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“When patients with COPD are receiving triple therapy but are not having frequent exacerbations, it’s safe to ‘de-escalate,’” Dr. Kenneth R. Chapman said.

Doug Brunk/MDedge News

In critically ill, lower glucose target linked to lower death risk

BY ANDREW D. BOWSER

MDedge News

FROM THE JOURNAL CHEST ■ In critically ill patients, treating blood glucose with a low target of 80-110 mg/dL was associated with a lower risk of 30-day mortality compared with patients with a target of 90-140 mg/dL, according to results of a retrospective cohort analysis.

With the computerized intravenous insulin protocol used in the study, the strict target could be achieved with a low rate of hypoglycemia, the authors wrote. The analysis was published in the journal *CHEST*.

These findings do not suggest that clinicians should practice counter to current guidelines, which recommend against intensive insulin therapy, noted Andrew M. Hersh, MD, of the division of pulmonary and critical care at San Antonio Military Medical Center, and his coauthors.

However, it does raise the possibility that earlier investigations finding an association between intensive insulin therapy and excess mortality “may have been accurate only in the setting of technologies which led to high rates of severe

REDUCING THE GLUCOSE TARGET // continued on page 7

Most COPD patients on triple therapy can withdraw steroids

BY DOUG BRUNK

MDedge News

SAN DIEGO – In patients on long-term triple therapy and up to one exacerbation in the previous year, the withdrawal of inhaled corticosteroids (ICS) led to a small decrease in lung function that was not clinically important, with no associated difference in the rates of chronic obstructive pulmonary disease (COPD) exacerbations, dyspnea, or as-needed bronchodilator use.

Those are key findings from the SUNSET trial, a 26-week, randomized, double-blind, parallel-group multicenter study to assess the efficacy and safety of the switch from long-term triple therapy to indacaterol/glycopyrronium (IND/

GLY, 110/50 mcg once daily) or continuation of triple therapy with tiotropium 18 mcg once daily and salmeterol/fluticasone propionate fixed-dose combination 50/500 mcg b.i.d.

“When patients with COPD are receiving triple therapy but are not having frequent exacerbations, it’s safe to ‘de-escalate’ to the bronchodilator foundation of second generation LABA/LAMA,” lead study author Kenneth R. Chapman, MD, FCCP, said in an interview prior to an international conference of the American Thoracic Society. “In a minority of patients with high blood eosinophil counts, one should make the move cautiously.”

Dr. Chapman, director of the asthma and

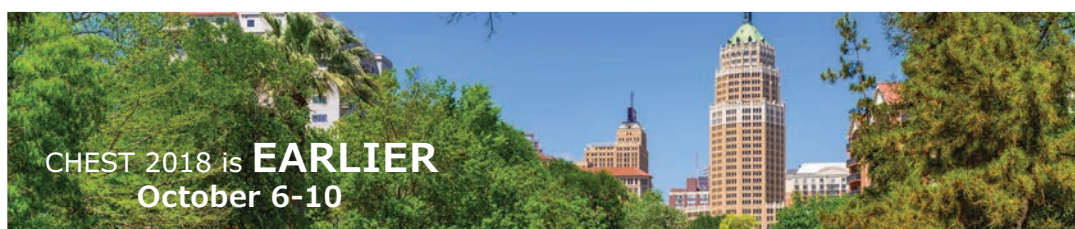
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FDA expands indication for COPD therapy

BY KATIE WAGNER LENNON

MDedge News

The Food and Drug Administration has approved a new indication for the chronic

obstructive pulmonary disease therapy fluticasone furoate/umeclidinium/vilanterol (Trelegy Ellipta), which allows physicians to prescribe the drug to a broader class of COPD patients, according to a

statement from two pharmaceutical companies.

This triple-therapy inhaler was approved for use as a long-term, once-daily maintenance treatment in some COPD patients back in Sep-

tember 2017. Those were defined as COPD patients who were already using the corticosteroid and long-acting beta₂-agonist (LABA) drug combination fluticasone furoate/vilanterol (Breo Ellipta) but required additional

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bronchodilation or those who were already using the same drugs contained in Trelegy Ellipta by taking both of the following two therapies: Breo Ellipta and the long-acting muscarinic antagonist (LAMA) umeclidinium (Incruse Ellipta). Physicians can now use fluticasone Trelegy Ellipta to treat all COPD patients who have airflow limitation or have experienced an

acute worsening of respiratory symptoms, according to the statement that GlaxoSmithKline and Innoviva released on April 24. In this new population of COPD patients who are now approved to use Trelegy Ellipta, the drug will continue to serve as a long-term once-daily maintenance therapy.

The results of the IMPACT trial, which was the first study to compare

a single-inhaler triple therapy with two dual therapies, were published on April 18 (N Engl J Med. 2018. doi: 10.1056/NEJMoa1713901).

This study randomized 10,355 symptomatic COPD patients with a history of moderate to severe exacerbations patients to 52 weeks of either triple inhaled therapy involving a once-daily combination of the

corticosteroid, 100 mcg fluticasone furoate; the LAMA, 62.5 mcg of umeclidinium; and the LABA, 25 mcg of vilanterol; or dual inhaled therapy involving either 100 mcg fluticasone furoate plus 25 mcg of vilanterol, or 62.5 mcg of umeclidinium plus 25 mcg of vilanterol.

After 1 year, the rate of moderate to severe COPD exacerbations in the triple-therapy group was 0.91 per year, compared with 1.07 in the fluticasone furoate–vilanterol group and 1.21 in the vilanterol–umeclidinium group. This translated to a 15% reduction with triple therapy compared with fluticasone furoate–vilanterol and a 25% reduction, compared with vilanterol–umeclidinium (*P* less than .001 for both).

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VIEW ON THE NEWS

Daniel Ouellette, MD, FCCP, comments: Mr.

Brown came to my clinic this week. He has severe COPD manifested by exertional dyspnea, chronic cough, and frequent exacerbations of his disease.



I have been treating him with tiotropium (LAMA), fluticasone (inhaled corticosteroid), and salmeterol (LABA). The latter two medicines are contained in a combination inhaler. He also has a rescue inhaler. He has quit smoking and completed a course of pulmonary rehabilitation, but still has daily symptoms. What else can I do?

I recently read a report about a new combination inhaler that was a “three-in-one” device: LAMA, LABA, and ICS all in the same delivery system. I was glad to see that “triple therapy” now has more robust objective, scientific support. I figured that a combination inhaler might be more convenient and may facilitate compliance. I wondered, though, whether this new device represents truly novel therapy or a re-packaging of existing therapies? Will other companies spend their research dollars to develop their own “triple threat,” or will they develop truly new drugs to help my patient with his breathing?

airways clinic at University Health Network, Toronto, noted that relatively few patients with COPD benefit from inhaled steroids. "Given the risk of adverse events (pneumonia, osteoporosis, etc.), we'd rather not give them when they're not needed," he said. "Inhaled steroids seem to play only one role in COPD: They tend to reduce exacerbations in the exacerbation-prone COPD patient. That's about 20% of the COPD population. Despite this, a great many patients end up on triple therapy [long-acting bronchodilators/long-acting muscarinic antagonist (LABA/LAMA) and ICS] needlessly."

For the study, Dr. Chapman and his associates enrolled 1,053 patients with moderate to severe COPD who'd had no more than one exacerbation in the previous year who had used triple therapy for at least 6 months prior to study inclusion. The primary endpoint of the study was noninferiority on change from baseline in postdose trough forced expiratory volume in 1 second (FEV₁) (with a noninferiority margin of -50 mL) after 26 weeks. Exacerbations, health-related quality of life as measured by the St. George's Respiratory Questionnaire (SGRQ-C), and breathlessness as measured by the Transition Dyspnea Index also were evaluated. Of the 1,053 patients, 527 were randomized to IND/GLY and 526 to triple therapy. Their mean age was 65 years and their mean postbron-

chodilator FEV₁ was 1.6 L.

The researchers found that ICS withdrawal led to a mean reduction in trough FEV₁ of -26 mL, which exceeded the noninferiority margin. This difference between treatments on trough FEV₁ was driven by the subset of patients with high blood eosinophil counts at baseline (a mean of -68 mL for patients with at least 300 cells/mcL and a mean of -13 mL for patients with fewer than 300 cells/mcL). The two treatments showed similar annualized rates of moderate/severe COPD exacerbations (rate ratio, 1.08) and all (mild/moderate/severe) exacerbations (RR, 1.07). ICS withdrawal led to a small difference in SGRQ-C (1.4 U on week 26), but no differences in Transition Dyspnea Index or use of rescue medication over 26 weeks. Safety and tolerability were balanced across the two treatment groups.

"Although we found no overall increase in exacerbations with 'de-escalation,' there were, of course, exacerbations that occurred during the trial," Dr. Chapman said. "We found that they tended to occur in the minority of patients who had elevated blood eosinophil counts, especially if the counts were elevated persistently (at screening and randomization). The relevant cut-point was blood eosinophil counts above 300/UL. If exacerbations did occur in this easily identifiable subpopulation, they tended to occur early, in the first month after de-escalation. This gives physicians a simple way to identify a population they might exercise caution and a period when careful monitoring is useful."

He acknowledged certain limitations of the study, including its 6-month duration, which is shorter than most exacerbation studies. "But by recruiting at multiple sites in multiple countries and across seasons, we don't think this was an importation limitation," he said. "Of course, like most investigators, I can always think of things I wish I had tracked. My personal hunch is that FeNO [exhaled nitric oxide levels] might offer some useful information but that will be a hunch to explore in another study."

SUNSET was sponsored by Novartis. Dr. Chapman disclosed that he has received fees for research, consulting and lectures from Novartis, as well as from several other pharmaceutical companies.

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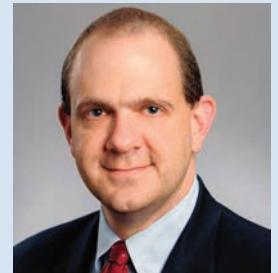
SOURCE: Chapman KR et al. *ATS* 2018, Abstract A1009.

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Female physicians face enduring wage gap

BY RICHARD FRANKI

MDedge News

Male physicians make more money than female physicians, and that seems to be a rule with few exceptions. Among

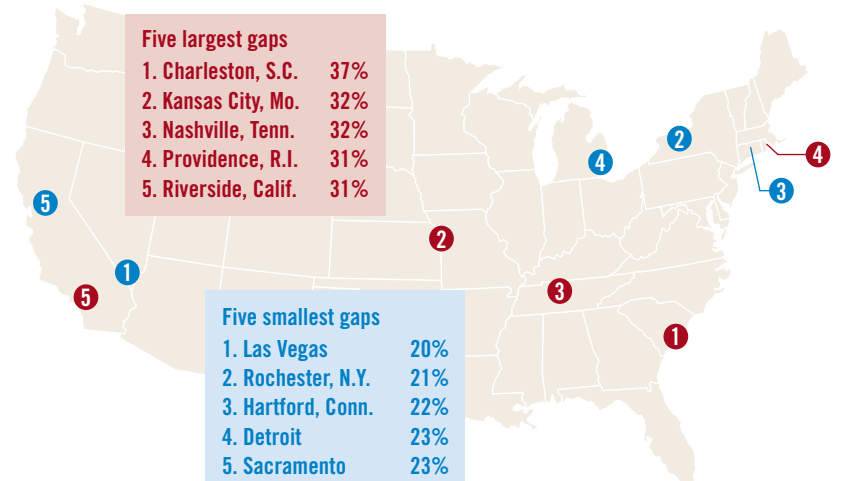
VIEW ON THE NEWS

Michael E. Nelson, MD, FCCP, comments: This is a rather damning revelation about pay parity in medicine, but not unexpected given similar findings in non-medical corporate America. As I do not sit on any compensation committees or negotiate contracts for female employees, I am at a loss to explain how these levels of inequality, in ALL 50 metropolitan areas, can exist unchecked. I would suggest that it is time for all male physicians to advocate for our female colleagues.

the 50 largest metro areas, there were none where women earn as much as men, according to a new survey by the medical social network Doximity.

The metro area that comes the closest is Las Vegas, where female physicians earned 20% less – that works out to \$73,654 – than their male counterparts in 2017. Rochester, N.Y., had the smallest gap in terms of dollars (\$68,758) and the second-smallest percent difference (21%), Doximity said in its 2018 Physician Compensation Report.

The largest wage gap on both measures can be found in Charleston, S.C., where women earned 37%, or \$134,499, less than men in 2017. The other members of the largest-wage-gap club are as follows: Kansas City, Mo., and Nashville, Tenn., both had differences of 32%, and Providence, R.I., and Riverside, Calif., had differences of 31%, Doximity said in the report, which was based on data from “compensation surveys completed in 2016 and 2017 by



Note: Compensation surveys were completed by more than 65,000 physicians in 2016 and 2017.

Source: Doximity

more than 65,000 full-time, licensed U.S. physicians who practice at least 40 hours per week.”

A quick look at the 2016 data shows that the wage gap between female and male physicians increased from 26.5% to 27.7% in 2017, going from more than \$92,000 to \$105,000. “Medicine is a highly

trained field, and as such, one might expect the gender wage gap to be less prominent here than in other industries. However, the gap endures, despite the level of education required to practice medicine and market forces suggesting that this gap should shrink,” Doximity said.

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Reducing the glucose target // continued from page 1

hypoglycemia,” they wrote.

The retrospective cohort analysis by Dr. Hersh and his colleagues included 1,809 adult patients treated at three different ICUs in two hospitals between January 2010 and December 2015. Treatment was delivered with a computerized ICU insulin infusion protocol that allows clinicians to choose between two blood glucose targets: 80-110 mg/dL or 90-140 mg/dL. The lower target was chosen for 951 patients, and the moderate target for 858 patients.

The most common primary admission diagnoses in the cohort included chest pain or acute coronary syndrome in 43.3%, cardiothoracic surgery in 31.9%, heart failure (including cardiogenic shock) in 6.8%, and vascular surgery in 6.0%.

While patients in the low blood glucose target group had a higher rate of moderate hypoglycemia, both groups had a low rate of severe hypoglycemia, at 1.16% in the low target group and 0.35% in the moderate target group ($P = .051$).

Unadjusted 30-day mortality was significantly lower in the 80- to 110-mg/dL group compared with the 90- to 140-mg/dL group (4.3% vs. 9.2%, respectively; P less than .001), according to the investigators.

Furthermore, logistic regression analysis showed that patients treated with a target of 80-110 mg/dL had a lower risk of 30-day mortality compared with patients with a target of 90-140

mg/dL (odds ratio 0.65; 95% confidence interval, 0.43-0.98; $P = .04$).

These results advance the debate over appropriate blood glucose targets in critically ill patients, as they suggest that the effects of targeting blood glucose and the effects of severe hypoglycemia “can be separated,” the investigators wrote.

Current guidelines on intensive insulin therapy are based in part on findings of the NICE-SUGAR trial, which found that, among adults treated in the ICU, intensive glucose control increased mortality. However, a post hoc analysis suggested the mortality increase in NICE-SUGAR was “largely driven by a significant incidence of moderate hypoglycemia, and to a greater degree severe hypoglycemia,” Dr. Hersh and his coauthors noted in their report.

“Given improvements in insulin delivery and glucose monitoring, a reassessment of potential benefits of [intensive insulin therapy] should once again be evaluated in a prospective randomized trial,” they wrote.

Dr. Hersh and his coauthors declared no financial or nonfinancial disclosures related to the study.

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SOURCE: Hersh AM et al. CHEST 2018. doi: 10.1016/j.chest.2018.04.025.

While patients in the low blood glucose target group had a higher rate of moderate hypoglycemia, both groups had a low rate of severe hypoglycemia.

Two therapies equally effective in obese OSA patients

BY KATIE WAGNER LENNON

MDedge News

The mortality rates were similar between patients using two different therapeutic regimens to treat obesity hypoventilation syndrome with severe obstructive sleep apnea, according to new research that was presented at the American Thoracic Society International Conference in San Diego.

In this multicenter open-label, randomized, controlled trial, Sanchez Quiroga et al. compared the long-term effectiveness of noninvasive ventilation (NIV) with continuous positive airway pressure (CPAP). The researchers analyzed the results for 202 patients who used one of the two treatments for at least 3 years.

Among this study’s findings were that the mortality rates and the number of cardiovascular events that occurred were similar in the two treatment groups. The mortality rate for patients who used CPAP was 14.7%, compared with 11.3% for the patients who received NIV (adjusted hazard ratio, 0.73; $P = .439$), and the cardiovascular events per 100 person-years were 5.1 for CPAP and 7.46 for NIV ($P = .315$).

The researchers concluded that both treatments are equally effective for the long term, but that CPAP should be “the preferred treatment modality,” because it’s cheaper and easier to implement.

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Two more and counting: Suicide in medical trainees

BY MICHAEL F. MYERS, MD

Like everyone in the arc of social media impact, I was shocked and terribly saddened by the recent suicides of two New York women in medicine – a final-year medical student on May 1 and a second-year resident on May 5. As a specialist in physician health, a former training director, a long-standing member of our institution's medical student admissions committee, and the ombudsman for our medical students, I am finding these tragedies harder and harder to reconcile. Something isn't working. But before I get to that, what follows is a bulleted list of some events of the past couple of weeks that may give a context for my statements and have informed my two recommendations.

- May 3, 2018: I give an invited GI grand rounds on stress, burnout, depression, and suicide in physicians. The residents are quiet and say nothing. Faculty members seem concerned about preventing and eradicating only burnout – and not that interested in anything more severe.
- May 5: A psychiatry resident from Melbourne arrives to spend 10 days with me to do an elective in physician health. As in the United States, there is a significant suicide death rate in medical students and residents Down Under. In the afternoon, I present a paper at the annual meeting of the American Academy of Psychodynamic Psychiatry and Psychoanalysis on the use of psychotherapy in treatment-resistant suicidal depression in physicians. There is increasing hope that this essential modality of care will return to the contemporary psychiatrist's toolbox.
- May 6: At the annual meeting of the American Psychiatric Association in New York, I'm the discussant for powerful heartfelt papers of five psychiatrists (mostly early-career psychiatrists and one resident) that talked about living with a psychiatric illness. The audience is huge, and we hear narratives about internal stigma, self-disclosure, external stigma, shunning, bullying, acceptance, rejection, alienation, connection, and love by peers and family. The authenticity and valor of the speakers create an atmosphere of safety, which enables psychiatrists in attendance from all over the world to share their personal stories – some at the microphone, some privately.
- May 7: Again at the APA, I chair and facilitate a workshop on physician suicide. We hear from four speakers, all women, who have lost a loved one to suicide – a husband, a father, a brother, a son – all doctors. Two of the speakers are psychiatrists. The stories are gripping, detailed, and tender. Yes, the atmosphere is very sad, but there is not a pall. We learn how these doctors lived, not just how they died. They all loved medicine; they were creative; they cared deeply; they suffered silently; and with shame, they lost hope. Again, a big audience of psychiatrists, many of whom share their own stories, that they, too, had lost a physician son, wife, or mother to suicide. Some of their deceased family members fell through the cracks and did

not receive the life-saving care they deserved; some, fearing assaults to their medical license, hospital privileges, or insurance, refused to see anyone. They died untreated.

- May 8: Still at the APA, a psychiatrist colleague and I collaborate on a clinical case conference. Each of us describes losing a physician patient to suicide. We walk the attendees through the clinical details of assessment, treatment, and the aftermath of their deaths. We talk openly and frankly about our feelings, grief, outreach to colleagues and the family, and our own personal journeys of learning, growth, and healing. The clinician audience members give constructive feedback, and some share their own stories of losing patients to suicide. Like the day before, some psychiatrists are grieving the loss of a physician son or sibling to suicide. As mental health professionals, they suffer from an additional layer of failure and guilt that a loved one died “under their watch.”
- May 8: I rush across the Javits Center to catch the discussant for a concurrent symposium on physician burnout and depression. She foregoes any prepared remarks to share her previous 48 hours with the audience. She is the training director of the program that lost the second-year resident on May 5. She did not learn of the death until 24 hours later. We are all on the edge of our seats as we listen to this grieving, courageous woman, a seasoned psychiatrist and educator, who has been blindsided by this tragedy. She has not slept. She called all of her residents and broke the news personally as best she could. Aided by “After A Suicide: A Toolkit for Residency/Fellowship Programs” (American Foundation for Suicide Prevention), she and her colleagues instituted a plan of action and worked with administration and faculty. Her strength and commitment to the well-being of her trainees is palpable and magnanimous. When the session ends, many of us stand in line to give her a hug. It is a stark reminder of how many lives are affected when someone you know or care about takes his/her own life – and how, in the house of medicine, medical students and residents really are part of an institutional family.
- May 10: I facilitate a meeting of our 12 second-year residents, many of whom knew of or had met the resident who died. Almost everyone speaks, shares their feelings, poses questions, and calls for answers and change. There is disbelief, sadness, confusion, some guilt, and lots of anger. Also a feeling of disillusionment or paradox about the field of psychiatry: “Of all branches of medicine, shouldn't residents who are struggling with psychiatric issues feel safe, protected, cared for in psychiatry?” There is also a feeling of lip service being paid to personal treatment, as in quoted statements: “By all means, get treatment for your issues, but don't let it encroach on your duty hours” or “It's good you're getting help, but do you still have to go weekly?”

In the immediate aftermath of suicide, feelings run high, as they should. But rather than wait it out – and fearing a return to “business as usual” –



Dr. Myers is a professor of clinical psychiatry at State University of New York, Brooklyn, and the author of “Why Physicians Die by Suicide: Lessons Learned From Their Families and Others Who Cared.”

In psychiatry, we need to redouble our efforts in fighting the stigma attached to psychiatric illness in trainees. It is unconscionable that medical students and residents are dying of treatable disorders. Too many are not availing themselves of services we provide.

let me make only two suggestions:

1. We need to come together and talk about this – medical students and residents and training directors and deans. A town hall forum would be ideal. Although there are amazing innovations on wellness emanating from the Association of American Medical Colleges and Accreditation Council for Graduate Medical Education, many current medical students and residents feel frustrated – “This is taking too long” or “This is top down and being imposed on us” or “What about our voices ... don't they count?” Although students and residents have representatives on faculty committees, feedback is not universal, and not all residents believe that their senior peers truly convey their concerns to those in power. They want to be present at the table and speak for themselves. Too many do not feel they have a voice.

2. In psychiatry, we need to redouble our efforts in fighting the stigma attached to psychiatric illness in trainees. It is unconscionable that medical students and residents are dying of treatable disorders (I've never heard of a doctor dying of cancer who didn't go to an oncologist at least once), yet too many are not availing themselves of services we provide – even when they're free of charge or covered by insurance. And are we certain that, when they knock on our doors, we are providing them with state-of-the-art care? Is it possible that unrecognized internal stigma and shame deep within us might make us hesitant to help our trainees in their hour of need? Or cut corners? Or not get a second opinion? Very few psychiatrists on faculty of our medical schools divulge their personal experiences of depression, posttraumatic stress disorders, substance use disorders, and more (with the exception of being in therapy during residency, which is normative and isn't stigmatized). Coming out is leveling, humane, and respectful – and it shrinks the power differential in the teaching dyad. It might even save a life.

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Americans are getting more sleep

BY KATIE WAGNER LENNON

MDedge News

Some Americans began getting more sleep over the period of 2003 through 2016, an analysis of data from the American Time Use Survey (ATUS) has suggested.

Many people living in the United States habitually sleep less than the recommended 7-9 hours each day. “Experimental studies have demonstrated that both acute total and chronic partial sleep restriction in healthy adults are associated with physiological changes that can be considered precursors of manifest diseases (e.g., decreased insulin sensitivity),” noted Mathias Basner, MD, PhD, and David F. Dinges, PhD, both of the division of sleep and chronobiology at the University of Pennsylvania, Philadelphia, in their paper.

This new study, which was published in the journal *Sleep*, is the first to have demonstrated that large parts of the U.S. population significantly increased their sleep between 2003 and 2016.

The investigators analyzed ATUS responses from 181,335 Americans aged 15 years and older; respondents included in the analysis were not active in the military or residing in institutions such as nursing homes or prisons. In 15- to 20-minute computer-assisted telephone interviews, the survey participants reported the activities they performed over a 24-hour period on a minute-by-minute basis. In-depth analyses included only groups “that showed a significant increase in sleep duration across survey years either on weekdays or weekends (or both): employed respondents, full-time students, and retirees.”

Using this data from ATUS, Dr. Basner and Dr. Dinges found that on workdays the prevalence of people who were sleeping 7 hours or less a day decreased by 0.44% per year (P less than .0001), while the percentage people who were sleeping more than 9 hours a day increased by 0.48% per year (P less than .0001).

Overall, respondents’ sleep increased by an average of 1.40 minutes during a weekday and 0.83 minutes during a weekend day every year.

These findings will be welcome news for or-

VIEW ON THE NEWS

David A. Schulman, MD, FCCP, comments:

For more than 15 years, we have had evidence that sleep deprivation is associated with not only increased accident risk, but also other common causes of mortality, including cardiovascular disease and cancer. Despite this knowledge, decades of trending in sleep patterns of the US population have continued to show declines in total sleep time, which have been attributed to multiple factors, including longer work hours and the pervasive use of electronics, which can serve both as a distraction from sleep and a contributor to circadian dysrhythmia.

The recent article by Basner and Dinges suggests, for the first time, that this trend may be reversing. Although the data suggest a minimal bump in sleep time (of approximately 1 minute per night, slight-

ly more during weeknights than weekend nights), it is at least a move in the right direction. In a related editorial in the same issue of *SLEEP*, Ogilvie and Patel identify some possible problems with the paper; these include a nonvalidated tool for data collection, and the possible conflation of time in bed and sleep time. Even if the data are accurate, it is difficult to imagine that such a modest improvement in sleep duration would yield meaningful benefits in terms of daytime function and sleep-related morbidity.

While our work in improving public awareness of sleep deprivation is far from done, perhaps this study is the first sign that a new day is dawning on improved sleep health for the country.



ganizations, such as the American Academy of Sleep Medicine, the Sleep Research Society, and the Centers for Disease Control and Prevention, that have been campaigning for years to increase sleep time among Americans.

The researchers also observed that the percentage of respondents in short sleep duration categories decreased significantly, and the percentage of respondents in long sleep duration categories increased significantly across survey years. One of the “most pronounced changes” occurred in the size of the group of patients receiving 6-7 hours of sleep. This group decreased by 0.23% per year. The biggest change was seen in the category of patients receiving 9-10 hours of sleep, which increased by 0.24% per year.

“[The] change in sleep duration across survey years on weekdays can mostly be explained by respondents going to bed earlier at night and, to a lesser degree, by getting up later in the morning,” the researchers said. “On weekends/holidays, ‘time to bed’ shifted significantly to earlier

bed times by 1.1 min/year across survey years, which was comparable to the shift observed on weekdays.”

Study participants aged 18-24 slept the most, with hours slept having “decreased with increasing age.” On weekdays, adults aged 45-54 years slept the least, and on weekends, adults aged 55-64 years got the least shut-eye. Hispanic, Asian, and black respondents slept more than white and “other race/ethnicity” survey participants. The researchers also found that women overall got more sleep than men.

Dr. Basner and Dr. Dinges expressed optimism about Americans’ ongoing battle against chronic sleep deficiency. “These findings presented here suggest that we are on the right track ... even if there is still a long way to go,” they said.

The authors reported no conflicts of interest.

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SOURCE: Basner M et al. *Sleep*. 2018 Apr 1;41(4):1-16.

8-Isoprostane levels predict OSA in children

BY MADHU RAJARAMAN

MDedge News

The oxidative stress biomarker 8-isoprostane (8-IsoP) predicted obstructive sleep apnea (OSA) and disease severity in children better than the fractional concentration of exhaled nitric oxide (FeNO), according to results published in *Sleep Medicine*.

In an analysis of 46 patients with sleep-disordered breathing and 20 controls, patients with OSA had higher levels of 8-IsoP in exhaled breath condensate (EBC) upon waking than patients with primary snor-

ing (PS) and controls. 8-IsoP values were also correlated with apnea hypopnea index (AHI) (r , 0.40; P = .003) and oxygen saturation, also

known as SaO₂ (r , -0.50; P = .001), reported Mario Barreto, MD, of the Pediatric Unit at Sant’Andrea Hospital in Rome and his coauthors.

The investigators studied 66 children aged 4.5-15.1 years, of whom 46 had sleep-disordered breathing (SDB) and were enrolled in the

hospital’s Pediatric Sleep Center. The 20 healthy controls had no history of sleep problems, including snoring, apneas, and restless

Patients with OSA had higher levels of 8-IsoP in exhaled breath condensate upon waking than patients with primary snoring and controls. 8-IsoP values were also correlated with apnea hypopnea index and oxygen saturation.

sleep. Exclusion criteria included acute respiratory infections in the 4 weeks preceding the study, chronic respiratory comorbidities, and therapy with corticosteroids or other anti-inflammatory drugs for at least 3 weeks.

Patients with SDB had a medical examination followed by overnight standard polysomnography (PSG), and EBC 8-IsoP and FeNO measurements were collected the next morning upon waking. The SDB group also had spirometry and skin prick testing for common allergens. The children in the

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control group had the same tests and measurements done, except for PSG, Dr. Barreto and his colleagues wrote.

Central, obstructive, and mixed apnea events were counted according to American Academy of Sleep Medicine (AASM) criteria. AHI was defined as the average number of apnea and hypopnea events per hour of sleep. OSA was diagnosed with an AHI of one episode per hour and confirmed by the presence of SDB symptoms with AHI of one episode per hour.

Children with snoring and an AHI of less than one episode per hour were diagnosed with primary snoring (PS). Patients with an AHI greater than one episode per hour and less than five episodes per hour were diagnosed with mild OSA. Children with an AHI of greater than five episodes per hour were diagnosed with moderate to severe OSA, the authors said.

While 8-IsoP concentrations correlated with OSA severity for AHI and SaO₂, FeNO did not, Dr. Barreto and colleagues reported.

The difference in 8-IsoP concentrations for children with SDB and controls (mean, 39.6; $P = .006$) was increased when adjusted using multiple linear regression (mean, 43.2; $P = .007$), and the difference was even more pronounced when adjusted for all potential confounding

variables (mean, 53.1; $P = .008$). The difference in FeNO levels between SDB patients and controls was not statistically significant (mean, 1.67; $P = .358$) and did not change significantly when adjusted for confounding variables.

High area under the curve values were observed for 8-IsoP as a pre-

dictor of OSA (.839; 95% confidence interval, .744-.933, $P = .000$). The sensitivity and specificity of cutoff values of 8-IsoP concentrations above the 50th percentile were 76.5% and 78.1%, respectively.

“[It] seems that biomarkers of oxidative stress reflect OSA severity in children more closely than biomark-

ers of atopic-eosinophilic airway inflammation,” the authors concluded.

No disclosures or conflicts of interest were reported.

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SOURCE: Barreto M et al. Sleep Medicine. 2018. doi: 10.1016/j.sleep.2018.01.011.

VIEW ON THE NEWS

Susan Millard, MD, FCCP,

comments: The field of biomarkers in different disease states

has exploded over the last few years and this article is fascinating.

Barreto et al. analyzed a biomarker for oxidative stress in pe-

diatric patients who presented to their sleep lab. The concentration of 8-isoprostane in the exhaled breath condensate correlated with the severity of the OSA in these patients who were 4.5 years of age to 15.1 years of age. We screen for OSA in difficult-to-control asthma patients, so it would be interesting to repeat this study in that population, too!



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Disrupted sleep tied to alexithymia

BY GINA L. HENDERSON

MDedge News

Heighted alexithymia may explain poor sleep quality, a pair of studies shows.

Alexithymia is a condition characterized by difficulty identifying and expressing one's emotions. "The mechanism by which alexithymia confers risk of disrupted sleep remains unclear, [but] suggestions

include increased nocturnal arousal as a result of poor verbalization of emotions and increased light sleep," wrote Jennifer Murphy, citing previous research.

In the first study, Ms. Murphy

and her associates recruited 86 men and women; 70 were included in the analyses. Participants' alexithymia scores were measured using the Toronto Alexithymia Scale, or TAS-20, which consists of three sub-

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scales – difficulty describing feelings, difficulty identifying feelings, and externally oriented thinking. Sleep quality was measured using the Pittsburgh Sleep Quality Index, or PSQI, a self-report measure that asks numerous questions, including: “During the past month, when have you usually gone to bed at night?” High scores on the TAS-20 and

“The mechanism by which alexithymia confers risk of disrupted sleep remains unclear, [but] suggestions include increased nocturnal arousal as a result of poor verbalization of emotions and increased light sleep,” wrote Jennifer Murphy.

PSQI “indicate elevated alexithymic traits and poor sleep quality, respectively,” wrote Ms. Murphy, a doctoral candidate in social, genetic, and

developmental psychiatry at King’s College London, and her associates in the journal *Personality and Individual Differences*.

The researchers found associations between total alexithymia scores and reduced sleep quality (P less than .001). They also found a significant association between the TAS-20 subscales and reduced sleep quality (all P less than .006).

In the second study, in which 73 men and women participated, Ms.

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Murphy and her associates sought to determine whether the association found in the first study was tied to depression or anxiety. Participants went online and completed three questionnaires: the TAS-20; the PSQI; and the Depression, Anxiety, & Stress Scale, or DASS-21, in a randomized order. Higher scores on the

DASS-21 correlate with greater levels of depression, anxiety, and stress. None of the questionnaires asked about any aspects of sleep.

Using a regression model, Ms. Murphy and her associates found that all of the measures correlated with poor sleep quality. But only depression ($P = .011$) and alexithymia ($P = .004$) explained unique vari-

ance in sleep quality.

Ms. Murphy said in an interview that, although it might be too early to make a clear clinical recommendation, the results suggest that “clinicians should be aware of the possibility of sleep problems characterized by heightened alexithymia and more generally in those with alexithymia.”

While further research is needed to confirm the direction of causality between disrupted sleep and alexithymia and how these subjective sleep reports in alexithymia map onto objectively measured sleep problems, these data suggest a link that is independent of depression and anxiety, she said.

Meanwhile, other researchers

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report that alexithymia is becoming more clinically relevant. Rising rates of alexithymia are being reported in psychiatric conditions such as autism, eating disorders, schizophrenia, and alcohol and substance abuse. The condition is also seen in neurologic conditions such as multiple sclerosis and traumatic brain injury (Neuropsychol

logica. 2018;11:229-40).

Ms. Murphy and her associates cited several limitations of their research. One is that they did not control for factors that affect sleep quality and alexithymia such as body composition. They also cited reports of discrepancies between objective and subjective measures – such as those made by self-report –

and the relatively small sample sizes.

The research was supported by the Economic and Social Research Council and the Baily Thomas Charitable Trust. No conflicts of interest were reported.

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SOURCE: Murphy J et al. Pers Individ Dif. 2018 Mar 27;129:175-8.



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Insomnia, major depressive episode linked in U.S.

BY CHRISTOPHER PALMER

Frontline Medical News

Insomnia is prevalent among U.S. soldiers, and the highest prevalence rate is among those with

current major depressive episode, according to a cross-sectional analysis.

“Psychiatric disorders moderated the relationship between insomnia and memory/concentration prob-

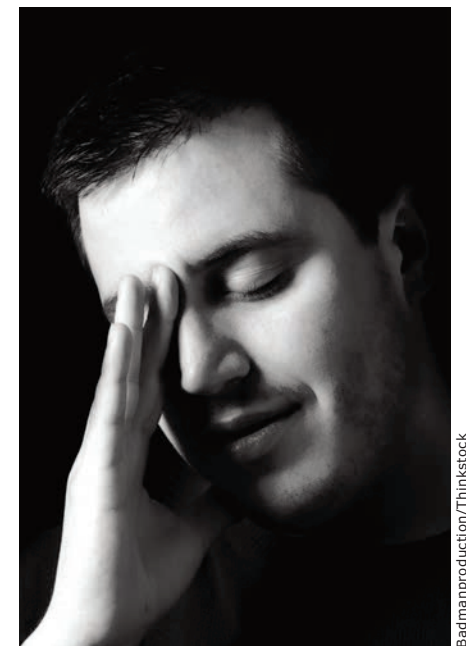
lems, suggesting the psychiatric disorders contribute unique variance to cognitive problems,” wrote Janeese A. Brownlow, PhD, of the University of Pennsylvania, Philadelphia, and her associates. “Results highlight the

importance of considering both insomnia and psychiatric disorders in the diagnosis and treatment of cognitive deficits in military soldiers.”

The researchers used the All Army Study of the Army Study to Assess Risk and Resilience in Servicemembers as their data source. They used the Composite International Diagnostic Interview (CIDI) and the Posttraumatic Stress Disor-

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der Checklist to assess psychiatric disorders; the CIDI also helped assess cognitive problems. One of the strengths of this study was its large sample size: It had an unweighted sample of 21,449 soldiers.

Dr. Brownlow and her associates found that the prevalence of insomnia among soldiers with current major depressive episode was 85%. The prevalence was 82.6% among soldiers with generalized anxiety disorder and 69.7% among those with PTSD. The likelihood of having insomnia grew with the number of comorbid psychiatric disorders.

One of the limitations of the study was that many of the measures were self-reported; for example, the psychiatric diagnoses and the determinations regarding insomnia were based on surveys and questionnaires rather than clinical interviews and assessments. Furthermore, the absence of a comprehensive neurocognitive battery might have limited the study's ability to assess cognitive problems. Nevertheless, the researchers wrote, “addressing insomnia may increase resiliency and the ability to perform and cope with the complexities of active duty.”

Read more about the study in the *Journal of Affective Disorders*.

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Vehicle crash risk linked to various sleep disorders

BY TARA HAELLE

MDedge News

Individuals with certain sleeping disorders may have a higher risk of crashes, near-crashes, or unsafe maneuvering prior to such events, suggests a study.

“The results confirm that some sleep disorders generally increase driving risk as defined by our dependent measures,” wrote Shu-Yuan Liu, a doctoral student, and two colleagues at Virginia Tech, Blacksburg (Sleep. 2018 Apr 1. doi: 10.1093/sleep/zsy023). “Furthermore, the results also provide some insights into how risk varies across specific types of sleep disorder and some moderating factors.”

The researchers analyzed data collected by the Second Strategic Highway Research Program (SHRP 2), the nation’s largest Naturalistic Driving Study, on 3,541 drivers between ages 16 and 98. The participants’ cars were outfitted with small cameras and other instruments that collected information on driver behavior, the driving environment, and the vehicle’s movements, such as speed and braking data.

The study involved licensed drivers who drove at least 3 days a week, had an eligible vehicle in good working condition, and agreed to participate for 1-2 years. At the start and end of the study, participants filled out a questionnaire on any medical conditions they had or had been treated for in the past year, any medications they were taking, and any aids they were using for a medical condition.

Among the conditions they were able to select were narcolepsy, sleep apnea, insomnia, shift-work sleep disorder, restless legs syndrome (RLS), periodic limb movement disorder, and migraine. All of these conditions have been linked in previous studies to a higher risk of vehicle collisions.

A total of 646 participants, 18.2% of the sample, had one of those disorders: 0.14% had narcolepsy, 7.4% had sleep apnea, 4.8% had insomnia, 3.4% had RLS, 0.37% had shift-work sleep disorder, 0.23% had periodic limb movement disorder, and 8.4% had migraine.

Analysis of vehicle data found that female driv-

ers with RLS and any drivers with insomnia had a higher risk of crashes or near-crashes (adjusted odds ratio, 2.26 and 1.49, respectively, *P* less than .05 for both). Drivers with narcolepsy had 9 times greater odds of being involved in a crash or near-crash, but the finding was not statistically significant (AOR, 10.24, *P* less than .1).

“Drivers who reported frequency of sleep-



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driving as ‘never,’ ‘rarely,’ and ‘sometimes’ also had higher a risk, indicating that crash or near-crash risk is also associated with sources other than these sleeping disorders,” the authors noted. These drivers’ increased odds of getting into or nearly getting into a crash ranged from 31% to 53% greater (*P* less than .05).

All drivers with shift-work sleep disorder, except for those aged 20-24, had a crash or near-crash rate that was 7.5 times greater than that of drivers without any sleeping disorders. The rate among drivers aged 20-24 with this disorder had a 90% lower rate (risk ratio, 0.1, *P* less than .05) compared with control drivers.

When the researchers analyzed the drivers’ maneuvers just before a crash or near-crash, they found females with sleep apnea had a 36% greater odds of doing an unsafe maneuver in crash/near-crash circumstances (AOR, 1.36). Females with RLS and any drivers with shift-work sleep disorder were more than twice as likely to perform unsafe maneuvers (AOR, 3.38 and 3.53, respectively, *P* less than .05).

The only drivers with a sleeping disorder who were more likely to be involved in crashes of greater severity were those with periodic limb movement disorder (AOR, 1.43, *P* less than .05).

However, young drivers, senior drivers, and nighttime drivers also all had higher odds of being involved in more severe crashes and in performing unsafe maneuvers prior to a crash or near-crash. Nighttime drivers seemed to be most at risk for these, and they were linked to having more than 5 times greater odds of unsafely maneuvering their vehicles prior to getting into a crash or near-crash (AOR, 6.71, *P* less than .05).

“This is a strong piece of evidence that nighttime driving is less safe than daytime driving and limiting amount of nighttime driving could be one method to moderate road risk for some individuals,” the authors wrote.

The study’s limitations include its observational nature, low numbers of participants with several of the sleeping disorders (at levels below the disorder’s prevalence in the general population), and the complexities involved in what causes a crash or near crash.

One limitation of this study was that sleep hygiene and sleep quality were not examined, even though these might contribute significantly to roadway safety, the researchers noted. This study also did not take into account what medications or other treatment (such as continuous positive airway pressure for those with sleep apnea) the participants might be receiving for their condition.

The study’s implications include the need for physicians to advise patients with insomnia or females with sleep apnea to use caution while driving without “exaggerating risks that introduce undue fear to patients with other sleep disorders and thereby limiting mobility unnecessarily,” the authors wrote. The researchers also suggested that employers consider providing alternative transportation to shift workers and/or that insurance companies offer employers lower rates for offering such alternatives.

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SOURCE: Liu S-Y et al. Sleep J. 2018 Apr 1. doi: 10.1093/sleep/zsy023.

Uvulopalatopharyngoplasty may cut CV events in OSA

BY BIANCA NOGRADY

MDedge News

Surgical remodeling of the tissues of the throat using uvulopalatopharyngoplasty (UPPP) could significantly reduce the cardiovascular complications of obstructive sleep apnea (OSA), according to a study published in Sleep Medicine.

Researchers examined the incidence of newly diagnosed myocardial infarction, congestive heart failure, and atrial fibrillation in 192,316 patients with a new diagnosis of obstructive sleep apnea – 22,213 of whom had undergone

UPPP – and 961,590 controls.

The individuals who had had UPPP had a significantly lower incidence of all three cardiovascular events, compared with those who had not undergone the procedure. The hazard ratios for myocardial infarction, congestive heart failure, and atrial fibrillation among individuals with OSA who had uvulopalatopharyngoplasty, compared with controls, were 1.002, 0.757, and 1.117, respectively. By comparison, those hazard ratios in patients with OSA who had not had UPPP, compared with controls, were 1.070, 1.165, and 1.39 for myocardial in-

farction, congestive heart failure, and atrial fibrillation, respectively.

These figures were after accounting for confounding factors, such as age, sex, diabetes, and dyslipidemia.

The authors wrote that the most distinctive finding of their study was that uvulopalatopharyngoplasty lowered the incidence of congestive heart failure and atrial fibrillation in patients with obstructive sleep apnea to the point that they had the same level of risk as individuals without obstructive sleep apnea.

“Prior studies have evaluated the success of UPPP based on reductions of AHI [apnea-hypopnea index],

with the average success rate for the surgery being low for most patients,” wrote Heung-Man Lee, MD, PhD, then from the Guro Hospital at Korea University, Seoul, and his coauthors.

“However, the current study suggests that the effects of UPPP, regardless of the effects on AHI, can significantly reduce cardiac morbidity in patients with OSA.”

Patients without diabetes showed more benefit from UPPP in reducing the incidence of congestive heart failure, compared with those with diabetes. However, those with diabetes showed greater reductions in the

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Three-pronged plan for universal flu vaccine proposed

BY NICK ANDREWS

MDedge News

Three specific research areas were proposed by the National Institute of Allergy and Infectious Diseases (NIAID) in its development plan for a universal influenza vaccine, as detailed in a



DR. FAUCI

report published online in the *Journal of Infectious Diseases*.

Anthony S. Fauci, MD, director of the NIAID, spoke with MDedge News in an interview regarding the plan and noted

that he and his colleagues felt that it was important to accelerate the effort for a universal vaccine.

The plan will focus on transmission, natural history, and pathogenesis studies utilizing prospective cohorts; influenza immunity and correlates of immune protection; and strategies in rational vaccine design to elicit broad, protective immune responses, according to Emily J. Erbelding, MD, MPH, director of microbiology and infectious diseases at the NIAID, and her associates in their report. They noted that the three research areas are not prioritized and that advances in each are expected to be interdependent.

“The strategic plan also includes a description of research resources

essential to advancing these three research areas that [the] NIAID will develop, support, and provide for the scientific community,” wrote Dr. Erbelding and her coauthors.

The development plan comes 8

months after scientists from academia, industry, and government convened for the NIAID Pathway to a Universal Influenza Vaccine workshop to address knowledge gaps and strategy, which was summarized

last year in the journal *Immunity* (2017;47: 599-603). The scientists at the workshop developed criteria that would define a universal vaccine and decided that a universal vaccine for influenza should do three things: be

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risk of atrial fibrillation, compared with those without diabetes.

Similarly, the incidence of atrial fibrillation was reduced after uvulopalatopharyngoplasty but only in patients with hypertension or dyslipidemia and not in those with normal blood pressure or lipid levels.

“These differences in outcomes after UPPP are probably due to the different etiologies of cardiovascular disease,” the authors wrote. Limitations included the absences of polysomnography information and information on whether patients used other sleep apnea therapies, such as CPAP or a mandibular advancing device.

The study was supported by the Korean Society of Otorhinolaryngology Head and Neck Surgery.

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SOURCE: Lee H-M et al. *Sleep Med.* 2018 May;45:11-6.

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at least 75% effective against symptomatic influenza infection; protect against group I and II influenza A viruses; and have durable protections that lasts at least 1 year and preferably through multiple seasons.

“Clearly, a vaccine that would cover most or all seasonal strains of influenza and also provide protection during a pandemic is highly

desirable,” wrote Catharine I. Paules, MD, of the University of Maryland, Baltimore, and her coauthors in the workshop summary.

Dr. Fauci told MDedge News how “experts from all over the country addressed their thoughts and concerns with us last year [at the workshop], and now we have a development plan,” he said. “But the

next step will be doing the research and finding more resources. ... The work is yet to be done.”

The development plan was published amid an ongoing historic flu season.

Dr. Fauci noted that this season had particular circumstances that made it worse than normal. “I don’t think that, had we had this plan in

place a year ago, it would have had an impact on this flu season,” he said.

The authors reported no relevant financial conflicts and that the National Institutes of Health produced this plan.

SOURCE: Erbeling EJ et al. J Infect Dis. 2018 Feb 28. doi: 10.1093/infdis/jiy103.

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Let clinical scenario guide sarcoidosis treatment

BY MICHELE G. SULLIVAN

MDedge News

SANDESTIN, FLA. – Don't be a slave to imaging when evaluating the patient with sarcoidosis.

"Sometimes, the worst-looking patients [on imaging] have the best prognosis," Daniel Culver, DO, said at the annual Congress of Clinical Rheumatology. Patients with Löfgren's syndrome are a very good example

of this tenet, he said in an interview. Scans can look alarming, with multiple widespread granulomas. But Löfgren's is generally a benign condition, despite its threatening mien.

Instead of imaging, "Let two

things drive your decision to treat: danger to an organ, and quality of life," said Dr. Culver, a pulmonologist and director of the Sarcoidosis Center of Excellence at the Cleveland Clinic in Ohio; he is also president of the World Association for Sarcoidosis.

He agrees with a decision schema published in 2015 (*Clin Chest Med.* 2015;36[4]:751-67).

"Sometimes, the worst-looking patients [on imaging] have the best prognosis," said Daniel Culver, DO, of the Cleveland Clinic.

Six factors weigh in favor of treatment:

- Symptomatic disease.
- Impaired organ function.
- Disease endangering an organ.
- Progressive disease.
- Clear-cut disease activity.
- Low likelihood of remission.

These must be balanced – with patient input as the fulcrum – against five factors that favor conservative management:

- Minimal symptoms.
- Good organ function.
- Low risk of danger to organs.
- Inactive disease.
- Higher likelihood of remission.

The decision to embark on a treatment program, usually starting with a steroid-based regimen, can't be taken lightly, Dr. Culver said. A 2017 study showed that steroids pose a cumulative risk of toxicities for sarcoidosis patients (*Respir Med.* 2017 Nov;132:9-14). Patients who started steroids faced more than a doubling in the risk of a toxic side effect by 96 months when compared with those who didn't. But even short-term steroid use increased the risk of a toxicity, Dr. Culver said. The study noted that problems can begin to occur in as little as 1 month, at a cumulative dose as low as 1 g.

For patients who fall onto the "treat" side of the risk teeter-totter, Dr. Culver recommended starting with an initial course of prednisone at 20-30 mg daily for no more than 4 weeks. Responders can taper to less than 10 mg/day. Those who continue to do well can maintain low-dose prednisone for up to 12 months and then complete the taper. Patients who relapse can add an immune modulator (methotrexate,

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Three days of beta-lactam beat clinically stable CAP

BY MICHELE G. SULLIVAN

MDedge News

MADRID – Three days of beta-lactam therapy was just as effective as 8 days for clinically stable patients presenting with community-acquired pneumonia.

In a randomized, placebo-controlled trial, 15-day cure rates were

in practice might lead to reduced rates of multidrug-resistant bacteria, fewer adverse events, and surely lower costs.”

The French PTC Trial (Short Duration Treatment of Non-Severe Community-Acquired Pneumonia) randomized 310 patients (mean age, 73.5 years) to either short- or long-course treatment with a beta-lactam antibiotic. Patients were eligible for the study if they were admitted to the hospital for community-acquired pneumonia based on respiratory signs, fever of 38° C or higher, and evidence of new infiltrate on chest radiograph.

All patients were treated with 3 days of amoxicillin/clavulanic acid (Augmentin) or third-generation cephalosporin. Those who had responded clinically by day 3 entered the 5-day randomization period, receiving placebo or 5 more days of active therapy with the same agent.

Clinical requirements for randomization included being afebrile with stable heart and respiratory rate, a systolic blood pressure of at least 90 mm Hg, and oxygen saturation of at least 90%.

The primary endpoint was clinical cure at day 15: no fever, absence of or improvement in respiratory symptoms (dyspnea, cough, purulent sputum, and crackles), and no need for additional antibiotic treatment for any indication.

Secondary endpoints were cure at day 30, 30-day mortality, adverse events, length of stay, return to usual activities by day 30, and quality of life at day 30.

Many of the generally elderly patient cohort had comorbid illnesses, including diabetes (about 20%), chronic obstructive pulmonary disease (about 35%), and coronary insufficiency (about 14%). About 20% were active smokers. Less than 10% had gotten a pneumococcal vaccine in the past 5 years.

At admission, more than half of patients were dyspneic, 80% had

cough, and 39% had purulent sputum. The median PSI/PORT Score was 82.

After 3 days of treatment, clinical cure was not significantly different between the 3- and 8-day groups, either in the intent-to-treat analysis (69.9% vs. 61.2%) or in the per-protocol analysis (75.7% vs. 68.7%).

“Reducing treatment time now appears to be manageable and effective in a number of infectious diseases. [This] change in practice might lead to reduced rates of multidrug-resistant bacteria, fewer adverse events, and surely lower costs.”

Because the trial had closed days before the ECCMID meeting, only the primary endpoints were available for discussion, Dr. Dinh said. Investigators are analyzing the secondary endpoint data, which he said would be published at a later date.

Despite the positive results, Dr. Dinh cautioned against using the study as justification for a one-size-fits-all treatment for community-acquired pneumonia.

“Although I think we demonstrated that 3 days of treatment with beta-lactam is not inferior to 8 days, this cannot be imposed without regard to individual patient status,” he cautioned. Such a treatment paradigm would not be advisable for patients with moderately severe pneumonia, who were excluded from the study, or those with compromised immune systems.

Nor does Dr. Dinh expect wholesale clinical embracing of the encouraging results, which bolster the ever-accumulating data in favor of shorter courses of antibiotics for some infectious diseases.

“I think there is a chance that clinicians who normally treat for 9 or 10 days may now feel comfortable reducing to 7,” he said with a chuckle.

The French Ministry of Health sponsored the study. Dr. Dinh had no competing financial interests.

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Michele G. Sullivan/MDedge News

Dr. Aurélien Dinh

69.9% in patients who took 3 days of antibiotics and 61.2% in those who took 8 days – a nonsignificant difference, Aurélien Dinh, MD, said at the European Society of Clinical Microbiology and Infectious Diseases annual congress.

The French study was one of a series at the meeting demonstrating that, for some groups of patients, short-term antibiotic therapy is a viable – and probably healthy – alternative to the traditional longer courses, said Dr. Dinh of the University of Paris Hospital.

“Reducing treatment time now appears to be manageable and effective in a number of infectious diseases,” Dr. Dinh explained. “Although there are some limits, surely, this change

Continued from previous page

azathioprine, leflunomide, or mycophenolate).

Those who have an inadequate response to the initial prednisone course should then get an immune modulator. If they do well, that can be maintained; a second modulator can be brought on board if necessary.

For those who don't respond at all to the initial prednisone course,

it's necessary to proceed immediately to an immunosuppressive regimen to prevent irreversible fibrosis.

Dr. Culver noted associations with multiple pharmaceutical companies, but said none were relevant to his talk. A video interview with Dr. Culver is available on mdedge.com/chestphysician.

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Four-meter gait speed predicts mortality in IPF

BY DOUG BRUNK

MDedge News

SAN DIEGO – Among patients with idiopathic pulmonary fibrosis (IPF), an improvement in 4-meter gait speed with pulmonary rehabilitation is an independent predictor of all-cause mortality at 1 year, suggest results from a multicenter study presented at an international conference of the American Thoracic Society.

The authors of the study found that patients who improved their gait speed had a longer survival time. In all, 11% of patients died within 1 year of completing pulmonary rehabilitation.

“Mortality is an attractive endpoint in IPF clinical research but requires large sample sizes and long follow-up duration, making clinical trials expensive and challenging to undertake,” lead study author Claire M. Nolan, MSc, said at the conference. “Consequently, there is much interest in surrogate endpoints of mortality. In the elderly population, a lot of work has been done on performance measures, in particular the 4-meter gait test. It’s a simple test to do from the assessor’s perspective, because you just need a 4-meter corridor and a stopwatch. From the patient’s perspective, they only have to walk at their usual speed, making it feasible in most settings.”

The study by Ms. Nolan, a National Institute for Health Research fellow, and her associates, involved recruiting 90 IPF patients referred to three outpatient pulmonary rehabilitation programs in London. All patients underwent the following assessments before and after 8 weeks of pulmonary rehabilitation: spirometry, Medical Research Council dyspnea score; anthropometry, 4-meter gait speed, incremental shuttle walk

test, and King’s Brief Interstitial Lung Disease questionnaire. Ms. Nolan, a respiratory physiotherapist with the Harefield Pulmonary Rehabilitation and Muscle Research Group, Royal Brompton and Harefield NHS Foundation Trust, London, and her associates drew from national databases to obtain data on all-cause mortality 1 year following pulmonary rehabilitation.

“We also identified a cutpoint, so if patients improved their walking speed by 0.009 meters per second or above, that was associated with a longer survival time at 1 year (area under the curve of 0.76, for sensitivity of 69.6% and a specificity of 70%; *P* less than 0.01),” she said. “Among patients who achieved that cutpoint or exceeded it, only 5% of them died in the 1-year follow-up period, compared with 23% in the group that didn’t achieve that cutpoint. That’s quite a big difference, but this requires external validation in another population.”

To determine the 4-meter gait speed change cut-off that best discriminated between patients who died and survived, the investigators plotted receiver operating characteristic curves. For validation, they conducted a Kaplan-Meier analysis to assess time to death, with significance assessed via the log-rank test. Finally, they used a multivariate Cox proportional hazards model to characterize the relationship between 4-meter gait speed change and all-cause mortality, adjusting for independent predictors of mortality (age, previous respiratory hospitalizations in the past year, forced vital capacity percent predicted) and baseline 4-meter gait speed.

At baseline, 70% of the 90 patients were male, mean age was 74 years, mean forced vital capacity was 72.8% predicted, and mean

Medical Research Council dyspnea score was 3. In addition, mean body mass index was 27.2 kg/m², mean 4-meter gait speed was 0.92 meters per second, mean incremen-



Doug Brunk/MDedge News

“[It’s] plausible that change in gait speed may be a surrogate marker for, say, improvement in exercise capacity or health status. But the precise mechanism requires verification,” noted Claire M. Nolan.

tal shuttle walk test measurement was 271 meters, and mean King’s Brief Interstitial Lung Disease total score was 56.4. Following 8 weeks of pulmonary rehabilitation, the patients’ 4-meter gait speed improved significantly by a mean of 0.15 meters per second (*P* less than .001). All other variables also improved significantly, with the exception of forced vital capacity.

In an interview, Ms. Nolan characterized the results as “one piece of the puzzle in answering whether 4-meter gait speed is a useful test for clinicians and researchers. It needs to be taken in the context of 4-meter gait speed in other populations as well as with what we’re finding in patients with IPF. We know that this test is reliable, valid, and responsive

to treatment. Now we know that it has predictive capacity as well.”

During her presentation, she cited potential reasons why change in gait speed is associated with survival. “Firstly, gait speed has been described as a clinical indicator of multisystem well-being and the ‘sixth vital sign,’” she said. “Walking ability and speed rely on multiple factors and the integration of many systems, cardiovascular and otherwise. We know that pulmonary rehab has multiple benefits and improves these systems, and it’s plausible that change in gait speed may be a surrogate marker for, say, improvement in exercise capacity or health status. But the precise mechanism requires verification.”

Ms. Nolan acknowledged certain limitations of the study, including the fact that contemporaneous measurement of full lung function testing and pulmonary hypertension diagnosis were not available at the time of the study. “Therefore, we were unable to account for [diffusing capacity of the lung for carbon monoxide] and pulmonary hypertension diagnosis,” she said. “Secondly, we were unable to identify the precise cause of death from the national database of harm and care records, but this corroborates previous data which suggest that it’s difficult to reliably discern if a death is IPF- or non-IPF related. Lastly, we know that the benefits of pulmonary rehab experienced by IPF patients tend to wane after 6 months. It would be interesting to compare the short-term improvements in gait speed that we observed to more sustained improvements, to identify whether this impacts prognostability.”

National Institute for Health Research funded the study.

Ms. Nolan reported having no financial disclosures.

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New ILD diagnostic test now available

BY KATIE WAGNER LENNON

MDedge News

A 190-gene test for interstitial lung diseases (ILD), including idiopathic pulmonary fibrosis (IPF), is now available through an early-access program.

IPF can be difficult to distinguish from other ILDs, S. Samuel Weigt, MD, of the University of California, Los Angeles, and director of UCLA Health’s Interstitial Lung Disease Center, said in a statement from Veracyte, the company marketing the test.

In fact, more than half of patients with ILDs were

misdiagnosed at least once, according to a study published by the Pulmonary Fibrosis Foundation.

The new test, known as the Envisia Genomic Classifier, combines RNA sequencing and machine learning to help physicians differentiate IPF from ILDs in samples obtained through transbronchial biopsy. Its specificity and sensitivity for detecting the genomic pattern of usual interstitial pneumonia, are 88% and 70%, respectively, according to the Veracyte statement.

“Multiple studies have demonstrated that the Envisia Genomic Classifier supports more confident IPF diagnosis and optimal patient manage-

ment,” Bonnie Anderson, chairman and CEO of Veracyte, said in the statement.

A benefit of the new test is that its use does not require patients to undergo risky, expensive surgery, which may not even be possible for some patients, noted Dr. Weigt. “We are pleased to be one of the few medical facilities in the country to have access to this breakthrough technology.”

More information about the Envisia Genomic Classifier and how to enter the early-access program can be obtained through emailing Veracyte at support@veracyte.com or by calling 844-464-5864.

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Ivacaftor reduced hospitalizations in CF

BY MADHU RAJARAMAN

MDedge News

Ivacaftor, a therapy that targets the G551D CFTR gene mutation to treat cystic fibrosis, significantly reduced hospital admission rates in patients with cystic fibrosis with a variety of mutations, according to results published May 7 in *Health Affairs*.

The study involved 143 patients being treated with ivacaftor (Kalydeco), which is manufactured for Vertex Pharmaceuticals, between February 2012 and February 2015. In 2014, the FDA expanded its approval for the use of ivacaftor by cystic fibrosis patients to include nine additional mutations, and patients with these mutations were included in this study.

The overall rate of inpatient admissions dropped by 55%, and cystic fibrosis–related admissions rates fell by 78% (*P* less than .0001) between the period 12 months before treatment and 12 months after the first filled prescription, wrote Lisa B. Feng and her coauthors.

Ms. Feng, who is senior director for policy and advocacy at the

tion. For each period, the numbers and percentages of patients hospitalized were calculated, for any reason and for cystic fibrosis–related reasons. Hospitalization rates also were calculated as numbers of admissions per

person-year. Data were analyzed for two subcohorts: the 86 patients who started using ivacaftor between Feb. 6, 2012, and Feb. 21, 2014, under the initial Food and Drug Administration label; and the 57 patients who

initiated use between Feb. 22, 2014, and Dec. 31, 2015, under the expanded FDA label, which included nine additional genetic mutations.

Of the 143 patients who had filled

Declines in hospital admissions also were similar between the initial label and the expanded FDA label groups, with declines in overall admissions of 59% and 57%, respectively. Hospital admissions related to cystic fibrosis decreased by 78%.

Cystic Fibrosis Foundation and her colleagues analyzed administrative claims data from the Truven Health Analytics Market Scan Commercial Research Database. All of the claims were for patients from the United States with employer-sponsored insurance plans. Eligibility criteria included an ICD-9 CM diagnosis of cystic fibrosis on one or more inpatient claims or two or more outpatient claims at least 30 days apart, a prescription claim for ivacaftor monotherapy, being at least 6 years of age at the time of the first filled prescription, and 12 months of continuous enrollment before and after the first filled prescription.

The “pre-ivacaftor” period was defined as the 12 months before the first filled prescription. The “post-ivacaftor” period was defined as the 12 months after the first filled prescrip-

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RSV immunoprophylaxis doesn't prevent asthma

BY CATHERINE COOPER NELLIST

MDEdge News

Respiratory syncytial virus immunoprophylaxis in premature

infants does not appear to prevent asthma at age 6 years, reported Nienke M. Scheltema, MD, of Wilhelmina Children's Hospital, Utrecht, the Netherlands, and associates.

In a study of 395 otherwise

healthy premature infants who were randomized to receive palivizumab for respiratory syncytial virus (RSV) immunoprophylaxis or placebo and followed for 6 years, 14% of the 199 infants in the RSV prevention

group had parent-reported asthma, compared with 24% of the 196 in the placebo group (absolute risk reduction, 9.9%). This was explained mostly by differences in infrequent wheeze, the researchers said. However, physician-diagnosed asthma in the past 12 months was not significantly different between the two groups at 6 years: 10.3% in the RSV prevention group and 9.9% in the placebo group.

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SOURCE: Scheltema NM et al. Lancet. 2018 Feb 27. doi: 10.1016/S2213-2600(18)30055-9.

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Continued from previous page

prescriptions for ivacaftor, 63% were aged 18 years or older. The rate of overall inpatient admissions decreased 55%, from 0.57 admissions per person-year in the pre-ivacaftor period to 0.26 admissions per person-year in the post-ivacaftor period.

The declines in hospital admissions also were similar between the initial label and the expanded FDA label groups, with declines in overall admissions of 59% and 57%, respectively.

Hospital admissions related to cystic fibrosis also decreased significantly, by 78%. Admissions with principal diagnosis codes for cystic fibrosis decreased from 42 in the preprescription period, to 8 after filling the prescription. Rates per person per year decreased by 82% in patients aged 6-17 years and 80% among adults aged 18 years and older. Additionally, patients who filled at least 10 prescriptions during the study period experienced a 68% reduction in inpatient admissions, compared with 45% for those with 3-9 prescriptions filled.

Ivacaftor also was associated with 60% lower per-person inpatient spending overall, with a greater proportional reduction in hospital costs for adults (68%) than for children (45%), and an absolute per-person reduction of \$10,567.

“To deliver the right care to the right patient,” the authors concluded, “cystic fibrosis care must continue to account for other aspects unique to individuals such as environment, physiology, patients’ preferences, and lifestyle.”

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SOURCE: Feng LB et al. Health Aff. 2018 May 8. doi: 10.1377/hlthaff.2017.1554.

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As-needed budesonide-formoterol prevented exacerbations in mild asthma

BY AMY KARON

MDedge News

Formoterol plus budesonide prevented exacerbations when inhaled as needed by patients with mild persistent asthma, according to the results of two large, double-blind, 52-week, randomized phase 3 trials.

In the SYGMA1 (Symbicort Given as Needed in Mild Asthma) trial, the regimen outperformed as-needed terbutaline in terms of asthma control (34.4% vs. 31.1% of weeks; $P = .046$) and exacerbations (rate ratio, 0.36; 95% confidence interval, 0.27-0.49). In the SYGMA2 study, it was noninferior to twice-daily budesonide for preventing severe exacerbations (RR, 0.97; upper one-sided 95% CI, 1.16). The findings were published in two reports in the *New England Journal of Medicine*.

Asthma often is undertreated because many patients adhere poorly to maintenance glucocorticoids, noted Paul M. O'Byrne, MD, of McMaster University in Hamilton, Ont., and his associates from SYGMA1 (NCT02149199). Instead, patients often rely on short-acting beta₂-agonists for symptom control, but these drugs don't stop exacerbations or treat underlying inflammation. "One potential strategy to address these issues is the use of a combination of a fast-acting beta₂-agonist and an inhaled glucocorticoid taken only on an as-needed basis," the researchers wrote.

Accordingly, they randomly assigned 3,849 patients aged 12 years and up who had mild persistent asthma (mean forced expiratory volume in 1 second [FEV₁] before bronchodilator use, 84% of predicted value) to receive one of three regimens: twice-daily placebo plus terbutaline (0.5 mg) used as needed, twice-daily placebo plus budesonide-formoterol (200 mcg of budesonide and 6 mcg of formoterol) used as needed, or maintenance twice-daily budesonide (200 mcg) plus as-needed terbutaline (0.5 mg), all for 52 weeks.

In the final analysis of 3,836 patients, annual rates of severe exacerbations were 0.20 with terbutaline, significantly worse than with budesonide-formoterol (0.07) or maintenance budesonide (0.09). Using budesonide-formoterol (Symbicort) as needed improved the odds



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of having well-controlled asthma by about 14%, when compared with using terbutaline as needed (odds ratio, 1.14; 95% CI, 1.00-1.30; $P = .046$).

Although maintenance budesonide controlled asthma best (44.4% of weeks; OR vs. budesonide-formoterol, 0.64; 95% CI, 0.57-0.73), 21% of patients did not adhere to it, the researchers reported. "Patients are often more concerned [than their health care providers] about adverse effects of inhaled glucocorticoids, even when low inhaled doses are used," they wrote. Notably, the budesonide-formoterol as-needed group received a median daily dose of only 57 mcg inhaled glucocorticoid, 17% of that received by the budesonide maintenance group.

In SYGMA2 (NCT02224157), 4,215 patients with mild persistent asthma aged 12 years and up were randomly assigned to receive either twice-daily placebo plus as-needed budesonide-formoterol or twice-daily maintenance budesonide plus as-needed terbutaline. Doses were the same as in the SYGMA1 trial. The regimens resembled each other in terms of severe exacerbations (annualized rates, 0.11 and 0.12, respectively) and time to first exacerbation, even though budesonide-formoterol patients received a 75% lower median daily dose of inhaled glucocorticoid, reported Eric D. Bateman, MD, of the University of Cape Town, South Africa, and his associates.

Results from both trials suggested that as-needed budesonide-formoterol provided better symptom control than did terbutaline but worse symptom control than did twice-daily budesonide. In SYGMA1, the change from baseline

on the Asthma Control Questionnaire-5 (ACQ-5) favored budesonide-formoterol over terbutaline by an average of 0.15 units and similarly favored twice-daily budesonide over budesonide-formoterol. In SYGMA2, the budesonide maintenance group averaged 0.11 units greater improvement on the ACQ-5 and 0.10 better improvement on the standardized Asthma Quality of Life Question-

naire, compared with as-needed budesonide-formoterol recipients.

Finally, lung function assessments favored as-needed budesonide-formoterol over terbutaline but not over maintenance budesonide. SYGMA1, mean changes (from baseline) in FEV₁ before bronchodilator use were 11.2 mL with terbutaline, 65.0 mL with budesonide-formoterol, and 119.3 mL with maintenance budesonide. In SYGMA2, these values were 104 mL with budesonide-formoterol and 136.6 mL with maintenance budesonide.

AstraZeneca provided funding. For SYGMA1, Dr. Byrne disclosed ties to AstraZeneca, Novartis, GlaxoSmithKline, Medimmune, and Genentech. For SYGMA2, Dr. Bateman disclosed ties to AstraZeneca, Novartis, Cipla, Vectura, Boehringer Ingelheim, and a number of other pharmaceutical companies.

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SOURCES: O'Byrne PM et al. *N Engl J Med*. 2018;378(20):1865-76. Bateman ED et al. *N Engl J Med*. 2018;378(20):1877-87.

VIEW ON THE NEWS

'Two out of three ain't bad'

In the SYGMA1 and SYGMA2 trials, as-needed budesonide-formoterol (Symbicort) prevented exacerbations and loss of lung function, the two worst outcomes of poorly controlled asthma, concluded Stephen C. Lazarus, MD, FCCP, in an editorial accompanying the studies in the *New England Journal of Medicine*.

"As-needed treatment was similar, or at least noninferior, to regular maintenance therapy with inhaled glucocorticoids with regard to the prevention of exacerbations, and exacerbations are the main contributor to loss of lung function, death, and cost," wrote Dr. Lazarus.

Patients typically received only 17%-25% as much inhaled glucocorticoid as did those on maintenance budesonide, which would help prevent side effects and would make the regimen more acceptable to "glucocorticoid-averse patients," he added. Another benefit to patients with mild persistent asthma using as-needed budesonide-formoterol instead of inhaled glucocorticoid maintenance therapy is that it would result in nearly \$1 billion in cost savings in the United States yearly.

Budesonide-formoterol did not control symptoms as well as did maintenance budesonide, but patients might accept "occasional mild symptoms and inhaler use if it [freed] them from daily use of inhaled glucocorticoids while preventing loss of lung function and exacerbations," he concluded. "For these patients, 'Two out of three ain't bad!'"

Dr. Lazarus is in the department of medicine and at the Cardiovascular Research Institute, University of California, San Francisco. He reported having no conflicts of interest. This comments are from his editorial (*N Engl J Med*. 2018 May 17. doi: 10.1056/NEJMe1802680).

In PAH trials, clinical worsening risk rose with time

BY ANDREW D. BOWSER

MDedge News

FROM THE JOURNAL CHEST® ■ Current clinical trials evaluating combination therapy for pulmonary artery

hypertension (PAH) may be longer than what is needed to demonstrate treatment benefit, results of a recent meta-analysis suggest.

In PAH trials of combination therapy, the absolute risk reduction

of clinical worsening beyond 6-12 months was relatively constant, according to results of the study published in the May issue of the journal *Chest*®.

That finding “questions the

requirement for longer-term event-driven trials beyond that duration in an orphan disease such as PAH,” wrote investigator Annie C. Lajoie, MD, of the Pulmonary Hypertension Research Group, Quebec

VIEW ON THE NEWS

Long-term follow-up questioned

Results of this study by Lajoie and colleagues question the need for long-term follow-up beyond 12 months in clinical trials of combination therapy in pulmonary arterial hypertension (PAH), according to authors of an editorial.

“While very short term follow-up trials fail to detect important patient-centered outcomes and adverse events, very long term follow-up may impact trial feasibility without improving power to detect meaningful efficacy,” wrote Rogerio Souza, MD, PhD, and Juliana C. Ferreira, MD, PhD.

The study also shows that relative risk of worsening is influenced by the duration of the trial. That suggests looking at relative risk in isolation may not be the optimal approach to evaluating the benefits of combination therapies for PAH, the authors added.

These findings, collectively, should inform the development of future clinical trials, they said. In particular, those trials could evaluate multiple markers of PAH improvement and a “time-limited observation” of morbidity events.

That “potential alternative” approach could make future studies more feasible, without compromising the robustness of findings, Dr. Souza and Dr. Ferreira said in their editorial.

Rogerio Souza, MD, PhD, and Juliana C. Ferreira, MD, PhD, are with the University of São Paulo, pulmonary division.

*These comments are derived from their editorial appearing in the journal *Chest*®. Dr. Ferreira reported speaker fees from Medtronic, and Dr. Souza reported speaker and consultancy fees from Actelion, Bayer, GSK, and Pfizer.*

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City, and her coauthors.

The meta-analysis by Dr. Lajoie and her colleagues included 3,801 patients enrolled in 1 of 15 previously published randomized clinical trials. Of those trials, four were long-term, event-driven studies, with a mean duration of 87 weeks, while the remainder were shorter studies with a mean duration of 15 weeks.



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For the long-term, event-driven trials, the mean number needed to treat (NNT) was 17.4 at week 16, gradually decreasing to 8.8 at 52 weeks of follow-up, remaining stable after that, according to investigators.

Consistent with that finding, the mean relative risk of clinical worsening was 0.38 at 16 weeks, and similarly, 0.41 at 26 weeks, investiga-

tors reported. After that, the relative risk progressively increased to 0.54 at 52 weeks and 0.68 at 104 weeks.

Looking at all trials combined, Dr. Lajoie and her colleagues observed that longer trial duration had a positive correlation with relative risk of clinical worsening ($P = .0002$).

Pragmatically, these results raise

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the possibility that PAH combination therapy trials could be shorter in duration. Some recent event-driven studies have lasted up to 6 years, with patients on treatment for about 2 of those years, investigators noted.

“In the context of an orphan disease with limited and competing recruitment for trials and the rapid-

ly changing treatment paradigm in PAH, the optimal duration of future trials should be revisited,” Dr. Lajoie and her colleagues wrote in a discussion of their findings.

Longer trial duration had a positive correlation with relative risk of clinical worsening.

They also cautioned that NNT, a measure of how many patient treatments are needed to prevent one additional adverse event, could be “misleading” despite its value

as a simple measure of treatment impact.

Dr. Lajoie’s coauthors had disclosures related to Actelion Pharmaceuticals, Bayer, and GlaxoSmithKline, among others.
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SOURCE: Lajoie AC et al. Chest. 2017 May;153(5):1142-52.

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Stroke-smoking link is dose-dependent in young men

BY JIM KLING

MDedge News

In men younger than 50 years, even just a reduction in the number of cigarettes smoked

may decrease the risk of ischemic stroke, according to a population-based, case-control study.

The odds ratio for a stroke was 1.21 for men who smoked fewer than 11 cigarettes per day, compared

with nonsmokers, and 5.24 for those who smoked 40 or more per day, reported Janina Markidan and her coinvestigators in *Stroke*.

A prior study showed a similar relationship in young women, but

the researchers decided to conduct a follow-up study in men in order to eliminate hormonal confounders (*Stroke*. 2008 Sep;39[9]:2439-43).

Ms. Markidan and her colleagues used data from the Stroke Prevention in Young Men Study, which recruited 615 men who had experienced a stroke in the previous 3 years, and compared these men with 530 age-, ethnicity-, and geography-matched controls.

There were some statistically significant differences in the two populations: Cases had lower levels of education and had greater incidences of hypertension, diabetes, myocardial infarction, angina, and obesity (all $P < .05$).

Current smokers were identified as those who had smoked more than 100 cigarettes in their lifetime and who had smoked a cigarette in the 30 days preceding the stroke. Never smokers were those who had smoked fewer than 100 cigarettes in their lifetime or who had never smoked five packs.

Compared with never smokers, current smokers had an odds ratio for stroke of 1.88 (95% confidence interval, 1.44-2.44). When the researchers stratified smokers by the number of cigarettes smoked, the stroke risk appeared to be dose dependent in the fully adjusted models: The OR for 1-10 cigarettes/day was 1.21 (95% CI, 0.83-1.77), 1.64 for 11-20 cigarettes/day (95% CI, 1.10-2.43), 3.51 for 21-39 cigarettes/day (95% CI, 1.65-7.45), and 5.24 for 40 or more cigarettes/day (95% CI, 1.90-14.42).

The study cannot prove causation and did not include smoking of nontobacco products, alcohol consumption, or physical activity.

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SOURCE: Markidan J et al. *Stroke*. 2018 May;49(5):1276-8.

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ED visits higher among pediatric asthma patients with comorbid depression, anxiety

BY DOUG BRUNK

MDedge News

TORONTO – Children with asthma who have a comorbid diagnosis of anxiety or depression are significantly more likely to make asthma-related visits to the emergency department, compared with their peers who do not have a mental health condition, results from a large administrative data analysis showed.

“There has been a fair bit of research on how comorbid mental health conditions can affect health care utilization for asthma in adults, but few studies have examined how comorbid mental health conditions like anxiety or depression can affect children with asthma,” one of the study authors, Caroline Neel, said in an interview in advance of the Pediatric Academic Societies meeting.

In an effort to assess whether anxiety or depression is associated with asthma-related ED usage in pediatric patients, Ms. Neel, a clinical research coordinator in the department of pediatrics at the University of California, San Francisco, and her associates evaluated data from the Massachusetts All Payer Claims Database for 2014-2015. They used the technical specifications from the Pediatric Quality Measures Program

to measure the rate of asthma-related ED visits. This measure identifies patients aged 2-21 years with asthma using ICD 9 and 10 codes and tracks ED utilization over the measurement year. Next, the researchers conducted univariate and multivariate analyses to assess the relationship between ED visit rate and an established diagnosis of comorbid anxiety or depression.



“We were surprised to see that anxiety and depression seemed to increase asthma emergency department visits as much as other medical chronic illnesses,” said Caroline Neel, a clinical research coordinator.

In all, the researchers identified 71,326 patients with asthma, with an overall rate of 16.3 ED visits per 100 child-years. Among these, children with a diagnosis of depression had significantly higher rates of ED visits (21.5 visits per 100 child-years; P less than .01), as did those with a diagnosis of anxiety (19.5 ED visits per 100 child-years; P less than .01). Being enrolled in a Medicaid managed care plan or Medicaid fee-for-service plan also increased the rates of asthma-related ED visits (20.3

and 21.5 ED visits per 100 child-years, respectively; P less than .01 for both associations.)

“We were surprised to see that anxiety and depression seemed to increase asthma emergency department visits as much as other medical chronic illnesses like cystic fibrosis or sickle cell disease, and that kids on Medicaid, who tend to be our poorer kids, also had an independent risk of going to the emergency department,” Ms. Neel said. “Having Medicaid as well as anxiety or depression were independently related to going to the emergency room for asthma, so the study suggests that some of our highest-risk kids for asthma have multiple

different contributors to getting sick and needing to go to the emergency room for an asthma attack.”

She acknowledged certain limitations of the analysis, including its reliance on administrative claims data to identify whether or not children had a diagnosis of anxiety or depression. “This doesn’t necessarily identify all the kids who may have these mental health conditions, since sometimes providers are less likely to document a diagnosis of a mental health conditions for children,”

VIEW ON THE NEWS

Susan Millard, MD, FCCP, comments:

This is a robust study and I am not surprised at all. Adding in the information about pediatric patients who have

Medicaid and anxiety or depression is also not surprising. This is why the Cystic Fibrosis Foundation now recommends that adolescent CF patients should be screened at every routine visit to a CF clinic. Maybe we should do the same for our asthma patients.



she said. “However, we still saw a significant association between a comorbid mental health condition and emergency department use for asthma, despite the potential that mental health conditions may have been under reported.”

The study’s senior author was Naomi Bardach, MD. The researchers reported having no financial disclosures.

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Interferon-gamma release assay trumps tuberculin skin test in school-aged children

BY HEIDI SPLETE

MDedge News

The interferon-gamma release assay (IGRA) was significantly more sensitive than a tuberculin skin test (TST) as an adjunct tuberculosis diagnosis of children aged 5 years and older, according to data from a population-based study of 778 cases.

VIEW ON THE NEWS

Susan Millard, MD, FCCP, comments:

Our pediatric infectious disease colleagues are using the IGRA test for the specific age groups cited in this article. The TB skin test has such variability in regards to how it is placed and read, so this is a welcomed method for the diagnosis of tuberculosis at least in many parts of the United States.

IGRAs have shown greater specificity than do TSTs, but data on their sensitivity to TB in children are limited, wrote Alexander W. Kay, MD, of the California Department of Public Health and his colleagues in a study published in Pediatrics.

The researchers reviewed data on children and teens aged 18 years and younger from the California TB registry for 2010-2015. Of 778 reported cases of TB, 360 were laboratory confirmed, and 95 children had both an IGRA and TST with complete results. Of these, IGRA was significantly more sensitive than TST (96% vs. 83%) in children aged 5-18 years. The sensitivities of IGRA and TST were similar in children aged 2-4 years (91% for both) and not significantly different in children younger than 2 years (80% vs. 87%, respectively).

Children younger than 1 year of age and those with CNS disease were significantly more likely to have indeterminate IGRA results, the researchers noted.

The study results were limited by the use

of mainly enzyme-linked immunosorbent assay-based IGRA, which limited the data on enzyme-linked immunospot tests, the researchers said. The findings also were limited by the small number of children younger than 5 years.

However, the study is the largest North American analysis of IGRA in children, and based on the findings, “we argue that an IGRA should be considered the test of choice when evaluating children 5-18 years old for TB disease in high-resource, low-TB burden settings,” Dr. Kay and his associates wrote.

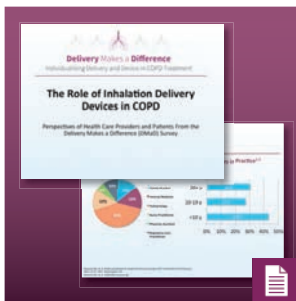
The study was funded by the Centers for Disease Control and Prevention. Coauthor Shamim Islam, MD, disclosed financial support from Qiagen, maker of the QuantiFERON test. Dr. Kay and the other investigators had no financial conflicts to disclose.

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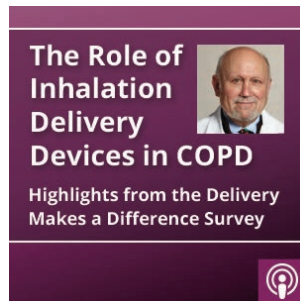
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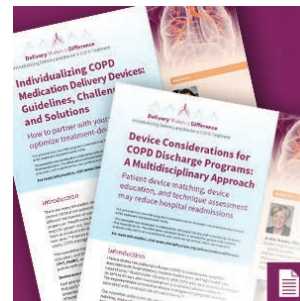
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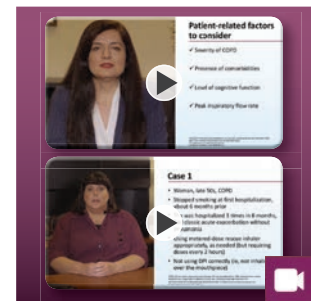
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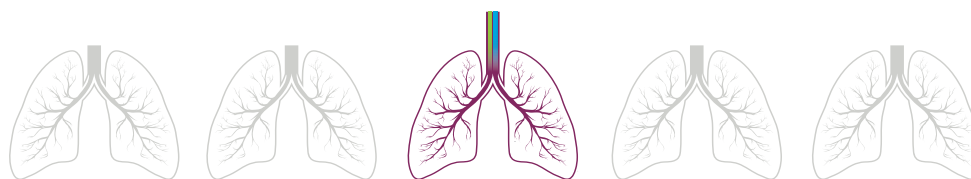
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Lung cancer palliative care may reduce suicides

BY KATIE WAGNER LENNON

MDedge News

Veterans with advanced-stage lung cancer who received palliative care were less likely to

commit suicide, according to new research presented at the international conference of the American Thoracic Society.

“Suicide is a significant national public health problem, especially

among lung cancer patients and among veterans,” said lead author, Donald R. Sullivan, MD, of the division of pulmonary and critical care medicine at Oregon Health & Science University and a member of

the OHSU Knight Cancer Institute, in a statement.

Dr. Sullivan, who also is a core investigator at the Center to Improve Veteran Involvement in Care at Portland Veterans Affairs, and his colleagues analyzed data on patients in the VA Healthcare System who were diagnosed with advanced-stage lung cancer (IIIB & IV) from January 2007 to December 2013.

The investigators found that veterans who experienced at least one “palliative care encounter” after

The suicide rate for the advanced stage lung cancer patients was 200/100,000 patient-years, five times higher than for all veterans using VA health care.

learning they had lung cancer were 82% less likely to die by suicide (odds ratio, 0.18; 95% confidence interval, 0.07-0.46; *P* less than .001), when compared with veterans who were diagnosed with lung cancer but did not receive palliative care.

The suicide rate for the advanced-stage lung cancer patients was 200/100,000 patient-years, which was more than five times higher than the suicide rate – adjusted for age, sex, and year – for all veterans using VA health care (37.5/100,000), according to the study abstract.

Of the 20,900 lung cancer patients analyzed, 30 committed suicide. Only six (20%) of the patients who died by suicide had received palliative care. Overall, most patients (18,192 or 87%) in the registry died of lung cancer. Other cancers, heart disease, and chronic obstructive pulmonary disease were some of the other common causes of death for the lung cancer patients, according to the abstract.

While several medical societies recommend palliative care for all patients with advanced-stage lung cancer, there is a gap between those recommendations and practice, noted Dr. Sullivan. “There are many barriers to palliative care, and unfortunately, some are related to clinician referrals. Not all doctors are aware of the benefits of palliative care,” he said in the statement.

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Delay of NSCLC surgery can lead to worse prognosis

BY RANDY DOTINGA

MDedge News

SAN DIEGO – A study suggests a delay of surgery in certain cases of non-small cell lung cancer (NSCLC) can mean patients will be upstaged and consequently have worse prognoses.

“There is significant upstaging with time from completion of clinical staging to surgical resection, with a 4% increase of upstaging per week for the overall study population,” said study coauthor Harmik J. Soukiasian, MD, FACS, of Cedars-Sinai Medical Center, Los Angeles, in an interview. “Upstaging impacts lung cancer prognosis as more advanced stages portend to a poorer prognosis.”

Dr. Soukiasian presented the study findings at the annual meeting of the American Association for Thoracic Surgery.

An estimated 80%-85% of lung cancer patients have NSCLC, according to the American Cancer

Society, and Dr. Soukiasian said surgery offers a chance at a cure for those diagnosed at stage I.

“National Cancer Comprehensive Network (NCCN) Guidelines recommend surgery within 8 weeks



“Although these guidelines are ... widely adopted, our study performs a more granular analysis,” said Dr. Harmik J. Soukiasian.

of completed clinical staging for NSCLC to limit cancer progression or upstaging,” Dr. Soukiasian said. “Although these guidelines are well established and widely adopted, our study performs a more granular analysis, studying time as a predictor of upstaging for those patients diagnosed with stage I NSCLC.”

For the new study, Dr. Soukiasian and colleagues tracked 52,406 pa-

tients in a cancer database who had stage I NSCLC but had not undergone preoperative chemotherapy. The researchers tracked their clinical stages for up to 12 weeks from initial staging.

Researchers found that, while staging levels rose with each successive week, just 25% of patients underwent surgery by 1 week, and only 79% had surgery in accordance with NSCLC guidelines by week 8. At 12 weeks, 9% had still not undergone surgery.

Upstaging was common: 22% at 1 week, 32% after 8 weeks, and 33% after 12 weeks.

“We demonstrate that patients diagnosed with stage I NSCLC benefit from surgery sooner than the 8-week window recommended by the NCCN guidelines,” Dr. Soukiasian said. “Exclusive of the rate of progression and in addition to time to surgery, our study also demonstrated academic centers, higher lymph node yield during surgery, and left-sided tumors to be inde-

pendent predictors of upstaging.”

The study design doesn't provide insight into why surgery is often delayed. However, “we can theorize factors associated with delays to surgery may be due to patient factors (personal scheduling, availability of support systems, etc.), delays in follow-up, operating room availability or scheduling, and issues with insurance approval,” Dr. Soukiasian said.

In his presentation, Dr. Soukiasian emphasized the role of the mediastinum. “Given the clinical impact of stage III disease, we analyzed upstaging rates of stage I NSCLC to stage IIIA and revealed a 1.3% increase per week of upstaging specifically to stage IIIA. Additionally, almost 5% of patients initially diagnosed with stage I NSCLC upstaged to IIIA disease. The significant rate of upstaging to IIIA disease makes the case for more accurate and aggressive mediastinal staging prior to surgical resection.”

No disclosures were reported.

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Nivolumab shows promise in early-stage resectable NSCLC

BY AMY KARON

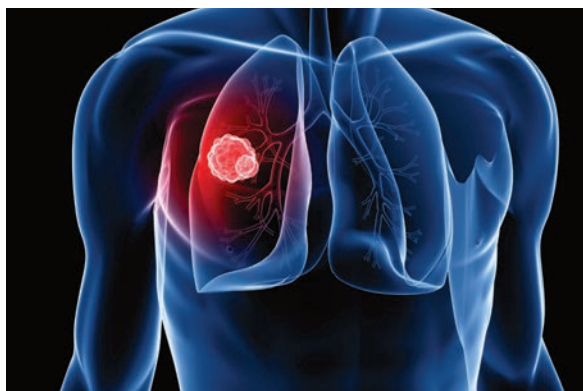
MDedge News

Noadjuvant nivolumab did not delay surgery and produced at least 90% tumor regression in nearly half of early-stage, resectable non-small cell lung cancers (NSCLC), according to the results of a 21-patient pilot trial.

Eighty percent of patients were alive and recurrence free a year after surgery, said Patrick M. Forde, MBBCh, and his colleagues from Johns Hopkins University, Baltimore. The only grade 3 or higher adverse event was treatment-related pneumonia, which did not prevent surgery. The findings were reported at the annual meeting of the American Association for Cancer Research and simultaneously in the *New England Journal of Medicine*.

Nivolumab targets the programmed cell death 1 (PD-1) pathway and is approved in several tumor types, including advanced NSCLC that has progressed despite platinum-based or epidermal growth factor receptor or anaplastic lymphoma kinase-targeted therapy. That approval was based on the CHECKMATE-057 trial, in which nivolumab significantly outperformed docetaxel in metastatic NSCLC (median overall survival, 12.2 vs. 9.4 months; $P = .002$). However, programmed cell death 1 inhibition in resectable NSCLC remained unexplored, Dr. Forde and his colleagues noted.

For the study (NCT02259621), 21 patients with treatment-naïve, stage I, II, or III NSCLC received two preoperative doses of nivolumab (3 mg/kg) 2 weeks apart, with surgery timed for 4 weeks after the first dose. In all, 62% of patients had adenocarcinoma, 81% had stage II or IIIA



SEBASTIAN KAULTZKI/THINKSTOCK

disease, and 86% were current or former smokers. Patients were followed for a median of 12 months after surgery (range, 0.8-19.7 months), and the researchers assessed safety, tumor response, programmed death ligand 1 mutational burden, and T-cell response.

Among 20 patients with evaluable resected primary tumors, nine (45%) showed a major pathologic response, defined as having 10% or fewer residual viable tumor cells. Twelve-month, recurrence-free survival was 83% (95% confidence interval, 66%-100%). The three progressors included one patient with 75% residual tumor at resection who subsequently developed a brain lesion, a patient with 5% residual tumor at resection who developed mediastinal lymph node recurrence, and a patient with 80% residual tumor at resection. The first two patients had durable responses to stereotactic radiotherapy or chemoradiotherapy, while the third patient developed fatal distal metastatic disease.

Sequencing of 11 completely resected tumors

linked major pathologic response with higher tumor mutational burden ($P = .01$). Mutational burden did not correlate with tumor programmed death ligand 1 expression. Deep sequencing of T-cell receptor-beta chain CDR3 regions also correlated major pathologic response with increased clonality of tumor-infiltrating T-cell clones that also expanded into peripheral blood. “Many of these clones were not detected in peripheral blood before treatment,” the investigators wrote.

In all, five (23%) patients developed treatment-related adverse events, and many developed more than one side effect. Grade 1-2 anorexia, taste distortion, vomiting, and diarrhea were most common, with isolated cases of grade 1-2 fever, infusion reaction, abdominal pain, abnormal liver function, dry skin, and delirium. The case of grade 3 pneumonia developed after the first dose of nivolumab.

The funders included Cancer Research Institute-Standard Up 2 Cancer; Johns Hopkins Bloomberg-Kimmel Institute for Cancer Immunotherapy; Bristol-Myers Squibb; International Immunology Network, LUNgevity Foundation; International Association for the Study of Lung Cancer; and Lung Cancer Foundation of America. Bristol-Myers Squibb makes nivolumab and supplied the study drug. Dr. Forde disclosed study grant support from Bristol-Myers Squibb, AbbVie, and other pharmaceutical companies outside the submitted work.

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SOURCE: Forde PM. AACR Annual Meeting 2018. Forde PM et al. *N Engl J Med*. 2018 Apr 16. doi: 10.1056/NEJMoa1716078.

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LUNG CANCER

Malignant pleural mesothelioma guidelines often ignored

BY RANDY DOTINGA

MDedge News

SAN DIEGO – National guidelines for the treatment of malignant pleural mesothelioma (MPM) often are not followed, a new study showed, with fewer than a third of patients receiving cancer-directed surgery.

Another 32% received no treatment, although that didn't seem to have an impact on median months of survival.

Still, “there can be a wide variation in median survival time, depending on clinical factors and tumor characteristics,” said study coauthor Harmik Soukiasian, MD, of Cedars-Sinai Medical Center, Los Angeles, at the annual meeting of the American Association for Thoracic Surgery. “Given the variation in prognosis, it is quite astonishing that over 30% of MPM patients are not receiving any form of treatment. As clinicians armed with these data, we need to investigate why that is.”

MPM, a rare cancer, is mainly linked to asbestos exposure. “MPM is almost always a fatal disease, and the prognosis can only be modestly influenced by oncological treatments,” according to the authors of guidelines released in 2013. “The diagnostic process can be complex, with highly specialized advice frequently required to arrive at a definite diagnosis. Treatment varies from therapeutic nihilism to radical combined-modality treatment approaches” (J Thorac Dis. 2013 Dec;5[6]:E254-307).

Surgical resection is a controversial treatment for MPM, Dr. Soukiasian said. It is “based on the principle of macroscopic resection of solid tumor with adjuvant therapy to treat micrometastatic disease,” he explained. “Cancer-directed surgery for MPM is usually reserved for localized epithelial type histology and is associated with a 5-year survival rate of 15%.”

For the new study, the investigators tracked 3,834 patients in the National Cancer Database (2004-2014) diagnosed with MPM clinical stages I-III. Most had epithelioid MPM (69%), with sarcomatoid (17%) and mixed subtype (15%) making up the rest. They examined whether patient treatment complied with the National Comprehensive Cancer Network (NCCN) guide-

lines, which recommend surgery in resectable epithelioid MPM.

“Our study revealed significant lack of compliance with NCCN guidelines, as well as many disparities in the management of MPM,” Dr. Soukiasian said. “For the overall cohort, 32.3% of patients did not receive any treatment, 18.1% had surgery plus chemotherapy, 38.6% chemotherapy alone, and only 7% received trimodality therapy. In patients with epithelial histology, surgery was significantly underutilized, with only 30% of patients receiving cancer-directed surgery.”

In addition, he said, “our study reveals several disparities that affect compliance with NCCN guidelines. Treatment disparities were observed in women, octogenarians, the uninsured, the Medicaid-insured, and in patients with comorbidities. Guideline adherence was significantly increased in academic and high-volume hospitals with an associated increase in survival.”

But the study also found that median survival estimates were similar regardless of treatment: 10 months for no treatment, 15 months for chemotherapy only, 17 months for surgery only, and 22 months for surgery plus chemotherapy.

During the AATS presentation, an audience member asked about how performance status – a measure of a person's ability to perform everyday activities – affects the eligibility for surgery.

“It's quite common for low performance status to exclude someone from surgery,” the audience member said.

Dr. Soukiasian acknowledged that performance status was not included in the data. The study was focused on the gap between guidelines and real-world practice, and generated questions of why and about the potential opportunity for improved treatment of these patients.

“Although our research does not provide data or conclusions on quality of life or cost, these topics will be important to address in follow-up studies to elucidate possible barriers in the treatment of MPM and the initiation of future educational opportunities for our patients,” Dr. Soukiasian noted.

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Diagnosis and management of Critical Illness-Related Corticosteroid Insufficiency (CIRCI): Updated guidelines 2017

BY STEPHEN M. PASTORES, MD, FCCP

Critical illness-related corticosteroid insufficiency (CIRCI) was first introduced in 2008 by a task force convened by the Society of Critical Care Medicine (SCCM) to describe the impairment of the hypothalamic-pituitary-adrenal (HPA) axis during critical illness (Marik PE, et al. *Crit Care Med.* 2008;36(6):1937).

CIRCI is characterized by dysregulated systemic inflammation resulting from inadequate cellular corticosteroid activity for the severity of the patient's critical illness. Signs and symptoms of CIRCI include hypotension poorly responsive to fluids, decreased sensitivity to catecholamines, fever, altered mental status, hypoxemia, and laboratory abnormalities (hyponatremia, hypoglycemia). CIRCI can occur in sepsis and septic shock, acute respiratory distress syndrome (ARDS), severe community-acquired pneumonia, and non-septic systemic inflammatory response syndrome (SIRS) states associated with shock, such as trauma, cardiac arrest, and cardiopulmonary bypass surgery. Three major pathophysiologic events constitute CIRCI: dysregulation of the HPA axis, altered cortisol metabolism, and tissue resistance to glucocorticoids (Annane D, Pastores SM, et al. *Crit Care Med.* 2017;45(12):2089; *Intensive Care Med.* 2017;43(12):1781). Plasma clearance of cortisol is markedly reduced during critical illness, due to suppressed expression and activity of the primary cortisol-metabolizing enzymes in the liver and kidney. Furthermore, despite the elevated cortisol levels during critical illness, tissue resistance to glucocorticoids is believed to occur because of insufficient glucocorticoid receptor alpha-mediated anti-inflammatory activity.

Reviewing the Updated Guidelines

Against this background of recent insights into the understanding of CIRCI and the widespread use of corticosteroids in critically ill patients, a panel of experts of the SCCM and the European Society of Intensive Care Medicine (ESICM) recently updated the guidelines for the diagnosis and management of CIRCI in a two-part guideline document (Annane D, Pastores SM, et al. *Crit Care Med.* 2017;45(12):2078; *Intensive Care Med.* 2017;43(12):1751; Pastores SM, Annane D, et al. *Crit Care Med.* 2018;46(1):146; Pastores SM, Annane D, et al. *Intensive Care Med.* 2018;44(4):474). For this update, the multidisciplinary task force used the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) methodology to formulate actionable recommendations. The recommendations and their strength (strong or conditional) required the agreement of at least 80% of the members. The task force spent considerable time and spirited discussions on the diagnosis of CIRCI and the use of corticosteroids for clinical disorders that most clinicians associate with CIRCI: sepsis/septic shock, ARDS, and major trauma.

Diagnosis

The task force was unable to reach agreement on a single test that can reliably diagnose CIRCI.

However, they acknowledged that a delta cortisol less than or equal to 9 µg/dL at 60 minutes after administration of 250 µg of cosyntropin and a random plasma cortisol level of less than or equal to 10 µg/dL may be used by clinicians. They also suggested against the use of plasma-free cortisol or salivary cortisol level over plasma total cortisol. Unequivocally, the panel acknowledged the limitations of the current diagnostic tools to identify patients at risk for CIRCI and how this may impact the way corticosteroids are used in clinical practice.

Sepsis and Septic Shock

Despite dozens of observational studies and randomized controlled trials (RCTs), the benefit-to-risk ratio of corticosteroids to treat sepsis and septic shock remains controversial with systematic reviews and meta-analyses either confirming (Annane D, et al. *Cochrane Database Syst Rev.* 2015;12:CD002243) or refuting (Volbeda M, et al. *Intensive Care Med.* 2015;41:1220) the survival benefit of corticosteroids. Based on the best available data, the task force recommended using corticosteroids in adult patients with septic shock that is not responsive to fluids and moderate-to-high vasopressor therapy but not for patients with sepsis who are not in shock. Intravenous hydrocortisone less than or equal to 400 mg/day for at least greater than or equal to 3 days at full dose was recommended rather than high dose and short course. The panel emphasized the consistent benefit of low-dose corticosteroids on shock reversal and the low risk for superinfection.

Since the publication of the updated CIRCI guidelines, two large RCTs (more than 5,000 combined patients) of low-dose corticosteroids for septic shock were reported: The Adjunctive Corticosteroid Treatment in Critically Ill Patients with Septic Shock (ADRENAL) trial (Venkatesh B, et al. *N Engl J Med.* 2018;378:797) and the Activated Protein C and Corticosteroids for Human Septic Shock (APROCCHSS) trial (Annane D, et al. *N Engl J Med.* 2018;378:809). The ADRENAL trial included 3,800 patients in five countries and did not show a significant difference in 90-day mortality between the hydrocortisone and the placebo groups (27.9% vs 28.8%, respectively, $P=.50$). In contrast, the APROCCHSS trial, involving 1,241 patients, reported a lower 90-day mortality in the hydrocortisone-fludrocortisone group compared with the placebo group (43% vs 49.1%, $P=.03$). Both trials showed a beneficial effect of hydrocortisone in the number of vasopressor-free and mechanical ventilation-free days. Blood transfusions were less common in the hydrocortisone group than those who received placebo in ADRENAL. Besides hyperglycemia, which was more common in the hydrocortisone group in both trials, the overall rates of adverse events were relatively low.

It is important to highlight the key differences between these two RCTs. First, in APROCCHSS, oral fludrocortisone (50-µg once daily for 7 days) was added to hydrocortisone to provide additional mineralocorticoid potency, although a previous study had shown no added benefit (Annane D, et al. *JAMA.* 2010;303:341). Second, hydrocortisone was administered as a 50-mg IV bolus every 6



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hours in APROCCHSS and given as a continuous infusion of 200 mg/day for 7 days or until death or ICU discharge in ADRENAL. It is noteworthy that the subjects in ADRENAL had a higher rate of surgical admissions (31.5% vs 18.3%), a lower rate of renal-replacement therapy (12.7% vs 27.6%), lower rates of lung infection (35.2% vs 59.4%) and urinary tract infection (7.5% vs 17.7%), and a higher rate of abdominal infection (25.5% vs 11.5%). Patients in APROCCHSS had high Sequential Organ Failure Assessment (SOFA) scores and Simplified Acute Physiology Score (SAPS) II values suggesting a sicker population and probably accounting for the higher mortality rates in both hydrocortisone and placebo groups compared with ADRENAL. In view of the current evidence, the author believes that survival benefit with corticosteroids in septic shock is dependent on several factors: dose (hydrocortisone less than or equal to 400 mg/day), longer duration (at least 3 or more days), and severity of sepsis. "The more severe the sepsis, the more septic shock the patient is in, the more likely it is for corticosteroids to help these patients get off vasopressors and mechanical ventilation. I consider the addition of fludrocortisone as optional."

ARDS

In patients with early moderate-to-severe ARDS ($\text{PaO}_2/\text{FIO}_2$ of less than or equal to 200 and within 14 days of onset), the task force recommended the use of IV methylprednisolone in a dose of 1 mg/kg/day followed by slow tapering over 2 weeks to prevent the development of a rebound inflammatory response, and adherence to infection surveillance. In patients with major trauma and influenza, the panel suggested against the use of corticosteroids. Corticosteroids were recommended for severe CAP (less than or equal to 400 mg/day of IV hydrocortisone or equivalent for 5 to 7 days), meningitis, adults undergoing cardiopulmonary bypass surgery, and adults who suffer a cardiac arrest. The task force highlighted that the quality of evidence for use of corticosteroids in these disease states was often low and that additional well-designed RCTs with carefully selected patients were warranted.

To conclude, as with any clinical practice guideline, the task force reiterated that the updated CIRCI guidelines were not intended to define a standard of care and should not be interpreted as prescribing an exclusive course of management. Good clinical judgment should always prevail!

Seven days of antibiotics is enough

BY MICHELE G. SULLIVAN

MDedge News

MADRID – Seven days of antibiotic therapy was just as effective as 14 days for patients with gram-negative bacteremias.

The shorter course was associated with similar cure rates and a faster return to normal activities, Dafna Yahav, MD, said at the European Society of Clinical Microbiology and Infectious Diseases annual congress.

“In patients hospitalized with gram-negative bacteremia and sepsis, a course of 7 antibiotic days was not inferior to 14 days, and resulted in a more rapid return to baseline activity,” said Dr. Yahav of the Rabin Medical Center, Petah Tikva, Israel. “This could lead to a change in accepted management algorithms and shortened antibiotic therapy. Potentially, though we did not show this in our trial, it may lead to reduced cost, reduced development of resistance, and fewer adverse events.”

During the past few years, a new dogma has emerged in antibiotic treatment paradigms, she said: Shorter is better. Brad Spellberg, MD, described this concept in his 2016 editorial in *JAMA Internal Medicine*, “The new antibiotic mantra” (Sep 1;176[9]:1254-5).

In it, Dr. Spellberg, of the University of Southern California, Los Angeles, addressed the long-held view that a full 10- or 14-day course of antibiotics was necessary to decrease the risk of creating a resistant strain, even if clinical symptoms were long resolved.

However, he noted, there is little evidence supporting the idea that longer courses suppress the rise of resistance – and, in fact, some data support the opposite.

“To the contrary, specifically for pneumonia, studies have shown that longer courses of therapy result in more emergence of antibiotic resistance,

which is consistent with everything we know about natural selection, the driver of antibiotic resistance,” he noted. “In only a few types of infections does resistance emerge at the site of infection; rather, resistance typically emerges off target, among colonizing flora away from the site of infection. Thus, all that is achieved by treating an infection with antibiotics for longer than the patient has symptoms is increased selective pressure driving antibiotic resistance among our colonizing microbial flora.”

The European Union and Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America have all recently updated their antibiotic stewardship guidelines to include a strong recommendation for the shortest effective duration of antimicrobial therapy.

However, most of the supporting data were drawn from randomized, controlled studies of patients with lung, skin, and kidney infections. Short-course treatments have not been adequately studied in bacteremia patients, Dr. Yahav said.

The aim of her study, which was investigator initiated and received no external funding, was to demonstrate the noninferiority of 7 days of antibiotic therapy, compared with 14 days, in patients with bacteremia arising from gram-negative infections.

The randomized, open-label study comprised 604 patients in three hospitals: two in Israel and one in Italy. Patients were eligible if they had an aerobic gram-negative bacteremia of any infection source that was either community or hospital acquired. The medication choice was left up to the treating physician. Patients were assessed at discharge, and at days 30 and 90.

The primary outcome was a composite 90-day endpoint of all-cause mortality, clinical failure (relapse, new local complications, or distant complications), and readmission or hospital stay longer than 14 days. There were a number of secondary outcomes, including new infection, emergence of antibiotic resistance, total hospital and total antibiotic days, time to return to baseline activity, and adverse events.

The cohort was a mean of 71 years old. About 60% were functionally independent, and the mean Charlson comorbidity score was 2. Most of the infections (90%) were nosocomial. The urinary tract was the largest source of infection (69%). Other sources were abdominal, respiratory, central venous catheter, and skin or soft tissue.

Escherichia coli was the most common infective organism (62%), followed by *Klebsiella* species and *Enterobacteriaceae*. A small number of patients had *Acinetobacter* and *Pseudomonas* infections.

In the intent-to-treat analysis, the primary composite outcome of all-cause mortality or extended hospital stay occurred in 46% of the 7-day group and 50% of the 14-day group – not significantly different. The results were nearly identical in the per-protocol analysis (46% vs. 49.6%).

Likewise, none of the secondary outcomes posted a significant difference in favor of one treatment arm, including relapse (2.9% vs. 2.7%) and resistance development (10.8% vs. 9.7%).

Dr. Yahav pointed out that total antibiotic-use



For gram-negative bacteremia and sepsis, 7 days of antibiotics was not inferior to 14 days, noted Dr. Dafna Yahav.

days were significantly less in the 7-day group, (5 days) than in the 14-day group (10 days). Patients in the short-duration group returned to their normal activities a day earlier than those in the longer-term group (2 days vs. 3 days), a difference that was statistically significant.

The total hospital stay from randomization to day 90 was only half a day shorter in the short-term group (mean, 3 days vs. 3.5 days). That was not a significant finding.

There were some differences in adverse events, although none was statistically significant. The short-duration arm had slightly more cases of kidney injury (0.5%), fewer cases of liver function abnormalities (–1.5%), and half as many rashes (two vs. four). There were two cases of *Clostridium difficile* in the short-use arm and one in the long-use arm, also not a significant difference.

A subgroup analysis looked at outcomes among the different sources of infection (urinary tract vs. other), whether empirical antibiotics were used, and whether the induced resistance was multidrug or non-multidrug. All of those differences hovered close to the null, but generally favored short antibiotic treatment, Dr. Yahav noted.

“I would conclude from these data that it is generally safe to stop antibiotics after 7 days of covering antibiotics for gram-negative bacteremia patients, if they are hemodynamically stable and nonneutropenic at 7 days, and have no uncontrolled source of infection,” she concluded.

The investigator-initiated study had no outside funding.

msullivan@mdedge.com



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Adding vasopressin in distributive shock may cut AF risk

BY ANDREW D. BOWSER

MDedge News

In patients with distributive shock, the risk of atrial fibrillation may be lower when vasopressin is administered along with catecholamine vasopressors, results of a recent systematic review and meta-analysis suggest.

The relative risk of atrial fibrillation was reduced for the combination of vasopressin and catecholamines versus the current standard of care, which is catecholamines alone, according to study results published in JAMA.

Beyond atrial fibrillation, however, findings of the meta-analysis were consistent with regard to other endpoints, including mortality, according to William F. McIntyre, MD, of McMaster University, Hamilton, Ont., and his coinvestigators.

The current study is one of the first to directly compare the combination of vasopressin and catecholamine to catecholamines alone, which is the current standard of care, wrote William F. McIntyre, MD, of McMaster University, and his coinvestigators, in their paper published in JAMA.

Mortality was lower with the combination approach when all studies were analyzed together. Yet, when the analysis was limited to the studies with the lowest risk of bias, the difference in mortality versus catecholamines alone was not statistically significant, investigators said.

Nevertheless, the meta-analysis does suggest that vasopressin may offer a clinical advantage regarding prevention of atrial fibrillation in patients with distributive shock, a frequently fatal condition most often seen in patients with sepsis.

Vasopressin is an endogenous peptide hormone that decreases stimulation of certain myocardial receptors associated with cardiac arrhythmia, the authors noted.

“This, among other mechanisms,

may translate into a reduction in adverse events, including atrial fibrillation, injury to other organs, and death,” they said in their report.

Dr. McIntyre and his colleagues included 23 trials that had en-

rolled a total of 3,088 patients with distributive shock, a condition in which widespread vasodilation lowers vascular resistances and mean arterial pressure. Sepsis is its most common cause. The current

study is one of the first to directly compare the combination of vasopressin and catecholamine to catecholamines alone, which is the current standard of care, the investigators wrote.

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They found that the administration of vasopressin was associated with a significant 23% reduction in risk of atrial fibrillation.

“The absolute effect is that 68 fewer people per 1,000 patients will experience atrial fibrillation when vasopressin is added to catecholaminergic vasopressors,” Dr. McIntyre

Pooled data showed administration of vasopressin along with catecholamines was associated with an 11% relative reduction in mortality, according to the investigators.

and his coauthors said of the results.

The atrial fibrillation finding was judged to be high-quality ev-

idence, they said, noting that two separate sensitivity analyses confirmed the benefit.

Mortality data were less consistent, they said.

Pooled data showed administration of vasopressin along with catecholamines was associated with an 11% relative reduction in mortality. In absolute terms, 45 lives would be saved for every 1,000 pa-

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tients receiving vasopressin, they noted.

However, the mortality findings were different when the analysis was limited to the two studies with low risk of bias. That analysis yielded a relative risk of 0.96 and was not statistically significant.

Studies show patients with distributive shock have a relative vasopressin deficiency, providing a theoretical basis for vasopressin administration as part of care, investigators said.

The current Surviving Sepsis guidelines suggest either adding vasopressin to norepinephrine to

help raise mean arterial pressure to target or adding vasopressin to decrease the dosage of norepinephrine. Those are considered weak recommendations based on moderate quality of evidence, Dr. McIntyre and colleagues noted in their report.

Authors of the study reported

disclosures related to Tenax Therapeutics, Orion Pharma, Ferring Pharmaceuticals, GlaxoSmithKline, and Bristol-Myers Squibb, among other entities.

chestphysiciannews@chestnet.org

SOURCE: McIntyre WF et al. JAMA. 2018;319(18):1889-900.

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CHEST past president honored by AACN

Curtis Sessler, MD, FCCP, has been honored with the American Association of Critical-Care Nurses (AACN) Pioneering Spirit Award. As one of AACN's

Visionary Leadership Awards, it recognizes significant contributions that influence high-acuity and critical care nursing regionally and nationally and relates to AACN's

mission, vision, and values.

Dr. Sessler is the Orhan Muren Distinguished Professor of Medicine at the Virginia Commonwealth University (VCU) Health System,

Richmond. He also serves as director of VCU's Center for Adult Critical Care, medical director of critical care, and medical director of the medical respiratory ICU. He has enjoyed a long career in critical care medicine focusing on patient care, teaching, clinical research, and advancing collaborative care of critically ill patients. He has a long-term collaboration with research colleagues from VCU School of Nursing, studying a variety of clinical problems, including ICU sedation,



DR. SESSLER

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prevention of nosocomial infection, mechanical ventilation, and procedural competency. Under his leadership, the interprofessional group created and validated the Richmond Agitation-Sedation Scale, which is used worldwide to help improve the management of pain, sedation, and delirium in critically ill patients.

Besides serving as CHEST President in 2014-2015, Dr. Sessler has held numerous leadership roles at CHEST and has been recognized for his research, leadership, and service with many honors, including the 2017 Distinguished CHEST Educator Award, 2016 Art Wheeler Memorial Lecture Award, and 2010 Roger C. Bone Memorial Lecture Award.

Dr. Sessler has also participated in many activities of the Critical Care Societies Collaborative, which links the leaders of AACN, CHEST, the American Thoracic Society, and the Society of Critical Care Medicine. This group has addressed numerous issues central to critical care, such as research priorities, workforce shortage, clinical competencies, Choosing Wisely in Critical Care, and, most recently, burnout among critical care health-care professionals.

CHEST congratulates Dr. Sessler on this distinguished honor!

NAMDRC legislative and regulatory agenda once again focuses on patient access

BY PHIL PORTE

Executive Director, NAMDRRC

NAMDRC's Mission Statement declares, "NAMDRRC's primary mission is to improve access to quality care for patients with respiratory disease by removing regulatory and legislative barriers to appropriate treatment." This mission is clear as we review our legislative and regulatory agenda on an ongoing and continuing basis.

Home Mechanical Ventilation:

Close to 20 years ago, HCFA (now CMS) was faced with an important reality: advances in technology



DR. PORTE

related to home mechanical ventilation are triggering an exponential growth in availability of these life supporting devices, but a price would be paid. At that time, Medicare law was quite explicit, indicating that certain ventilators would be paid under a "frequent and substantial servicing" payment methodology, authorizing payment on an ongoing basis as long as the prescribing physician documented medical necessity. To circumvent that statutory reality, the agency created a new category of medical device – a respiratory assist device/RAD – and declared that these devices are no longer ventilators and are now subject to capped rental rules and regulations.

NAMDRC was determined to work within the system, but roadblocks were consistently encountered, ie, contractor policies that did not reflect current medical

standards of care, peer reviewed literature, etc. Even defining a "respiratory assist device" was (and still

is) a challenge, as the term does not appear in the medical literature or in FDA vernacular.

Spin forward to 2018 and numerous realities come into play. Physicians still struggle with the concept

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of RADs without a definitive, consistent definition and no FDA language to guide usage. Today, it is easier to secure a ventilator if a physician documents the patient experiences some level of respiratory failure than it is to prescribe a simple ventilator with a back-up

NAMDRC was determined to work within the system, but roadblocks were consistently encountered, such as contractor policies that did not reflect current medical standards of care.

rate. Because of that dichotomy, the growth of life support ventilator usage is well documented.

If one takes the approach that a device should be paired with the actual clinical characteristics/medical

need of the patient, changes in policy are necessary. While CMS clearly has the authority to act to improve policy and match clinical need to patient access, years and years of back and forth have signaled a definite unwillingness of the agency to

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move in that direction; therefore, the only genuine recourse is to seek legislative relief.

NAMDRC is working closely with the United States Senate, particularly the Finance Committee, Senator Cassidy (R-LA), and the Office of

Senate Legislative Counsel to craft legislative language to address the myriad of issues associated with home mechanical ventilation.

Home Oxygen Therapy: In 1986, Congress revamped the statute governing coverage and payment of

home oxygen. Pondering the reality of a segment of pulmonary medicine that has seen dramatic technological improvements and enhancements over the past 30-plus years, coupled with a payment system that is stuck with e-cylinders and competitive bidding, it is no wonder that both

patients and physicians experience ongoing frustration trying to match a patient's needs with an oxygen system that reflects the patient's needs.

It's a challenge to even consider where to start a reasonable discussion of home oxygen therapy. While the concept of supplemental oxygen is well accepted, the actual clinical evidence relies heavily on a very small number of studies. While virtually no one challenges the concept of the therapy, the actual science has progressed modestly in 30-plus years. But the technology surrounding oxygen therapy has become an industry all to itself. There are

NAMDRC is working with the Senate Finance Committee, Senator Cassidy (R-LA), and the Office of Senate Legislative Counsel to craft legislative language to address the myriad of issues associated with home mechanical ventilation.

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concentrators, portable oxygen concentrators, liquid systems, transfill systems, transtracheal oxygen therapy, and so on.

Add to the environment the growing demand for high flow systems that would deliver continuous flow oxygen at rates in excess of 4 L/min, and you begin to realize that the current payment system is a barrier to access. After all, the current payment system has problematic characteristics:

1. A flawed competitive bidding methodology;
2. Payment tied to liter flow pegged at a baseline of 2 L/min, regardless of actual patient need;
3. The major shift from a "delivery model" of care to a nondelivery model that reflects these newer technologies;
4. Virtual disappearance of liquid system availability as an option for physicians/patients;
5. The total failure of CMS to monitor, let alone act on, patient concerns.

Again, taking the NAMDRC Mission Statement into context, NAMDRC is working with all the key societies to craft a broad strategy to address these problems, acknowledging that it will likely take a mix of legislative and regulatory actions to bring home oxygen therapy into the 21st century, let alone to reflect realities of care in 2018.

PULMONARY PERSPECTIVES®

From ECMO to post-ICU discharge clinics

BY JOHN MADARA, MD, AND
MICHAEL BARAM, MD, FCCP

As extracorporeal membrane oxygenation (ECMO) is utilized more frequently,¹ there will be more survivors of prolonged hospitalizations with new challenges that they will need to face. As health-care providers, we must be involved with establishing a system to deal with the longitudinal effects of the expanding treatment options. Some of the interventions to improve post-ECMO quality of life require hospital-based initiatives but also should incorporate post-hospital discharge care.

The ECMO patient population represents some of the sickest patients in the hospital. With the average ECMO patient having an APACHE II score of greater than 25, this carries an estimated mortality rate of at least 55%.^{2,3} When the decision is made that the patient no longer needs ECMO support and is removed from the circuit, there still remains a possibility of a multitude of complications during their hospitalization. One of the more common occurrences after ECMO is a continued systemic inflammatory response syndrome (SIRS).⁴ A meta-analysis published in 2013 reported frequent ECMO complications, such as renal failure requiring hemodialysis (52%), pneumonia (33%), liver disease (16%), and GI bleeding (7%).⁵ Many patients require tracheostomy for prolonged mechanical ventilation and percutaneous enteral access. There are high rates of critical care-related myopathies and neuropathies that usually require prolonged treatment courses of physical therapy and occupational therapy. This is not to mention one of the more dreaded complications of prolonged ICU stays—delirium, leading to posttraumatic stress disorder (PTSD). Due to the pharmacokinetics of the ECMO circuit and high levels of discomfort, higher amounts of opioids and benzodiazepines are required when compared with the general critical care population. It is common to see patients receiving high doses of continuous IV infusions of lorazepam, fentanyl, and ketamine. ICU delirium leads to increased days in the ICU, adds the additional risks of developing complications seen from long hospitalizations, and

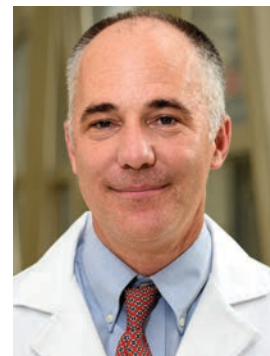
contributes to long-term cognitive deficits.

Once these critically ill patients are discharged from the hospital, they are left with a multitude of long-term medical, psychological, and cognitive deficits. Post-Intensive Care Unit Syndrome (PICS) is becoming more recognized as a group of health problems that patients suffer after a prolonged course of treatment in the ICU. Recent studies have shown the long-term negative deficits in critically ill patients. Iwashyna and colleagues demonstrated that survivors of severe sepsis revealed increased rates of cognitive impairments and functional disabilities.⁶ The same phenomena that patients with septic shock suffer are seen in ECMO survivors, as well. ECMO survivors are frequently left with residual cognitive, psychological, and medical complications.

It is known that patients who survive long ICU stays suffer from PICS, and patients who survive ECMO are at high risk for developing complications, but there is a dearth of literature examining the long-term outcomes in these patients. High levels of sedation are required while on pump increases delirium that is a known risk factor for cognitive impairments in the long term. Prolonged bedrest, paralytics, and steroids are frequently needed for these patients, all risk factors in developing ICU-acquired weakness. An article published by Schmidt and colleagues⁷ in 2013 showed that survivors of ECMO had decreased SF-36 scores, which is a single measure patient health-related quality of life questionnaire, indicating worse quality of life when compared with the general population. Hodgson and colleagues⁸ also noted a similar decrease in SF-36 scores in ECMO survivors at 8 months postdischarge. Beyond the cognitive and quality of life impairments, significant long-term psychiatric issues develop. A case-series published in 2013 showed an extremely high prevalence (71%) of mental disorders in ECMO survivors.⁹

During a long and complicated hospital course for these patients, there is often a major component to the care of the patient that goes overlooked. While the patient

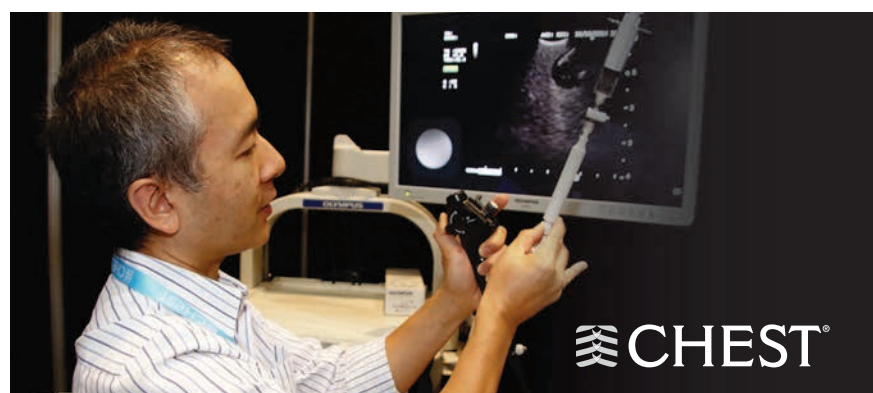
remains sedated with anti-anxiety, analgesics, and amnesic medications throughout their ICU stay, the family members and caregivers of the patient remain at bedside, often for hours, days, or weeks on end. It is sometimes difficult to explain the nuisances, risks, and details of the care of ECMO patients to other health-care practitioners, yet alone family members who are undergoing one of the most stressful periods of their life, leaving anxiety amongst decision makers. An article published in 2016,¹⁰ demonstrated that the long-term negative outcomes affect not only the patients but their caregivers, as well. Primary caregivers of critically ill patient survivors suffered from high rates of depression that persisted for the year of the study. It has been shown that including family members in daily discussions and scheduling frequent family meetings helps to avoid confusion and stress.



Dr. Madara and Dr. Baram (pictured) are with the Division of Pulmonary Care, Department of Medicine, Jefferson University, Philadelphia, Pennsylvania.

To further hospital-based strategies to reduce PICS, there have been several interventions proposed and implemented to decrease these long-term negative outcomes. Daily rounds are performed to identify who may benefit from physical therapy, and patients are receiving early treatments. Emphasis is placed on minimizing sedation, as well as daily sedation holidays to decrease the amount of pharmacologic that patients are receiving. Family members are incorporated into rounds and updated daily to decrease uncertainty in their loved one's care. Time is

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Continued from previous page

spent to make sure medications are reconciled, specialist recommendations are incorporated, and then patients are discharged from the hospital with follow-up plans usually to their primary care physician. Historically, the intensivist role in caring for the patient classically ends there—this is changing. The newest literature about PICS supports longer engagement by intensivists. Intensivists are the ones who have identified this is an issue and increasingly are involved with the patient care and family after discharge.

Post-ICU discharge clinic

We have begun a post-ICU discharge clinic at our institution to start screening our patient population for the cognitive, psychological, and medical disease processes that are common, yet underrecognized. Incorporating the health-care providers who care for the critically ill patients in the hospital will help give us an understanding of what challenges and difficulties these patients may face once discharged. A lot of focus in the medical literature is on mortality benefits. We argue that if we

are having more patients survive critical illness, our focus should broaden on how to deal with the complications that our survivors are left with. We can work together to help our patients and their families in their most vulnerable time in their lives. Patients should be provided an ongoing service after they leave the ICU and focus on improving their quality of life.

Models for a post-ICU clinic vary per site. But the goals of these clinics are to help bridge the gaps as patients try to rebuild their lives. A prolonged critical illness can leave a devastated life that needs to be restructured. Using multiple services, the goal of the clinic is to recognize the difficulties of recovering from critical care. Internists often do not realize the stress that surviving ICU can leave. Some people look at surviving ARDS as a miracle, while others carry financial, social, physical, and emotional scars as indicated by SF-36 scores. The goal of the clinic is to acknowledge deficits left by a prolonged stay with multidisciplinary services being involved. There are screening tools to identify PTSD; rehabilitation medicine specialists; and pharmacists to help address issues. Although many of the identified issues will not be

addressed directly in clinic, the goal is to refer patients to specialists who can provide long-term care. In many ways, the goal of the clinic is to offer patients recognition/substantiation of what they have gone through (which is a plus in itself) but also refers patients to subspecialty services that our university program can provide.

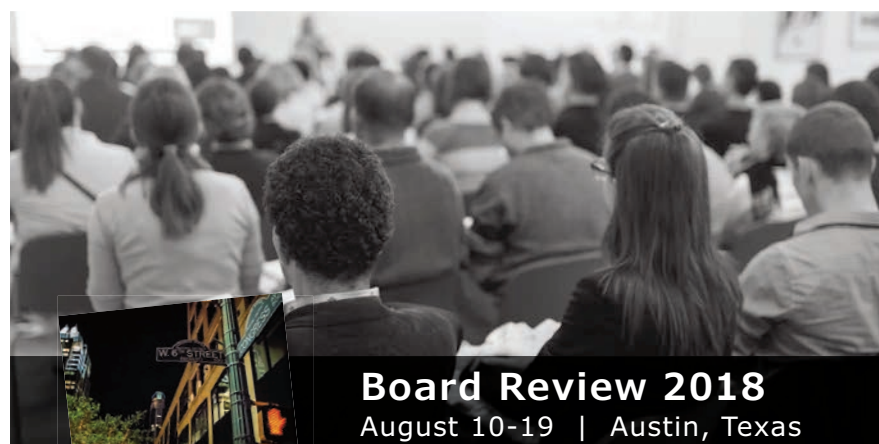
Each person in the clinic has a unique role. The physician presence is to describe to the patient and their loved ones the ongoing medical complications from the hospitalization. Families are informed that cognitive and psychological problems are common in this particular condition. A critical care pharmacist can review lists of medications and doses to ensure no problems occurred in the transition to outpatient. Physical and occupational therapy are present to screen for both neuromuscular and cognitive defects and provide tips and exercises to help rebuild patients' strength of muscle and mind. We also involve one of the most important parts of the patients care while in the ICU, critical care-trained nurses and nurse practitioners. These are the members of the team who the patients and families are always happiest to see. Also, seeing patients in the outpatient setting, after significant recovery has occurred, comes as a significant morale booster for the health-care practitioners who deal with so much stress and anxiety on a daily basis. The team feels gratified that all of their energy spent in the ICU yields very meaningful outcomes.

Utilizing the expertise of multiple disciplines, our post-ICU clinic is to help ICU survivors gain control over their lives. The Society of Crit-

ical Care Medicine (SCCM) has embraced the idea of treating PICS. As intensivists we embrace the idea of helping our survivors regain independence in life, support family members through their needs, and help fulfill our own need to see survivors achieve a higher quality of life.

References

1. Extracorporeal Life Support Organization, ECLS Registry Report International Summary, January, 2017.
2. Lin CY, Tsai FC, Tian YC, et al. Evaluation of outcome scoring systems for patients on extracorporeal membrane oxygenation. *Ann Thoracic Surg.* 2007;84:1256-62.
3. Natt BS, Desai H, Singh N, et al. Extracorporeal membrane oxygenation for ARDS: National trends in the United States 2008-2012. *Respir Care.* 2016;61(10):1293-98.
4. Thangappan K, Cavarocchi NC, Baram M, et al. Systemic inflammatory response syndrome (SIRS) after extracorporeal membrane oxygenation (ECMO): Incidence, risks, and survivals. *Heart Lung.* 2016;45:449-53.
5. Zangrillo A, Landoni G, Biondi-Zoccai G, et al. A meta-analysis of complications and mortality of extracorporeal membrane oxygenation. *Crit Care Resusc.* 2013;15(3):172-78.
6. Iwashyna TJ, Ely EW, Smith DM, et al. Long-term cognitive impairment and functional disability among survivors of severe sepsis. *JAMA.* 2010;304(16):1787-94.
7. Schmidt M, Zogheib E, Rozé H, et al. The PRESERVE Mortality Risk Score and analysis of long-term outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. *Intensive Care Med.* 2013;39(10):1704-13.
8. Hodgson CL, Hayes K, Everard T, et al. Long-term quality of life in patients with acute respiratory distress syndrome requiring extracorporeal membrane oxygenation for refractory hypoxemia. *Crit Care.* 2012;16(5):R202.
9. Risnes I, Haldal A, Wagner K, et al. Psychiatric outcome after severe cardiopulmonary failure treated with extracorporeal membrane oxygenation: A case-series. *Psychosomatics.* 2013;54(5): 418-27.
10. Cameron JJ, Chu LM, Matte A, et al. One-Year outcomes in caregivers of critically ill patients. *N Engl J Med.* 2016;374:1831-41.



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CHEST NETWORKS

Sinus rhythm, physician burnout, difficult-to-treat pulmonary infections, and more

Cardiovascular Medicine and Surgery

Sinus rhythm is superior for heart failure with atrial fibrillation

It is a question that is frequently asked: is rhythm or rate control better for non-valvular atrial fibrillation (AFib)? The Atrial Fibrillation Follow-up Investigation of Rhythm Management (AFFIRM) [*N Engl J Med.* 2002;347[23]:1825-33] and Rate Control versus Electrical Cardioversion for Persistent Atrial Fibrillation (RACE) (Van Gelder et al. *N Engl J Med.* 2002;347[23]:1834-40) trials demonstrated that the strategies are equivalent. However, AFib and heart failure are concurrent in up to 50% of patients (Santhanakrishnan et al. *Circulation.* 2016;133[5]:484-92) and several trials have shown that decreasing the time spent in AFib leads to improved left ventricular ejection fraction (LVEF), 6-minute walk distance (6MWD), quality of life, and may even reduce mortality and hospitalizations (Khan et al. *N*

Engl J Med. 2008;359[17]:1778-85; Hunter et al. *Circ Arrhythm Electrophysiol.* 2014[1];7:31-8; DiBiase et al. *Circulation.* 2016;133[17]:1637-44). The AFFIRM trial demonstrated a reduced mortality in those achieving sinus rhythm, but this was negated by adverse effects from antiarrhythmic medications. The Catheter Ablation versus Standard Conventional Therapy in Patients with Left Ventricular Dysfunction and Atrial Fibrillation (CASTLE-AF) trial examined the benefits of rhythm control in patients with AFib and CHF via pulmonary vein ablation (Marrouche et al. *N Engl J Med.* 2018;378[5]:417-27). This was a multicenter, randomized, open label trial that included patients with symptomatic AFib, an LVEF less than or equal to 35%, and at least NYHA class II heart failure. Results demonstrated a significant reduction in all-cause mortality and heart failure hospitalizations in those undergoing ablation (NNT of 9). Exploratory results also demonstrated reduced cardiovascular death, decreased

AFib burden, increased 6MWD, and improved LVEF with ablation. Post-ablation patients received anticoagulation therapy for at least 6 months. However, the study did have some limitations: it was not blinded, there was no sham group, the sample size was relatively small, and experienced, high volume medical centers performed the procedures (*N Engl J Med.* 2018;378:468-469). CASTLE-AF provides additional evidence for the benefits of reducing the burden of AFib in congestive heart failure while avoiding the detrimental effects of antiarrhythmic medications.

David J. Nagel, MD, PhD
Steering Committee Member

Follow-up study of HeartMate 3 LVAD

Since commercially available in 2008, enthusiasm for continuous flow LVADs as treatment of end-stage heart failure has increased with over 22,000 implantations to date. However, the 2-year survival rate of 70% is limited mostly by neurologic

complications - the consequence of the perilous imbalance between thrombosis and bleeding (Kirklin et al. *JHLT* 2017;36 [10]:1080).




DR. SHAH

In this context, the MOMENTUM 3 trial (Mehra et al. *N Engl J Med.* 2018;378:1386), a head-to-head study of the HeartMate 3 (newest durable

LVAD) vs HeartMate II (the first and most popular model) is a significant milestone. In this trial, compared with the HM II, patients with HM 3 had fewer strokes and reoperation for pump malfunction at 2 years. Although rate of severe strokes was similar in both arms, HM 3 has the lowest rate of overall strokes or pump thrombosis compared with other continuous flow device trials thus far. The rates of bleeding were the

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same among the two models in this trial, but given the low rate of pump thrombosis, lower anticoagulation targets might be considered for the HM 3. Whether new modifications of the anticoagulation strategy reduce bleeding complications down the road remains to be seen. Currently, the HM 3 is FDA-approved for bridge to transplant only, but, after this trial, the indication will likely expand to include destination therapy.

As technological breakthroughs lead to improved long-term patient survival, we will inevitably be tending to a growing number of LVAD implanted patients in our clinics and units.

Nimesh S. Shah, MD, FCCP
Steering Committee Member

Chest Infections Inhaled antibiotics for difficult-to-treat pulmonary infections

That the lungs constantly interface with the environment is both a



DR. KEYT

blessing and a curse: while the lungs are continually exposed to environmental pathogens and irritants, this also provides a relatively unique route for delivery of effective medications

directly to the site of disease. For chronic lung diseases characterized by recurrent infections, such as cystic fibrosis (CF) and non-CF bronchiectasis, this means delivery of antimicrobials via inhalation. For individuals with CF, inhaled antibiotics are considered standard of care in the management of Pseudomonas infections. A recent Cochrane review concluded that inhaled anti-pseudomonal treatments improve lung function and reduce exacerbation rates in this population (Smith, et al. *Cochrane Database Syst Rev.* 2018;Mar 30;3:CD001021).

What is the next frontier for inhaled antimicrobial therapies in CF? The focus is now on increasingly common and difficult-to-treat pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA) and nontuberculous mycobacteria (NTM). Vancomycin inhalation powder (AeroVanc™) is an inhaled dry powder version of vancomycin, which significantly reduced sputum MRSA density in a recent phase 2 trial; a phase 3 trial is currently underway. For infections caused by NTM, inhaled amikacin has been shown to be

safe and efficacious in small subsets of patients with CF and non-CF bronchiectasis (Yagi, et al. *BMC Infect Dis.* 2018;17[1]:558). Other inhaled therapies currently under investigation for use in CF pulmonary infections include fosfomycin/tobramycin inhalation and a new inhaled glycopolymer (SNSP113) that disrupts bacterial biofilms.

In non-CF bronchiectasis, the evidence showing benefit for use of inhaled antibiotics is not as well established. A recent Cochrane review reported no evidence indicating whether oral or inhaled antibiotics are better for non-CF bronchiectasis (Spencer, et al. *Cochrane Database Syst Rev.* 2018; Mar 27;3:CD012579). The heterogeneity of this population limits the ability to extend positive findings in a small subgroup to the population at large; however, investigation in this area is ongoing.

Inhaled antibiotics have been studied and used for decades in patients with chronic infections, and interest in the development of even more efficacious and better-tolerated medications is stronger than ever. Look for more information on this topic at the upcoming CHEST 2018 Annual Meeting in San Antonio this October.

Holly Keyt, MD
Steering Committee Member

Clinical Pulmonary Medicine Prevent and treat burnout now

Burnout is a work-related syndrome that manifests with symptoms of emotional exhaustion, depersonalization, and a sense of reduced personal accomplishment (Moss, et al. *Chest.* 2016;150[1]:17-26). In a 2018 Medscape survey, critical care physicians had



DR. DOO

the highest rates of burnout at 48%, with pulmonary medicine physicians reporting rates at 41% (Medscape. <https://www.medscape.com/sites/public/lifestyle/2018>. Accessed Apr 13, 2018). Studies show approximately 25% to 33% of critical care nurses experience burnout (Shanafelt, et al. *Arch Intern Med.* 2012;172[18]:1377-1385). Resident and fellow trainees also have a high prevalence (60%) of burnout (Dyrbye, et al. *Acad Med.* 2014;89[3]:443-451). Burnout has been shown to contribute to staff turnover and, thus, impact access to care, patient satisfaction, and quality of care. Excessive staff turnover

rates also increase health-care costs. Replacing a critical care nurse and primary care physician is estimated to cost at least \$65,000 and \$250,000, respectively. Drivers of burnout (ie, excessive workload, lack of work support, lack of work-home integration, loss of control and autonomy, and loss of meaning from work) can be solved with organizational (ie, optimizing electronic medical records) and individual solutions (ie, prioritizing tasks and mindfulness) (West, et al. *J Intern Med.* 2018; Mar 5. doi: 10.1111/joim.12752 [Epub ahead of print]).

The American College of Chest Physicians is part of the Critical Care Societies Collaborative (CCSC), which was convened to acknowledge and raise awareness of burnout in the healthcare community (Moss M, et al. *Chest.* 2016;150[1]:17-26). To combat this crisis, all stakeholders in healthcare must work together to develop evidence-based strategies to prevent and treat burnout.

Saiprakash B. Venkateshiah,
MD, FCCP
Vice-Chair
Kathleen Doo, MD
Fellow-in-Training Member

Interprofessional Team When standard ACLS fails for the hospitalized patient

The current standard of care for the management of hospitalized adult patients who suffer cardiac arrest is standard ACLS. This population still suffers significant mortality even after the incorporation of rapid response teams (Solomon et al. *J Hosp Med.* 2016 Jun;11(6):438-45. doi: 10.1002/jhm.2554. Epub 2016 Feb 1). Addition of technology and mechanical support with chest compression devices has also demonstrated survival improvement (Couper, et al. *Resuscitation.* 2016 Jun;103:24-31. doi: 10.1016/j.resuscitation.2016.03.004. Epub 2016 Mar 11). As ECMO becomes more commonplace in various centers (Abrams and Brodie. *Chest.* 2017;152[3]:639-649), expanding those programs to provide E-CPR services has become the next step in some facilities. ELSO registry reports demonstrate an approximate 40% survival rate for adults treated with ECPR (Extracorporeal Life Support Organization. 2017. *ECLS Registry Reports*. Retrieved from <https://www.else.org/Portals/0/Files/Reports/2017/US%20Summary%20July%202017.pdf>). This potentially represents fertile ground hospitals to improve in-hospital arrests. Guidelines exist for consideration of

ECPR when standard measures fail. A two-physician model has been described; however, this resource may not always be available. Models have been described whereby advanced practice providers (APPs) can be



DR. BAETEN

key leaders in critical care and to initiate ECPR (Baeten, et al. Shifting the paradigm towards advanced practice providers managing the coronary care units. SCAI 40th Annual Scientific Sessions, May 10-13, 2017, New Orleans, LA). Limiting factors for expedient cannulation can include the time for arrival of a perfusionist and/or ECMO-capable physician.

A multiprofessional approach, including RTs, RNs, APPs, and MDs can be used to optimize appropriate resources. In-house staff, including a respiratory therapist to secure and manage the airway, nurses ensure appropriate compressions or operation of a chest compression device, and APPs to determine ECMO/ECPR candidacy in conjunction with the appropriate physician. While the physician is en route, ACLS continues; however, the patient is prepped and draped and initial femoral veno-arterial access is achieved. This facilitates rapid catheter exchange to large peripheral VA-ECMO cannulas immediately upon arrival of the ECMO physician.

Robert Baeten II, PA-C
Steering Committee Member

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Catching up with our CHEST past presidents

Where are they now? What have they been up to? CHEST's Past Presidents each forged the way for the many successes of the American College of Chest Physicians, leading to enhanced patient care around the globe. Their outstanding leadership and vision are evidenced today in many of CHEST's strategic initiatives. Let's check in with Dr. D. Robert McCaffree, Master FCCP.

**D. Robert McCaffree, MD, MSHA, Master FCCP
CHEST President 1997 - 1998**

I received the chain of office (yes, there is an actual chain) from Dr. Bart Chernow in New Orleans during CHEST 1997. I remember this time as being a time of beginnings, challenges, and changes. Bart had been the stimulus for the CHEST Foundation and the form and function of this foundation was being developed. The women's caucus (probably not the official name) was becoming more organized and more of a force under the leadership of Dr. Diane Stover and Dr. Deborah Shure and others, and the Woman, Girls, Tobacco, and Lung Cancer educational program was being refined. It was this program that got my wife, Mary Anne, involved with CHEST, and she became a Fellow (FCCP). The American College of Chest Physicians was in the midst of the national tobacco settlement efforts at this time. Our involvement began when Mike Moore, Attorney-General of Mississippi, filed the first suit against the tobacco industry in 1994. Under the stimulus of Dr. John Studdard, our current President, the college was the only medical organization to file an *amicus curiae* brief supporting this, thus thrusting us into the midst of the tobacco settlement debates and in a leadership position. During the time I was President-elect and President, I was fortunate to represent us both in the ENACT Coalition (composed



Dr. Mary Anne McCaffree and Dr. D. Robert McCaffree

of national health groups, such as the American Cancer Society), as well as on the Koop-Kessler Congressional Advisory Committee. I also testified before Congress on the tobacco issues and met at the White House with DHHS Secretary Donna Shalala. On a different front, our international activities were not as developed as now, but we did make two memorable trips to India. Many thanks to Dr. Kay Guntupalli for helping make those trips so memorable. After this absolutely wonderful year, I passed the chain to Dr. Allen Goldberg in Toronto.

My experiences with tobacco control continue to influence my life. After the national tobacco settlement failed, there was enacted the multistate tobacco settlement. Oklahoma was the only state to place the majority of those settlement dollars into a constitutionally protected trust fund, the Oklahoma Tobacco Settlement Endowment Trust Fund (TSET). I was fortunate to be appointed to the Board of Directors of TSET by our Attorney General and was elected the first chair. Since then, the corpus has grown to over one billion

dollars, and TSET has been able to effect many positive changes toward helping tobacco control in Oklahoma. One of these was to fund the Oklahoma Tobacco Research Center (OTRC) as part of the Stephenson Cancer Center at Oklahoma University. I stepped off the TSET Board to join Dr. Laura Beebe in this endeavor, which started with two people and one office and has now grown to occupy over 15,000 square feet with nine faculty and several postdoctoral students.

Among other activities, I was Chief of Staff at the Oklahoma City VAMC for 18 years, retiring from that position in 2009. I was honored by having the MICU at the VA named after me. In the community, I helped start the Hospice of Oklahoma County and then the Hospice Foundation of Oklahoma, both of which I served as first chairman. I also helped start Palliative Care Week on the OUHSC campus. I am currently the vice-chair of the Health Alliance for the Uninsured in Oklahoma City, which helps support the many free clinics in our city. My wonderful wife, Mary Anne, is also involved in many community activities. On a personal level, we try to see our two children and two grandchildren as often as possible, which is not often enough. My free time activities include reading, playing the piano, fly fishing (not often enough), and exercise.

My time as President of the American College of Chest Physicians was one of the best and most important experiences of my life. My memories of working with Al Lever, David Eubanks, Marilyn Lederer, Lynne Marcus, Steve Welch, and all the other staff and physician leaders during that time remain very dear to me. The influence of CHEST continues to this very day. I can never repay all that I have gained from this experience. I wish I had the space allowance to expand on my experiences. But while my word allowance is limited, my gratitude is unlimited.

Explore the Culture in San Antonio During CHEST 2018

With the level of history and culture in San Antonio, there are plenty of options when experiencing what the city has to offer. Here are a few ways you can enjoy the arts and culture of San Antonio.

San Antonio Museum of Art

200 West Jones Avenue
The San Antonio Museum of Art contains the largest and most comprehensive collection of ancient Egyptian, Greek, Roman, and Asian art in the southern United States. The museum also has a significant collection of Latin American art. Also, check out the growing contemporary art collection with notable Texan and regional art, special exhibitions, films, concerts, gallery talks, and more!

Centro de Artes

101 S. Santa Rosa Avenue
Monday: Closed
Tuesday to Sunday: 11:00 a.m. to 6:00 p.m.

Head over to Centro de Artes to experience local and regional art, as well as history and culture, revealing the story of the Latino experience in the United States with a focus on San Antonio and South Texas.

King William Historic District

122 Madison Street
Historic King William District spans 25 blocks of downtown San Antonio. In the late 1800s, the King William District was considered the most elegant residential area in the city and zoned as the state's first historic district. You can now view these 19th century residences on the

south bank of the San Antonio River where some have been preserved and reincarnated into cafes, art galleries, museums, and shops.

GO RIO River Shuttle

Daily: 10:00 a.m. to 9:00 p.m.
Want an open tour of San Antonio? Look for the GO RIO River Shuttle signs and boats (labeled with GO RIO) along the River Walk from downtown to Museum Reach. Shuttles run approximately every 60 minutes with tickets available for purchase on the boat, online, or at any GO RIO ticket booth.

Market Square

514 W. Commerce Street
Open Daily: 10:00 a.m. to 6:00 p.m.
Explore the Historic Market Square where you'll find authentic hand-

crafted art and the gourmet Mexican cuisine of old Mexico at over 100 locally owned shops and stalls, all at a festive indoor mall. There's also the Farmers Market Food Court where you can enjoy a show on the stage.

City Sightseeing San Antonio Bus Tours

Get a double decker view starting from Alamo Plaza, then head north toward the San Antonio Museum of Art, the Pearl Brewery Entertainment Complex, and more. There are 18 stops where you can get off and explore. Then, just go back to where you were dropped off, and wait for the next bus to arrive. There's a bus every 20 minutes at each stop during the operating hours from 8:40 a.m. to 5:30 p.m..

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THE SECTION OF PULMONARY, CRITICAL CARE & SLEEP MEDICINE, YALE SCHOOL OF MEDICINE, IS SEEKING OUTSTANDING INDIVIDUALS FOR THE FOLLOWING POSITIONS:

Associate Clinic Director

Section of Pulmonary, Critical Care and Sleep Medicine, Yale School of Medicine (Yale PCCSM), is seeking candidates for Associate Director of our rapidly growing Ambulatory Pulmonary program (Winchester Chest Clinic). This academic position will be filled at a rank of: Instructor, Assistant Professor, or Associate Professor commensurate with qualifications. The successful candidate is expected to assist the Clinic director with the day to day management of the Winchester Chest Clinic, as well as develop initiatives to improve and optimize patient care and experience in the clinic. The candidate is expected to see patients in the Comprehensive Pulmonary Program but may also work in our sub-specialty practices as well dependent on interest. All candidates are expected to have outstanding skills in the clinical and educational arena, will take an active role teaching and mentoring fellows and residents and other opportunities for career development in the thriving academic environment of Yale PCCSM. Successful applicants are expected to make a significant contribution to the clinical, educational, and research missions of the section. Minimum requirements include: board eligibility or certification in pulmonary diseases and critical care medicine. Experience in pulmonary ambulatory care, medical education and management is encouraged.

All applications materials should be submitted electronically to:
<http://apply.interfolio.com/41048>

Review of applications will begin immediately, and will continue until the position is filled.

Yale University is an affirmative action/equal opportunity employer. Yale values diversity in its faculty, students, and staff and especially welcomes applications from women, persons with disabilities, protected veterans and members of minority groups.

For more information on Yale PCCSM

Website <https://medicine.yale.edu/intmed/pulmonary/>

Facebook <https://www.facebook.com/yalepccsm/>

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YouTube <https://www.youtube.com/channel/UC12y2CWB9774zxNZwy1TmbA/videos>



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THE SECTION OF PULMONARY, CRITICAL CARE & SLEEP MEDICINE, YALE SCHOOL OF MEDICINE, IS SEEKING OUTSTANDING INDIVIDUALS FOR THE FOLLOWING POSITION

Ambulatory Clinician

Section of Pulmonary, Critical Care and Sleep Medicine at Yale School of Medicine (Yale PCCSM), is seeking applicants to practice in our Ambulatory Pulmonary program (Winchester Chest Clinic) and satellite practices. The successful candidate is expected to see the majority of their patients in the general comprehensive pulmonary practice but may also work in our sub-specialty practices as well dependent on interest. All candidates are expected to have outstanding skills in the clinical and educational arena and will have the opportunity to take an active role teaching and mentoring fellows and residents. Successful applicants are expected to make a significant contribution to the clinical, educational, and research missions of the section. Minimum requirements include: board eligibility or certification in pulmonary diseases and critical care medicine.

Review of applications will begin immediately, and will continue until the position is filled.

Yale University is an affirmative action/equal opportunity employer. Yale values diversity in its faculty, students, and staff and especially welcomes applications from women, persons with disabilities, protected veterans and members of minority groups.

For more information please contact Dr. Jonathan Siner, Clinical Chief, Yale PCCSM e-mail, jonathan.siner@yale.edu or phone 203-737-4523

For more information on Yale PCCSM

Website <https://medicine.yale.edu/intmed/pulmonary/>

Facebook <https://www.facebook.com/yalepccsm/>

Twitter @YalePCCSM

YouTube <https://www.youtube.com/channel/UC12y2CWB9774zxNZwy1TmbA/videos>

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*Sterling, K. "Long-term Results of the OPTALYSE PE trial" as presented at the International Symposium on Endovascular Therapy (ISET) meeting, Hollywood, FL, Feb 2018.

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