan, and will likely increase in the future with greater improvements in health care overall.

*“People with disabilities are the best teachers about disability, because they have expertise that comes from their lived experience.”*

Dr. Harris reviewed the current conceptual model that forms the basis for the World Health Organization definition of functioning disability. This “functional model” defines disability as caused by interactions between health conditions and the environment, and the response is to “prioritize function to meet patient goals,” Dr. Harris said at the meeting, sponsored by the Society of Hospital Medicine, the American Academy of Pediatrics, and the Academic Pediatric Association.

This model is based on collaboration between health care providers and their patients with disabilities, and training is important to help providers make this collaboration successful, said Dr. Harris. Without training, physicians may be ineffective in communicating with patients with disabilities by not speaking directly to the patient, not speaking in a way the patient can understand clearly, and not providing accessible patient education materials. Physicians also tend to minimize the extent of the patient’s expertise in their own condition based on their

lived experiences, and tend to underestimate the abilities of patients with disabilities.

However, direct experience with disabled patients and an understand-

ing of the health disparities they endure can help physicians look at these patients “through a more intersectional lens,” that also takes into account social determinants of

health, Dr. Harris said. “I have found that people with disabilities are the best teachers about disability, because they have expertise that comes from their lived experience.”

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The Hospitalist



**Patients are the best teachers**

Several initiatives are helping physicians to bridge this gap in understanding and reduce disparities in care. One such program is FRAME: Faces Redefining the Art of Medical Education. FRAME is a web-based film library designed

to present medical information to health care providers in training, clinicians, families, and communities in a dignified and humanizing way. FRAME was developed in part by fashion photographer Rick Guidotti, who was inspired after meeting a young woman with albi-

nism to create Positive Exposure, an ongoing project featuring children and adolescents with various disabilities.

FRAME films are “short films presenting all the basic hallmark characteristics of a certain genetic condition, but presented by some-

body living with that condition,” said Mr. Guidotti in his presentation during the session.

The National Curriculum Initiative in Developmental Medicine (NCIDM) is designed to incorporate care for individuals with disabilities

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into medical education. NCIDM is a project created by the American Academy of Developmental Medicine and Dentistry (AADMD).

“The need for this program is that there is no U.S. requirement for medical schools to teach about

intellectual and developmental disabilities,” Priya Chandan, MD, also of the University of Louisville, said in her presentation during the session. “Approximately 81% of graduating medical students have no training in caring for adults with disabilities,” said Dr. Chandan, who serves as di-

rector of the NCIDM.

The current NCIDM was created as a 5-year partnership between the AADMD and Special Olympics, supported in part by the Centers for Disease Control and Prevention, Dr. Chandan said. The purpose was to provide training to medical students

in the field of developmental medicine, meaning the care of individuals with intellectual/developmental disabilities (IDD) across the lifespan. The AADMD has expanded to 26 medical schools in the United States and will reach approximately 4,000 medical students by the conclusion of the current initiative.

One challenge in medical education is getting past the idea that people living with disabilities need to be fixed, said Dr. Chandan. The NCIDM approach reflects Mr. Guidotti’s approach in both the FRAME initiatives and his Positive Exposure foundation, with a focus on treating people as people, and letting individuals with disabilities represent themselves.

Dr. Chandan described the NCIDM curriculum as allowing for flexible teaching methodologies and materials, as long as they meet the NCIDM-created learning goals and objectives. The curriculum also includes standardized evaluations. Each NCIDM program in a participating medical school includes a faculty champion, and the curriculum supports meeting people with IDD not only inside medical settings, but also outside in the community.

NCIDM embraces the idea of community-engaged scholarship, which Dr. Chandan defined as “a form of scholarship that directly benefits the community and is consistent with university and unit missions.” This method combined teaching and conducting research while providing a service to the community.

The next steps for the current NCIDM initiative are to complete collection of data and course evaluations from participating schools by early 2022, followed by continued dissemination and collaboration through AADMD.

Overall, the content of the curriculum explores how and where IDD fits into clinical care, Dr. Chandan said, who also emphasized the implications of communication. “How we think affects how we communicate,” she added. Be mindful of the language used to talk to and about patients with disabilities, both to colleagues and to learners.

When talking to the patient, find something in common, beyond the diagnosis, said Dr. Chandan. Remember that some disabilities are visible and some are not. “Treat people with respect, because you won’t know what their functional level is just by looking,” she concluded.

The presenters had no financial conflicts to disclose.

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The Hospitalist

# Vaccine

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with their peers, other hospital staff, patients and families, and their communities. They can play key roles in advocating for the vaccine, answering questions, clarifying the science, and dispelling misinformation – for those who are willing to listen.

Becker's Hospital Review, which has kept an ongoing tally of announced vaccine mandate policies in hospitals, health systems, and health departments nationwide, reported on Aug. 13 that 1,850 or 30% of U.S. hospitals, had announced vaccine mandates.<sup>1</sup> Often exceptions can be made, such as for medical or religious reasons, or with other declarations or opt-out provisions. But in many settings, mandating COVID vaccinations won't be easy.

Amith Skandhan, MD, SFHM, FACP, a hospitalist at Southeast Health Medical Center in Dothan, Ala., and a core faculty member in the internal medicine residency program at Alabama College of Osteopathic Medicine, said that implementing vaccine mandates will be more difficult in smaller health systems, in rural communities, and in states with lower vaccination rates and greater vaccine controversy.

Alabama has the lowest vaccination rates in the country, reflected in the recent rise in COVID cases and hospitalizations, even higher than during the surge of late 2020, Dr. Skandhan said. "In June we had one COVID patient in this hospital." By late August the number was 119 COVID patients and climbing.

But where he works, in a health system where staffing is already spread thin, a vaccine mandate would be challenging. "What if our staff started leaving? It's only 10 minutes from here to the Florida or Georgia border," Dr. Skandhan said. Health care workers opposed to vaccinations would have the option of easily seeking work elsewhere.

When contacted for this article, he had been off work for several days but was mentally preparing himself to go back. "I'm not even following the [COVID-19] numbers but I am prepared for the worst. I know it will be mostly COVID. People just don't realize what goes into this work."

Dr. Skandhan, who said he was the third or fourth person in Alabama to receive the COVID vaccine, often finds himself feeling frustrated and angry – in the midst of a surge in cases that could have been prevented – that such a beneficial medical

advance for bringing the pandemic under control became so politicized. "It is imperative that we find out why this mistrust exists and work to address it. It has to be done."

## Protecting health care professionals

On July 26, the Society of Hospital Medicine joined 50 other health care organizations including the American Medical Association, American Nurses Association, and American Academy of Pediatrics in advocating for all health care employers to require their employees to be vaccinated against COVID, in order to protect the safety of all patients and residents of health care facilities.<sup>2</sup>

"As an organization, we support vaccinating health care workers, including hospitalists, to help stop the spread of COVID-19 and the increasingly dominant Delta variant," said SHM's chief executive officer Eric E. Howell, MD, MHM, in a prepared statement. "We aim to uphold the highest standards among hospitalists and other health care providers to help protect our fellow health care professionals, our patients, and our communities."

To that end, Dr. Skandhan has started conversations with hospital staff who he knows are not vaccinated. "For some, we're not able to have a civil conversation, but in most cases I can help to persuade people." The reasons people give for not getting vaccinated are not based in science, he said. "I am worried about the safety of our hospitalists and staff nurses." But unvaccinated frontline workers are also putting their patients at risk. "Can we say why they're hesitating? Can we have an honest discourse? If we can't do that with our colleagues, how can we blame the patients?"

Dr. Skandhan encourages hospitalists to start simply in their own hospitals, trying to influence their own departments and colleagues. "If you can convince one or two more every week, you can start a chain reaction. Have that conversation. Use your trust." For some hospitalized patients, the vaccination conversation comes too late, after their infection, but even some of them might consider obtaining it down the road or trying to persuade family members to get vaccinated.

Adult hospitalists, however, may not have received training in how to effectively address vaccine fears

and misconceptions among their patients, he said. Because the patients they see in the hospital are already very sick, they don't get a lot of practice talking about vaccines except, perhaps, for the influenza vaccine.

Pediatric hospitalists have more experience with such conversations involving their patients' parents, Dr. Skandhan said. "It comes more naturally to them. We need to learn quickly from them about how to talk about vaccines with our patients."

## Pediatric training and experience

Anika Kumar, MD, FHM, FAAP, a pediatric hospitalist at the Cleveland Clinic and the pediatric editor of *The Hospitalist*, agrees that pediatricians and pediatric hospitalists often have received more training in how to lead vaccination conversations. She often talks about vaccines with the parents of hospitalized children relative to chicken pox, measles, and other diseases of childhood.

Pediatric hospitalists may also ask to administer the hepatitis B vaccine to newborn babies, along with other preventive treatments such as eye drops and vitamin K shots. "I often encourage the influenza vaccine prior to the patient's hospital discharge, especially for kids with chronic conditions, asthma, diabetes, or premature birth. We talk about how the influenza vaccine isn't perfect, but it helps to prevent more serious disease," she said.

"A lot of vaccine hesitancy comes from misunderstandings about the role of vaccines," she said. People forget that for years children have been getting vaccines before starting school. "Misinformation and opinions about vaccines have existed for decades. What's new today is the abundance of sources for obtaining these opinions. My job is to inform families of scientific facts and to address their concerns."

It has become more common recently for parents to say they don't want their kids to get vaccinated, Dr. Kumar said. Another group is better described as vaccine hesitant and just needs more information. "I may not, by the time they leave the hospital, convince them to allow me to administer the vaccine. But in the discharge summary, I document that I had this conversation. I've done my due diligence and tried to start a larger dialogue. I say: 'I encourage you to continue this discussion with the pediatrician you trust.' I also communicate with the outpatient team," she said.

"But it's our responsibility, be-

cause we're the ones seeing these patients, to do whatever we can to keep our patients from getting sick. A lot of challenging conversations we have with families are just trying to find out where they're at with the issue – which can lead to productive dialogue."

Ariel Carpenter, MD, a 4th-year resident in internal medicine and pediatrics at the University of Louisville (Ky.), and a future pediatric hospitalist, agreed that her combined training in med-peds has been helpful preparation for the vaccine conversation. That training has



Dr. Carpenter

included techniques of motivational interviewing. In pediatrics, she explained, the communication is a little softer. "I try to approach my patients in a family-centered way."

Dr. Carpenter recently wrote a personal essay for *Louisville Medicine* magazine from the perspective of growing up homeschooled by a mother who didn't believe in vaccines.<sup>3</sup> As a teenager, she independently obtained the complete childhood vaccine series so that she could do medical shadowing and volunteering. In medical school she became a passionate vaccine advocate, eventually persuading her mother to change her mind on the subject in time for the COVID vaccine.

"There's not one answer to the vaccination dilemma," she said. "Different approaches are required because there are so many different reasons for it. Based on my own life experience, I try to approach patients where they are – not from a place of data and science. What worked in my own family, and works with my patients, is first to establish trust. If they trust you, they're more likely to listen. Simply ask their worries and concerns," Dr. Carpenter said.

"A lot of them haven't had the opportunity before to sit down with a physician they trust and have their worries listened to. They don't feel heard in our medical system. So I remind myself that I need to understand my patients first – before inserting myself into the conversation."

Many patients she sees are in an information bubble, with a very different understanding of the issue than their doctors. "A lot of well-meaning people feel they are making the safer choice. Very few truly don't care about protecting

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others. But they don't feel the urgency about that and see the vaccine as the scarier option right now."

**Frontline vaccine advocates**

Hospitalists are the frontline advocates within their hospital system, in a position to lead, so they need to make vaccines a priority, Dr. Carpenter said. They should also make sure that their hospitals have ready access to the vaccine, so patients who agree to receive it are able to get it quickly. "In our hospital they can get the shot within a few hours if the opportunity arises. We stocked the Johnson & Johnson vaccine so that they wouldn't have to connect with another health care provider in order to get a second dose."

Hospitals should also invest in access to vaccine counseling training and personnel. "Fund a nurse clinician who can screen and counsel hospitalized patients for vaccination. If they meet resistance, they can then refer to the dedicated physician of the day to have the conversation," she said. "But if we don't mention it, patients will assume we don't feel strongly about it."

Because hospitalists are front and center in treating COVID, they need

to be the experts and the people offering guidance, said Shyam Odeti, MD, SFHM, FFAFP, section chief for hospital medicine at the Carilion Clinic in Roanoke, Va. "What we're trying to do is spread awareness. We educated physician groups, learners, and clinical teams during the initial phase, and now mostly patients and their families." COVID vaccine reluctance is hard to overcome, Dr. Odeti said. People feel the vaccine was developed very quickly. But there are different ways to present it.

"Like most doctors, I thought people would jump on a vaccine to get past the pandemic. I was surprised and then disappointed. Right now, the pandemic is among the unvaccinated. So we face these encounters, and we're doing our best to overcome the misinformation. My organization is 100% supportive. We talk about these issues every day."

Carilion, effective Oct. 1, has required unvaccinated employees to get weekly COVID tests and wear an N95 mask while working, and has developed Facebook pages, other social media, and an Internet presence to address these issues. "We've gone to the local African American community with physician leaders active in that community. We had a Spanish

language roundtable," Dr. Odeti said.

Dr. Skandhan reported that the Wiregrass regional chapter of SHM recently organized a successful statewide community educational event aimed at empowering community leaders to address vaccine misinformation and mistrust. "We surveyed religious leaders and pastors regarding the causes of vaccine hesitancy and reached out to physicians active in community awareness." Based on that input, a presentation by the faith leaders was developed. Legislators from the Alabama State Senate's Healthcare Policy Committee were also invited to the presentation and discussion.

**Trying to stay positive**

It's important to try to stay positive, Dr. Odeti said. "We have to be empathetic with every patient. We have to keep working at this, since there's no way out of the pandemic except through vaccinations. But it all creates stress for hospitalists. Our job is made significantly more difficult by the vaccine controversy."

Jennifer Cowart, MD, a hospitalist at Mayo Clinic in Jacksonville, Fla., has been outspoken in her community about vaccination and masking, talking to reporters, attending rallies and press conferences, posting on social media, and speaking in favor of mask policies at a local school board meeting. She is part of an informal local group called Doctors Fighting COVID, which meets online to strategize how to share its expertise, including writing a recent letter about masks to Jacksonville's mayor.

"In July, when we saw the Delta variant surging locally, we held a webinar via local media, taking calls about the vaccine from the community. I'm trying not to make this a political issue, but we are health officials." Dr. Cowart said she also tries not to raise her voice when speaking with vaccine opponents and tries to remain empathetic. "Even though inwardly I'm screaming, I try to stay calm. The misinformation is real. People are afraid and feeling pressure. I do my best, but I'm human, too."

Hospitalists need to pull whatever levers they can to help advance understanding of vaccines, Dr. Cowart said. "In the hospital, our biggest issue is time. We often don't have it, with a long list of patients to see. But every patient encounter is

an opportunity to talk to patients, whether they have COVID or something else." Sometimes, she might go back to a patient's room after rounds to resume the conversation.

Hospital nurses have been trained and entrusted to do tobacco abatement counseling, she said, so why not mobilize them for vaccine education? "Or respiratory therapists, who do inhaler training, could talk about what it's like to care for COVID patients. There's a whole bunch of staff in the hospital who could be mobilized," she said.

"I feel passionate about vaccines, as a hospitalist, as a medical educator, as a daughter, as a responsible member of society," said Eileen Barrett,



Dr. Barrett

MD, MPH, SFHM, MACP, director of continuing medical education at the University of New Mexico, Albuquerque. "I see this as a personal and societal responsibility. When I speak about the

vaccine among groups of doctors, I say we need to stay in our lane regarding our skills at interpreting the science and not undermining it."

Some health care worker hesitancy is from distrust of pharmaceutical companies, or of federal agencies, she said. "Our research has highlighted to me the widespread inequity issues in our health care system. We should also take a long, hard look at how we teach the scientific method to health professionals. That will be part of a pandemic retrospective."

Sometimes with people who are vaccine deliberative, whether health care workers or patients, there is a small window of opportunity. "We need to hear people and respond to them as people. Then, if they are willing to get vaccinated, we need to accomplish that as quickly and easily as possible," Dr. Barrett said.

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Dr. Cowart

## Key Clinical Question

# Opioid-induced adrenal insufficiency for the hospitalist

Consider OIAI, even among patients with common infections

By John M. Cunningham, MD; Anna Maria Muñoz, MD; Kimberly A. Indovina, MD

## Case

A 60-year-old woman with metastatic breast cancer using morphine extended release 30 mg twice daily and as-needed oxycodone for cancer-related pain presents with fever, dyspnea, and productive cough for 2 days. She also notes several weeks of fatigue, nausea, weight loss, and orthostatic lightheadedness. She is found to have pneumonia and is admitted for intravenous antibiotics. She remains borderline hypotensive after intravenous fluids and the hospitalist suspects opioid-induced adrenal insufficiency (OIAI).

How is OIAI diagnosed and managed?

## Brief overview of issue

In the United States, 5.4% of the population is currently using long-term opioids.<sup>1</sup> Patients using high doses of opioids for greater than 3 months are 40%-50% more likely to be hospitalized than those on a lower dose or no opioids.<sup>2</sup> Hospitalists frequently encounter common opioid side effects such as constipation, nausea, and drowsiness, but may be less familiar with their effects on the endocrine system. Chronic, high-dose opioids can suppress the hypothalamic-pituitary-adrenal (HPA) axis and cause secondary, or central, adrenal insufficiency (AI).<sup>1</sup>

Recognition of OIAI is critical given the current opioid epidemic and life-threatening consequences of AI in systemically ill patients. While high-dose opioids may acutely suppress the HPA axis,<sup>3</sup> OIAI is more commonly associated with long-term opioid use.<sup>4</sup> The prevalence of OIAI among patients receiving long-term opioids ranges from 8.3% to 29%. This range reflects variations in opioid dose, duration of use, and different methods of assessing the HPA axis.<sup>1,4</sup> When screening for HPA-axis suppression in subjects taking chronic opioids, Lamprecht and colleagues found a prevalence of 22.5%.<sup>5</sup> In comparison, Gibb and colleagues found the prevalence of

secondary AI to be 8.3% in patients enrolled in a chronic pain clinic.<sup>6</sup> Despite the high prevalence on biochemical screening, the clinical significance of OIAI is less clear. Clinical AI and adrenal crisis among patients on opioids are less frequent and mostly limited to case reports.<sup>7,8</sup> In one retrospective cohort, 1 in 40 patients with OIAI presented with adrenal crisis during a hospitalization for viral gastroenteritis.<sup>9</sup>

With this prevalence, one would expect to diagnose OIAI more commonly in hospitalized patients. A concerning possibility is that this diagnosis is underrecognized because of either a lack of knowledge of the

disease or the clinical overlap between the nonspecific symptoms of AI and other diagnoses. In patients reporting symptoms suggestive of OIAI, the diagnosis was delayed by a median of 12 months.<sup>9</sup> The challenge for the hospitalist is to consider OIAI, even among patients with common infections such as pneumonia, viral gastroenteritis, or endocarditis who present with these nonspecific symptoms, while also avoiding unnecessary testing and treatment with glucocorticoids.

## Overview of the data

Opiates and opioids exert their physiologic effect through activation of the mu, kappa, and delta receptors. These receptors are located throughout the body, including the hypothalamus and pituitary gland.<sup>4</sup> Activation of these receptors results in tonic inhibition of the HPA axis and results in central AI.<sup>4</sup> Central AI is characterized by a low a.m. cortisol, low adrenocorticotropic hormone (ACTH), and low dehydroepiandrosterone sulfate (DHEAS) levels.<sup>1,4</sup> The low ACTH is indicative of central etiology. This effect of opioids is likely dose dependent with patients using more than 60 morphine-equivalent daily dose at greater risk.<sup>1,5</sup>

Unexplained or unresolved fatigue, musculoskeletal pain, nausea, vomiting, anorexia, abdominal pain, and orthostatic hypotension in a patient on chronic opioids should

prompt consideration of OIAI.<sup>9</sup> Once suspected, an 8 a.m. cortisol, ACTH level, and DHEAS level should be ordered. Because of the diurnal variation of cortisol levels, 8 a.m. values are best validated for diagnosis.<sup>10</sup> While cutoffs differ, an 8 a.m. cortisol less than 5 mcg/dL combined with ACTH less than 10 pmol/L, and DHEAS less than 50 mcg/dL are highly suggestive of OIAI. Low or indeterminate baseline a.m. cortisol levels warrant confirmatory testing.<sup>4,10</sup> While the insulin tolerance test is considered the gold standard, the high-dose (250 mcg) cosyntropin stimulation test (CST) is the more commonly used test to diagnose and confirm AI. A CST peak response greater than 18-20 mcg/dL suggests an intact HPA axis (see Figure 1).<sup>10</sup> This testing will diagnose central AI, but is not specific for OIAI. Other causes of central AI such as exogenous steroid use, pituitary pathology, and head trauma should be considered before attributing AI to opioids (see Table 1).<sup>4</sup>

The abnormal CST in central AI is from chronic ACTH deficiency and lack of adrenal stimulation resulting in adrenal atrophy. Adrenal atrophy leaves the adrenal glands incapable of responding to exogenous ACTH. This process takes several weeks; therefore, those with ACTH suppression caused by recent high-dose opioid use or subacute pituitary injury may have an

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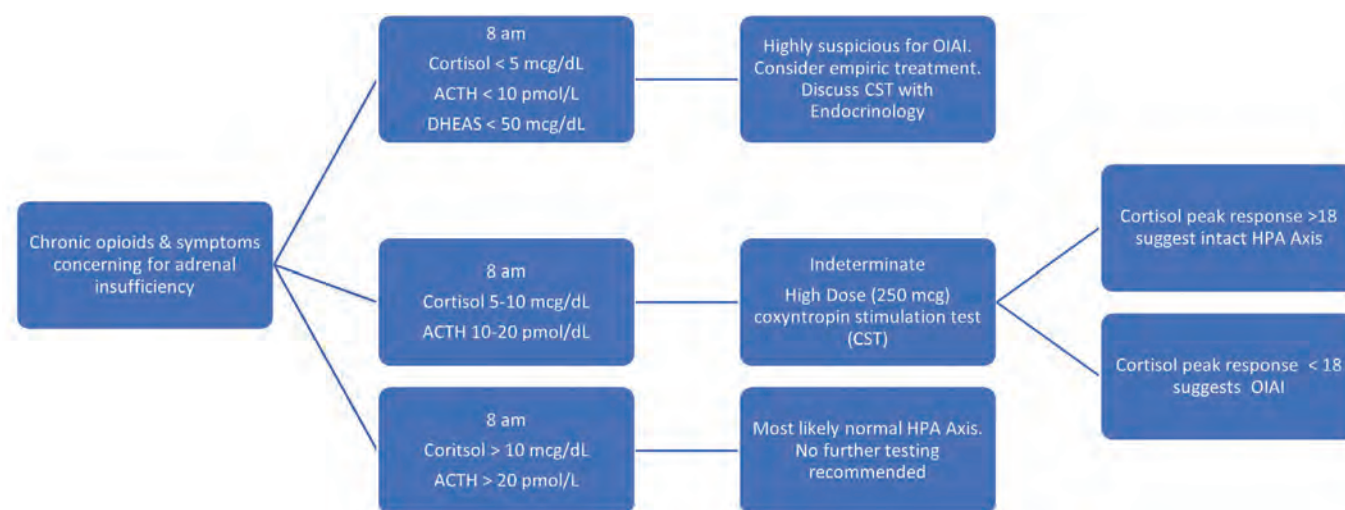


Figure 1: Diagnostic pathway of OIAI

Continued from previous page

indeterminate or normal cortisol response to high-dose exogenous ACTH.<sup>4</sup> Even in the setting of a normal CST, there may remain uncertainty in the diagnosis of OIAI. For evaluation of central AI, the sensitivity and negative likelihood ratio of the CST are only 0.64 and 0.39, respectively.<sup>4</sup> In the same cohort of 40 patients with OIAI, 11 patients had a normal CST.<sup>9</sup> The

low-dose (1 mcg) CST may increase the sensitivity, but the use of this test is limited because of technical challenges.<sup>1</sup> Endocrinology consultation can assist when the initial diagnostic and clinical presentation is unclear.

To manage a patient on opioid therapy who has laboratory data consistent with central AI, the clinician must weigh the severity of symptoms, probability of opioid

weaning, and risks associated with glucocorticoid treatment. Patients presenting with acute adrenal crisis, hypotension, or critical illness should be managed with intravenous steroid replacement per existing guideline recommendations (see Table 2).<sup>10,11</sup>

Patients with mild symptoms of nausea, vomiting, or orthostatic symptoms that resolve with treatment of their admitting diagnosis but who have evidence of an abnormal HPA axis should be considered for weaning opioid therapy. Evidence suggests that OIAI is reversible with reduction and cessation of chronic opioid use.<sup>4,9</sup> These patients may not need chronic steroid replacement; however, they should receive education on the symptoms of AI and potentially rescue steroids for home use in the setting of severe illness. Patients with OIAI admitted for surgical procedures should be managed in accordance with existing guidelines for perioperative stress dosing of glucocorticoids for AI.

Those with persisting symptoms of OIAI and an abnormal HPA axis require endocrinology consultation and glucocorticoid replacement. There is limited evidence that sug-

gests low-dose steroid replacement in patients with OIAI can improve subjective perception of bodily pain, activity level, and mood in chronic opioid users.<sup>9</sup> Li and colleagues found that 16 of 23 patients experienced improvement of symptoms on glucocorticoids, and 15 were able to discontinue opioids completely.<sup>9</sup> The authors speculated that the improvement in fatigue and musculoskeletal pain after steroid replacement is what allowed for successful opioid weaning. Seven of 10 of these patients with available follow-up had recovery of the HPA axis during the follow-up period.<sup>9</sup> In central AI, doses as low as 10-20 mg/day of hydrocortisone have been used.<sup>10,11</sup> Hospitalists should educate patients on recognizing symptoms of AI, as this low dose may not be sufficient to prevent adrenal crisis.

All patients with evidence of abnormalities in the HPA axis should receive a Medic-Alert bracelet to inform other providers of the possibility of adrenal crisis should a major trauma or critical illness render them unconscious.<sup>4,10</sup> Since OIAI is a form of central AI, mineralocorticoid replacement is not generally necessary.<sup>11</sup> Endocrinology follow-up can help wean steroids as the HPA axis

Causes of Central Adrenal Insufficiency	
•	Pituitary or metastatic tumor
•	Other tumors (e.g., craniopharyngioma, meningioma)
•	Pituitary surgery or radiation
•	Lymphocytic hypophysitis
•	Head trauma/TBI
•	Pituitary apoplexy/Sheehan's Syndrome
•	Pituitary infiltration (sarcoidosis, histiocytosis)
•	Empty Sella Syndrome
•	Chronic opioids

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Table 1: Causes of central adrenal insufficiency



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recovers after weaning opioid therapy. Recognizing and diagnosing OIAI can identify patients with untreated symptoms who are at risk for adrenal crisis, improve communication with patients on benefits of weaning opioids, and provide valuable patient education and safe transition of care.

### Application of the data to the original case

To make the diagnosis of OIAI, 8 a.m. cortisol, ACTH, and DHEAS should be obtained. Her cortisol was less than 5 mcg/dL, ACTH was 6 pmol/L and DHEAS was 30 mcg/dL. A high-dose CST was performed with 30-minute and 60-minute cortisol values of 6 mcg/dL and 9 mcg/dL, respectively. The abnormal CST and low ACTH indicate central AI. She should undergo testing for oth-

er etiologies of central AI, such as a brain MRI and pituitary hormone testing, before confirming the diagnosis of OIAI.

The insufficient adrenal response to ACTH in the setting of infection and hypotension should prompt glucocorticoid replacement. Tapering opioids could result in recovery of the HPA axis, though may not be realistic in this patient with chronic cancer-related pain. If the patient is at high risk for adverse effects of glucocorticoids, repeat testing of the HPA axis in the outpatient setting can assess if the patient truly needs steroid replacement daily rather than only during physiologic stress. The patient should be given a Medic-Alert bracelet and instructions on symptoms of AI and stress dosing upon discharge.



Dr. Cunningham



Dr. Muñoz



Dr. Indovina

Dr. Cunningham, Dr. Muñoz, and Dr. Indovina are based in the division of hospital medicine at Denver Health and Hospital Authority.

Management of Adrenal Insufficiency		
	Acute management	Discharge planning
Adrenal crisis	<ul style="list-style-type: none"> <li>• IV crystalloids</li> <li>• 100 mg IV hydrocortisone followed by 50-100 mg of IV hydrocortisone every 6 hours<sup>11</sup></li> </ul>	<ul style="list-style-type: none"> <li>• Education on the signs and symptoms of adrenal insufficiency and adrenal crisis</li> <li>• Consider prescription of rescue steroids</li> </ul>
Chronic OIAI	<ul style="list-style-type: none"> <li>• Hydrocortisone 15-20mg per 24 hours in 2-3 divided doses.</li> <li>• If borderline abnormal CST, consider 10mg daily or stress doses only with close monitoring<sup>11</sup></li> <li>• Stress dosing for severe illness, surgery, or trauma</li> <li>• Endocrinology consult</li> </ul>	<ul style="list-style-type: none"> <li>• Medic-Alert bracelet to inform possibility of adrenal insufficiency</li> <li>• Endocrinology referral</li> <li>• Determine feasibility of opioid taper</li> </ul>

Table 2: Management of adrenal insufficiency

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### Bottom line

OIAI is underrecognized because of central adrenal insufficiency. Knowing its clinical characteristics, diagnostic pathways, and treatment options aids in recognition and management.

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### Key points

- Opioids can cause central adrenal insufficiency because of tonic suppression of the HPA axis. This effect is likely dose dependent, and reversible upon tapering or withdrawal of opioids.
- The prevalence of biochemical OIAI in chronic opioid users of 8%-29% clinical AI is less frequent but may be underrecognized in hospitalized patients leading to delayed diagnosis.
- Diagnosis of central adrenal insufficiency is based upon low 8 a.m. cortisol and ACTH levels and/or an abnormal CST. OIAI is the likely etiology in patients on chronic opioids for whom other causes of central adrenal insufficiency have been ruled out.
- Management with glucocorticoid replacement is variable depending on clinical presentation, severity of HPA axis suppression, and ability to wean opioid therapy. Patient education regarding symptoms of AI and stress dosing is essential.

### Quiz

A 55-year-old man with chronic back pain, for which he takes a total of 90 mg of oral morphine daily, is admitted for pyelonephritis with fever, nausea, vomiting, dysuria, and abdominal pain. He is febrile and tachycardic on presentation, but his vitals quickly normalize after hydration and antibiotics. About 48 hours into his hospitalization his fevers, dysuria, and abdominal pain have resolved, but he has persistent nausea and headaches. On further questioning, he also reports weight loss and fatigue over the past 3 weeks. He is found to have a morning cortisol level less than 5 mcg/dL, as well as low levels of ACTH and DHEAS. OIAI is suspected.

Which of the following is true about management?

- A.** Glucocorticoid replacement therapy with oral hydrocortisone should be considered to improve his symptoms.
- B.** Tapering off opioids is unlikely to resolve his adrenal insufficiency.
- C.** Stress dose steroids should be started immediately with high-dose intravenous hydrocortisone.

**D.** Given high clinical suspicion for OIAI, further testing for other etiologies of central adrenal insufficiency is not recommended.

### Explanation of correct answer

The correct answer is A. This patient's ongoing non-specific symptoms that have persisted despite treatment of his acute pyelonephritis are likely caused by adrenal insufficiency. In a symptomatic patient with OIAI, treatment with oral hydrocortisone should be considered to control symptoms and facilitate tapering opioids. Tapering and stopping opioids often leads to recovery of the HPA axis and resolution of the OIAI. Tapering opioids should be considered a mainstay of therapy for OIAI when clinically appropriate, as in this patient with chronic benign pain. Stress dose steroids are not indicated in the absence of critical illness, adrenal crisis, or major surgery. OIAI is a diagnosis of exclusion, and patients should undergo workup for other causes of secondary adrenal insufficiency.



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# My experience of a COVID-19 vaccine breakthrough infection

By Thomas McIlraith, MD,  
SFHM, CLHM

Friday, July 16, 2021, marked the end of a week on duty in the hospital, and it was time to celebrate with a nice dinner out with my wife, since COVID-19 masking requirements had been lifted in our part of California for people like us who were fully vaccinated.

We always loved a nice dinner out and missed it so much during the pandemic. Unlike 6 months earlier, when I was administering dexamethasone, remdesivir, and high-flow oxygen to half of the patients on my panel, not a single patient was diagnosed with COVID-19, much less treated for it, during the previous week. We were doing so well in Sacramento that the hospital visitation rules had been relaxed and vaccinated patients were not required to have a negative COVID-19 test prior to hospital admission.

Saturday was game 5 of the NBA finals, so we had two couples join us for the game at our house; no masks because we were all vaccinated. On Sunday, we visited our neighbors who had just had a new baby boy and made them the gift of some baby books. The new mom had struggled with the decision of whether to get vaccinated during her pregnancy, but eventually decided to complete the vaccination cycle prior to delivery. She was fully immune at the time of the baby's birth, wisely wanting the baby to have passive immunity through her. We kept an appropriate distance, and never touched baby or mom, but since masking guidelines had been lifted for the vaccinated, we didn't bother with them.

On Monday, I felt a little something in my nose but still pursued my usual workout. Interestingly, my performance wasn't up to my usual standards. There was a meeting that evening that I had to prepare for, when all of a sudden I felt very fatigued. I lay down and slept for a good hour, which disrupted my preparation. I warned the participants that I was feeling a little under the weather, but they wanted to proceed. At this point, I decided it was time to start wearing a mask again.

More meetings on Tuesday morning, but I made sure that I was

fully masked. That little thing in my nose had blown up into a full-scale rhinitis, requiring Kleenex and decongestants. Plus, the fatigue was hitting me very hard. "Dang!" I thought. "I haven't had a cold since 2019. All those COVID-19 precautions not only worked against COVID-19 (which I never got) but also worked against the common cold, which I had now."

I finished up my meetings and laid down for a good hour and a half. As the father of two, I had plenty of experience with the common cold, and I knew that plenty of rest and hydration was the key to kicking this thing. Besides, my 55th birthday was coming up, and I wanted to make sure I was fully recovered for the festivities my wife was planning for me. Nonetheless, I scheduled myself for a COVID-19 test. I knew this couldn't be COVID-19 because I was fully vaccinated, but it was hitting me so hard. It had to be a virus that my body had never seen before; maybe the human metapneumovirus. That was my line of reasoning, anyway.

Wednesday was another day on the couch because of continued severe fatigue and myalgias. I figured another good day of rest would help me kick this cold in time for my birthday celebration. Then the COVID-19 results came back positive. "How could this be? I was vaccinated?!" Admittedly I had been more relaxed with masking, per the CDC and county guidelines, but I always wore a mask when I was seeing patients in the hospital. Yeah, I wasn't wearing an N95 anymore, and I had given up my goggles months ago, but we just weren't seeing much COVID-19 anymore, so a plain surgical mask was all that was required and seemed sufficient. I had been reading articles about the new Delta variant that was becoming dominant across the country, and reports were that the vaccine was still effective against the Delta variant. However, I was experiencing the COVID-19 vaccine breakthrough infection because of the remarkable talent the Delta variant has for replicating and producing high levels of viremia.

My first thoughts were for my family, of course. As my illness unfolded, I had kept checking in with them to see if they had any of these "cold" symptoms I had; none of them

did. When my test came back positive, we all went into quarantine immediately and they went to get tested; all of them were negative. Next, I contacted the people I had been meeting with that week and warned them that I had tested positive. Despite my mask, and their fully vaccinated status, they needed to get tested. They did, and they were negative. I realized that I was probably contagious, though asymptomatic, on Saturday night when we had friends over to watch the NBA finals. Yeah, everyone was vaccinated, but if I could get sick from this new Delta variant, they could too. The public health department sent me a survey when they found out about my positive test, and they pinpointed Saturday as the day I started to be contagious. I told my friends that I was probably contagious when they were over for the game, and that they should get tested. They did, and everyone came back negative for COVID-19.

Wait a minute; what about Sunday night? The newborn baby and the sleep-deprived mom. Oh no! I was contagious then as well. We kept our distance, and were only there for about 10 minutes, but if I felt bad from COVID-19, I felt worse for exposing them to the virus.

I am no Anthony Fauci, and I am grateful that we have had level-headed scientists like him to lead us through this terrible experience. I am sure there will be many papers written about COVID-19 breakthrough infections in the future, but I have many thoughts from this experience. First, my practice of wearing an N95 and goggles for all patients, not just COVID-19 patients, during the height of the pandemic was effective. Prior to getting vaccinated, my antibody tests were negative, so I never contracted the illness when I stuck to this regimen. Second, we all want to get back to something that looks like "normal," but because there are large unvaccinated populations in the community the virus will continue to propagate and evolve, and hence everyone is at risk. While the guidelines said it was okay to ease up on our restrictions, because so many people are not vaccinated, we all must continue to keep our guard up. Third, would a booster shot have saved me from this fate? Because I was on



Dr. McIlraith is the founding chairman of the hospital medicine department at Mercy Medical Group in Sacramento. He received the SHM Award for Outstanding Service in Hospital Medicine in 2016.

the front lines of the pandemic as a hospitalist, I was also among the first members of my community to get vaccinated, receiving my second shot on Jan. 14, 2021. My wife was not in any risk group, was not on any vaccine priority list, and didn't complete the series until early April. If I was going to give the infection to anyone, it would have been her. Not only did she never develop symptoms, but she also repeatedly tested negative, as did everyone else that I was in contact with when I was most contagious. The thing that was different about me from everyone else was that I had gotten the vaccine well ahead of them. Had my immunity waned over the months?

The good news is that, while I wouldn't characterize what I had as "mild," it certainly wasn't protracted. Yes, I was a good boy, and did the basics: stay hydrated and get plenty of sleep. I was really bad off for about 3 days, and I hate to think what it would have been like if I had coexisting conditions such as asthma or diabetes. We all know what a bad case of COVID-19 looks like in the unvaccinated, with months in the hospital, intravenous infusions, and high-flow oxygen for the lucky ones. I had nothing remotely like that. The dominant symptom I had was incapacitating fatigue and significant body aches. The second night I had some major chills, sweats, and

*Continued on following page*

# Beta-blocker reduces lung inflammation in critical COVID-19

By Fran Lowry

In a small study, intravenous administration of the beta-blocker metoprolol to critically ill COVID-19 patients with acute respiratory distress syndrome (ARDS) safely blunted lung inflammation associated with the disease.

Metoprolol administration also resulted in better oxygenation and fewer days on intensive mechanical ventilation and in the ICU, compared with no treatment.

These data suggest that metoprolol repurposing for the treatment of ARDS in COVID-19 patients is a safe and inexpensive strategy with the potential to improve outcomes, the researchers said.

“Metoprolol repurposing for the treatment of ARDS associated with COVID-19 is a safe and cheap intervention that can help to alleviate the massive personal and health care burden associated with the pandemic,” they concluded.

The results, from the MADRID-COVID pilot trial from Agustin Clemente-Moragon, BSc, Centro Nacional de Investigaciones Cardiovasculares, Madrid, and colleagues, were published online Aug. 30, 2021, in the *Journal of the American College of Cardiology* (doi: 10.1016/j.jacc.2021.07.003).

In previous work, the researchers showed that metoprolol, but not other clinically available intravenous beta-blockers, abrogates neutrophil-driven exacerbated inflammation, neutrophil-platelet interaction, and formation of neutrophil extracellular traps in a mouse model of acute lung injury.

These results prompted the current pilot trial in 20 patients, ages 18-80 years, with COVID-19-associated ARDS.

Randomization was stratified by age (59 and younger vs. 60 and older), history of hypertension (yes or no), and circulating neutrophil counts (<6,000 vs. ≥6,000). Bronchoalveolar lavage (BAL) fluid and blood samples were obtained from patients at randomization and 24 hours after the third metoprolol dose in the treatment group, and on day 4 in controls.

*“I think this study really shows that medications like metoprolol can help blunt that initial sympathetic effect.”*

Because of the cardiovascular effects of metoprolol, patients were monitored invasively and by echocardiography, the authors noted.

As expected, metoprolol significantly reduced heart rate ( $P < .01$ ) and systolic blood pressure ( $P < .05$ ), although both remained within the physiological range. Echocardiography showed no deterioration of cardiac function after metoprolol treatment.

To assess the ability of metoprolol to address neutrophil-mediated exacerbated lung inflammation, the researchers analyzed leukocyte populations in BAL samples by flow cytometry at baseline and on day 4.

At baseline, the metoprolol and control groups showed no differences in BAL neutrophil content. But on day 4, after 3 days of treatment with metoprolol, neutrophil content was significantly lower in the metoprolol group (median, 14.3 neu-

trophils/mcL) than in the control group (median, 397 neutrophils/mcL).

Metoprolol-treated patients also had lower total inflammatory-cell content and lower monocyte/macrophage content. Lymphocytes did not differ between the groups.

The investigators also explored the impact of metoprolol on the chemokine, monocyte chemoattractant protein-1 (MCP-1), as it has been shown to promote pulmonary fibrosis in late-stage ARDS.

They found that MCP-1 was significantly attenuated after 3 days of metoprolol treatment. At baseline, the median MCP-1 level was 298 pg/mL; on day 4 after metoprolol, it was 203 pg/mL ( $P = .009$ ).

MCP-1 levels remained unchanged in control patients.

In an accompanying editorial (*J Am Coll Cardiol.* 2021 Sep;78[10]:1012-4), Mourad H. Senussi, MD, assistant professor at Baylor College of Medicine, Houston, wrote: “Although the study has a small sample size, we commend the authors, who attempt to shed light on the important pathophysiological underpinnings that help establish biological plausibility for this inexpensive, safe, and widely available medication.”

In an interview, Dr. Senussi added that metoprolol is not itself something primarily used to treat COVID-19. “Rather, the drug blunts the sympathetic-host response. There is a fine balance between that sympathetic surge that is helpful to the body, and then a sympathetic surge that, if left unchecked, can lead to significant damage. I think this study really shows that medications like metoprolol can help blunt that initial sympathetic effect.” A larger study is warranted, he added, “The study design here was simple and most importantly, showed biological plausibility.”

*Continued from previous page*

wild dreams. From a respiratory standpoint, I had bad rhinitis and a wicked cough for a while that tapered off. My oxygen saturations dropped into the mid 90's, but never below 94%. But if I had been 10 times sicker, I doubt I would have survived. I was on quarantine for 10 days but I highly doubt I was at all contagious by day 5, based on my symptoms and the fact that nobody around me turned COVID positive with repeat testing.

I was so relieved that none of my contacts when I was most contagious turned positive for COVID-19. Though not scientific, I find that illustrative. While I should have canceled my meetings on Monday and Tuesday, everybody knew I had a “cold” and nobody wanted to cancel. Nobody thought it possible that I had COVID-19, especially me. The Delta variant is notorious for gen-

erating high levels of viremia, yet I didn't get anybody sick, not even my wife. That suggests to me that, while the vaccine doesn't eliminate the risk of infection – which we already knew – it probably significantly reduced my infectivity. For that I am very grateful. Now that I can say that I had the COVID-19 experience, I can tell you it feels terrible. But I would have felt much worse if I had gotten others ill. My personal belief is that, while the vaccine didn't save me from disease, it dramatically truncated my illness, and significantly reduced my risk of passing the virus on to my friends and family.

So where did I contract the virus? We were unmasked at dinner on Friday night, which was acceptable in Yolo County at that time. By the way, I actually live in Yolo County, not YOLO (you only live once) county. You can imagine the latter

would be a bit more loosey-goosey with the masking requirements. That notwithstanding, I don't think the dinner was where I picked it up because it was too short of an incubation period. My wife and I obviously reacted differently, as I discussed, but we were both at the restaurant. She didn't get COVID-19 and I did. I think that I probably picked it up at the hospital, because, while I was wearing a mask there, I was wearing only a surgical mask, not an N95. And I wasn't wearing goggles anymore. While none of my patients were officially diagnosed with COVID-19, I was encountering a lot of people, getting in relatively close contact, and guidelines were being relaxed, including preadmission COVID-19 testing.

I was an outlier, as I have pointed out; none of my other close contacts contracted COVID-19. A lot of politics and public opinion is driven by

outlier cases, and even pure fabrications these days; we certainly can't create public health policy based on an outlier. I am not suggesting that my experience is any basis for rewriting the rules of COVID-19. The experience has given me pause to think through many facets of this horrible illness we have had to deal with in so many ways, however. And I have also reexamined my own practice for protecting myself in the hospital. Clearly what I was doing in the height of the pandemic was effective, and my more relaxed recent practices were not. Now that I am fully recovered after a relatively unique encounter with the condition, I look forward to seeing what the scientists and public policy makers do with COVID-19 vaccine breakthrough cases. So, among us hospitalist friends and colleagues, regardless of the policy guidelines, I say we keep on masking.

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